DURECT CORP
Form S-3
October 13, 2005
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As filed with the Securities and Exchange Commission on October 13, 2005

Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

DURECT CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**94-3297098**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

10240 Bubb Road

Cupertino, California 95014

(408) 777-1417

(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

James E. Brown

Chief Executive Officer

DURECT Corporation

10240 Bubb Road

Cupertino, California 95014

(408) 777-1417

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copy to:

Mark B. Weeks

Stephen B. Thau

Heller Ehrman LLP

275 Middlefield Road

Menlo Park, CA 94025

(650) 324-7000

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

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

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price (1)	Amount of Registration Fee (2)
Common Stock, par value $0.0001 per share (3)	$ 75,000,000	$ 8,827.50

(1) In no event will the aggregate offering price of all securities issued from time to time pursuant to this registration statement exceed $75,000,000.

(2) Calculated pursuant to Rule 457(o) under the Securities Act.

(3)

Associated with the common stock are series A participating preferred stock purchase rights that will not be exercisable or be evidenced separately from the common stock prior to the occurrence of certain events. Prior to the occurrence of certain events, the Series A participating preferred stock purchase rights will not be exercisable or evidenced separately from the registrant s common stock and have no value except as reflected in the market price of the shares to which they are attached.

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

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The information 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 we are not soliciting offers to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED OCTOBER 13, 2005

PROSPECTUS

$75,000,000

DURECT CORPORATION

Common Stock

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE *RISK FACTORS* BEGINNING ON PAGE 3.

We may offer from time to time up to $75,000,000 in total of shares of our common stock, which may include up to 347,256 shares of our common stock from our selling stockholders. We will not receive any of the proceeds from the sale of the shares being sold by the selling stockholders.

Our common stock trades on the Nasdaq National Market under the symbol DRRX . On October 11, 2005, the last reported sale price of the common stock on the Nasdaq National Market was $6.56 per share.

We will provide specific terms of these securities in supplements to this prospectus. The prospectus supplement will also describe the specific manner in which we will offer the securities and may also supplement, update or amend information contained in this document. You should read this prospectus and any supplement carefully before you purchase any of our securities.

This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement.

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.

We may offer the securities in amounts, at prices and on terms determined at the time of offering. We may sell the securities directly to you, through agents we select or through underwriters and dealers we select. If we use agents, underwriters or dealers to sell the securities, we will name them and describe their compensation in a prospectus supplement.

The date of this prospectus is , 2005

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No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement in connection with the offering described in this prospectus and any accompanying prospectus supplement, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any prospectus supplement shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. Neither the delivery of this prospectus or any prospectus supplement nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference in this prospectus or in any prospectus supplement is correct as of any date subsequent to the date of this prospectus supplement or of any prospectus supplement.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Under this shelf registration process, we may, from time to time, issue and sell to the public any part of the securities described in this prospectus in one or more offerings up to a total dollar amount of $75,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell the securities, we will provide a prospectus supplement containing specific information about the terms of that offering. The prospectus supplement may also add, update or change information in this prospectus or in documents incorporated by reference in this prospectus. To the extent that any statement that we make in a prospectus supplement is inconsistent with statements made in this prospectus or in documents incorporated by reference in this prospectus, the statements made or incorporated by reference in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. You should carefully read both this prospectus and any prospectus supplement together with the additional information described under the heading Where You Can Find More Information before buying any securities offered in this offering. **THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.**

The registration statement containing this prospectus, including exhibits to the registration statement, provides additional information about us and the securities offered under this prospectus. The registration statement can be read at the Securities and Exchange Commission (the SEC) web site or at the SEC offices mentioned under the heading Where You Can Find More Information .

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ABOUT DURECT

We are an emerging specialty pharmaceuticals systems company focused on the development of pharmaceutical systems based on the following proprietary drug delivery technology platforms: the SABER Delivery System (a patented and versatile depot injectable useful for protein and small molecule delivery), the TRANSDUR Delivery System (a proprietary transdermal technology), the ORADUR sustained release oral gel-cap technology (an oral sustained release technology with potential abuse deterrent properties), the DURIN Biodegradable Implant (a biodegradable drug-loaded implant), the DUROS® System, (an osmotic implant technology licensed to us for specified fields from ALZA Corporation, a Johnson & Johnson Company) and the MICRODUR Biodegradable Microparticulates (a microspheres injectable system).

Our pharmaceutical systems combine engineering innovations and delivery technology with our proprietary pharmaceutical and biotechnology drug formulations. By integrating these technologies, we are able to control the rate and duration of drug administration as well as target the delivery of the drug to its intended site of action, allowing our pharmaceutical systems to meet the special challenges associated with treating medical conditions over an extended period of time. Our pharmaceutical systems can enable new drug therapies or optimize existing therapies based on a broad range of compounds, including small molecule pharmaceuticals as well as biotechnology molecules such as proteins, peptides and genes.

We were incorporated in Delaware in February 1998. Our principal executive offices are located at 10240 Bubb Road, Cupertino, California 95014 and our telephone number at that address is (408) 777-1417. Our website is www.durect.com. The information contained or incorporated in our website is not part of this registration statement.

Securities We Are Offering

We may offer shares of common stock with a total value of up to $75,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of the offering, which may include up to 347,256 in total of shares of our common stock from our selling stockholders. Our common stock currently is quoted on the Nasdaq National Market under the symbol DRRX . Shares of common stock that may be offered in this offering will, when issued and paid for, be fully paid and non-assessable.

We refer to our common stock in this prospectus as securities . This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, as described below under Plan of Distribution .

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RISK FACTORS

An investment in our securities involves a high degree of risk. You should consider carefully the following risk factors, along with other information contained or incorporated by reference in this prospectus, in deciding whether to invest in our securities. These factors, among others, may cause actual results, events or performances to differ materially from those expressed in any forward-looking statements we made in this prospectus, resulting in a decline in the value of our securities and a loss of all or part of your investment.

RISKS RELATED TO OUR BUSINESS

Development of our pharmaceutical systems is not complete, and we cannot be certain that our pharmaceutical systems will be able to be commercialized

To be profitable, we or our collaborative partners must successfully research, develop, obtain regulatory approval for, manufacture, introduce, market and distribute our pharmaceutical systems under development. For each pharmaceutical system that we or our third-party collaborators intend to commercialize, we must successfully meet a number of critical developmental milestones for each disease or medical condition targeted, including:

- selecting and developing drug delivery platform technology to deliver the proper dose of drug over the desired period of time;
- determining the appropriate drug dosage for use in the pharmaceutical system;
- developing drug compound formulations that will be tolerated, safe and effective and that will be compatible with the system;
- demonstrating the drug formulation will be stable for commercially reasonable time periods;
- selecting and developing catheter or other targeting technology, if appropriate, to deliver the drug to a specific location within the body; and
- demonstrating through clinical trials that the drug and system combination is safe and effective in patients for the intended indication.

The time frame necessary to achieve these developmental milestones for any individual product candidate is long and uncertain, and we may not successfully complete these milestones for any of our product candidates in development. We have not yet selected the drug dosages nor finalized the formulation or the system design of any pharmaceutical systems, including our SABER-Bupivacaine and TRANSDUR-Sufentanil product candidates, Remoxy, our DURIN-Leuprolide (Memryte) product candidate and our CHRONOGESIC product candidate, and we have limited experience in developing such products. We may not be able to finalize the design or formulation of any of our product candidates. In addition, we may select components, solvents, excipients or other ingredients to include in our pharmaceutical systems that have not been previously approved for use in pharmaceutical products, which may require us to perform additional studies and may delay clinical testing and regulatory approval of our pharmaceutical systems. Even after we complete the design of the product candidate, the product candidate must still complete required clinical trials and additional safety testing in animals before approval for commercialization. See We must conduct and

satisfactorily complete required laboratory performance and safety testing, animal studies and clinical trials for our pharmaceutical systems before we can sell them. We are continuing testing and development of our product candidates and may explore possible design or formulation changes to address issues of safety, manufacturing efficiency and performance. We may not be able to complete development of any product candidates that will be safe and effective and that will have a commercially reasonable treatment and storage period. If we or our collaborative partners are unable to complete development of our SABER-Bupivacaine, TRANSDUR-Sufentanil, Remoxy, DURIN-Leurpolide (Memryte), CHRONOGESIC or other product candidates, we will not be able to earn revenue from them, which would materially harm our business.

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We or our collaborative partners must conduct and satisfactorily complete required laboratory performance and safety testing, animal studies and clinical trials for our pharmaceutical systems before they can be sold

Before we or our collaborative partners can obtain government approval to sell any of our pharmaceutical systems, we or they, as applicable, must demonstrate through laboratory performance studies and safety testing, preclinical (animal) studies and clinical (human) trials that each system is safe and effective for human use for each targeted disease. The clinical development status of our most advanced programs is as follows:

SABER-Bupivacaine Phase I trial completed and Phase II trial initiated in Australia and the United Kingdom. Dosing of all three cohorts consisting of an aggregate of approximately 80 patients in the Phase II clinical trial in Australia completed as of September 2005. Dosing for the United Kingdom trial is ongoing.

TRANSDUR-Sufentanil Patch Dosing of Phase I trial completed and first trial of Phase II program initiated as of February 2005.

ORADUR-Oxycodone (Remoxy) Phase I and Phase III trials completed by Pain Therapeutics. In September 2005, Pain Therapeutics announced positive results from the first Phase III study and that they intend to initiate a second Phase III study by year-end 2005.

DURIN-Leuprolide (Memryte) for Alzheimer s disease Dosing completed in one Phase I trial by Voyager Pharmaceuticals. One Phase II proof of concept trial using the drug but not our DURIN-Leuprolide (Memryte) dosage form completed and a second such trial ongoing by Voyager. Voyager is currently recruiting patients for pivotal Phase III clinical studies using Memryte as an adjunctive therapy with acetyl cholinesterase inhibitors (ACIs) for the treatment of mild to moderate Alzheimer s disease.

CHRONOGESIC Phase I, Phase II and Pilot Phase III completed. Redesigning the system to address performance problems and will resume clinical trials when system design is completed.

We are currently in the preclinical or research stages with respect to all our other product candidates under development. We plan to continue extensive and costly tests, clinical trials and safety studies in animals to assess the safety and effectiveness of our product candidates. These studies include laboratory performance studies and safety testing, clinical trials and animal toxicological studies necessary to support regulatory approval of product candidates in the United States and other countries of the world. These studies are costly, complex and last for long durations, and may not yield the data required for regulatory approval. We may not be permitted to begin or continue our planned clinical trials for our potential product candidates. If our trials are permitted, our potential product candidates may not prove to be safe or produce their intended effects. In addition, we may be required by regulatory agencies to conduct additional animal or human studies regarding the safety and efficacy of our product candidates which we have not planned or anticipated that could delay commercialization of such product candidates and harm our business and financial conditions.

The length of our clinical trials will depend upon, among other factors, the rate of trial site and patient enrollment and the number of patients required to be enrolled in such studies. We or our third-party collaborators may fail to obtain adequate levels of patient enrollment in our clinical trials. Delays in planned patient enrollment may result in increased costs, delays or termination of clinical trials, which could have a material adverse effect on us. In addition, even if we or our third-party collaborators enroll the number of patients we expect in the time frame we expect, such clinical trials may not provide the data necessary to support regulatory approval for the product candidates for which they were conducted. Additionally, we or our third-party collaborators may fail to effectively oversee and monitor these clinical trials, which would result in increased costs or delays of our clinical trials. Even if these clinical trials are completed, we or our third-party collaborators may fail to complete and submit a new drug application as scheduled. The Food and Drug Administration (FDA) may not clear any such application in a timely manner or may deny the application entirely.

Data already obtained from preclinical studies and clinical trials of our pharmaceutical systems do not necessarily predict the results that will be obtained from later preclinical studies and clinical trials. Moreover, preclinical and clinical data such as ours is susceptible to varying interpretations, which could delay, limit or

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prevent regulatory approval. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. The failure to adequately demonstrate the safety and effectiveness of a product candidate under development could delay or prevent regulatory clearance of the potential product candidate, resulting in delays to the commercialization of our product candidates, and could materially harm our business. Clinical trials may not demonstrate the sufficient levels of safety and efficacy necessary to obtain the requisite regulatory approvals for our product candidates, and thus our product candidates may not be approved for marketing.

We and our third-party collaborators may not be able to manufacture sufficient quantities of our products and components to support the clinical and commercial requirements of our collaborators and ourselves at an acceptable cost or in compliance with applicable government regulations, and we have limited manufacturing experience

We or our third-party collaborators to whom we have assigned such responsibility must manufacture our product candidates and components in clinical and commercial quantities, either directly or through third parties, in compliance with regulatory requirements and at an acceptable cost. The manufacture processes associated with our pharmaceutical systems are complex. We and our third-party collaborators, where relevant, have not yet completed development of the manufacturing process for any product candidates or components including SABER Bupivacaine, TRANSDUR-Sufentanil, Remoxy, DURIN-Leurpolide (Memryte) and CHRONOGESIC. If we and our third-party collaborators, where relevant, fail to timely complete the development of the manufacturing process for our product candidates, we and our third-party collaborators, where relevant, will not be able to timely produce product for clinical trials and commercialization of our product candidates. We have also committed to manufacture and supply product or components under a number of our collaborative agreements with third-party companies. We have limited experience manufacturing pharmaceutical products, and we may not be able to timely accomplish these tasks. If we and our third-party collaborators, where relevant, fail to develop manufacturing processes to permit us to manufacture a product candidate or component at an acceptable cost, then we and our third-party partners may not be able to commercialize that product candidate or we may be in breach of our supply obligations to our third-party partners.

Our manufacturing facility in Cupertino is a functional multi-discipline site that we have used to manufacture only research and clinical supplies of several of our pharmaceutical system product candidates under good manufacturing practices (GMP), including SABER-Bupivacaine, TRANSDUR-Sufentanil, DURIN-Leuprolide (Memryte), Remoxy and CHRONOGESIC. We have not manufactured commercial quantities of any of our pharmaceutical system product candidates. In the future, we intend to develop additional manufacturing capabilities for our pharmaceutical systems and components to meet our demands and those of our third-party collaborators by contracting with third-party manufacturers and by construction of additional manufacturing space at our current facilities in Cupertino, CA, Vacaville, CA and Pelham, AL. We have limited experience building and validating manufacturing facilities, and we may not be able to timely accomplish these tasks.

If we and our third-party collaborators, where relevant, are unable to manufacture product or components in a timely manner or at an acceptable cost, quality or performance level, and attain and maintain compliance with applicable regulations, the clinical trials and the commercial sale of our pharmaceutical systems and those of our third-party partners could be delayed. Additionally, we may need to alter our facility design or manufacturing processes, install additional equipment or do additional construction or testing in order to meet regulatory requirements, optimize the production process, increase efficiencies or production capacity or for other reasons, which may result in additional cost to us or delay production of product needed for the clinical trials and commercial launch of our product candidates and those of our third-party collaborators. We and our third-party collaborators, where relevant, may also need or choose to subcontract with third-party contractors to perform manufacturing steps of our pharmaceutical systems or supply required components for our pharmaceutical systems in which case we will be subject to the schedule, expertise and performance of third parties as well as incur significant additional costs. See We rely heavily on third parties to support development, clinical testing and manufacturing of our product candidates and Key Components of our pharmaceutical systems are provided

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by limited numbers of suppliers, and supply shortages or loss of these suppliers could result in interruptions in supply or increased costs. Under our development and commercialization agreement with ALZA, we cannot subcontract the manufacture of subassemblies of the DUROS system components of our DUROS-based pharmaceutical system product candidates to third parties which have not been approved by ALZA.

If we or our third-party collaborators cannot manufacture product or components in time to meet the clinical or commercial requirements of our partners or ourselves or at an acceptable cost, our operating results will be harmed.

Failure to obtain product approvals could delay or limit introduction of our product candidates and result in failure to achieve anticipated revenues

The manufacture and marketing of our product candidates and our research and development activities are subject to extensive regulation for safety, efficacy and quality by numerous government authorities in the United States and abroad. We or our third-party collaborators must obtain clearance or approval from applicable regulatory authorities before we or they, as applicable, can market or sell our product candidates in the United States or abroad. Clinical trials, manufacturing and marketing of products are subject to the rigorous testing and approval process of the FDA and equivalent foreign regulatory authorities.

The Federal Food, Drug and Cosmetic Act and other federal, state and foreign statutes and regulations govern and influence the testing, manufacture, labeling, advertising, distribution and promotion of drugs and medical devices. These laws and regulations are complex and subject to change. Furthermore, these laws and regulations may be subject to varying interpretations, and we may not be able to predict how an applicable regulatory body or agency may choose to interpret or apply any law or regulation. As a result, clinical trials and regulatory approval can take a number of years to accomplish and require the expenditure of substantial resources. We or our third-party collaborators, as applicable, may encounter delays or rejections based upon administrative action or interpretations of current rules and regulations. We or our third-party collaborators, as applicable, may not be able to timely reach agreement with the FDA on our clinical trial protocols or on the required data we or they must collect to continue with our clinical trials or eventually commercialize our product candidates.

We or our third-party collaborators, as applicable, may also encounter delays or rejections based upon additional government regulation from future legislation, administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. We or our third-party collaborators, as applicable, may encounter similar delays in foreign countries. Sales of our product candidates outside the United States are subject to foreign regulatory standards that vary from country to country. The time required to obtain approvals from foreign countries may be shorter or longer than that required for FDA approval, and requirements for foreign licensing may differ from FDA requirements. We or our third-party collaborators, as applicable, may be unable to obtain requisite approvals from the FDA and foreign regulatory authorities, and even if obtained, such approvals may not be on a timely basis, or they may not cover the clinical uses that we specify. If we or our third-party collaborators, as applicable, fail to obtain timely clearance or approval for our product candidates, we or they will not be able to market and sell our product candidates, which will limit our ability to generate revenue.

Failure to comply with ongoing governmental regulations for our product candidates could materially harm our business in the future

Marketing or promoting a drug is subject to very strict controls. Furthermore, clearance or approval may entail ongoing requirements for post-marketing studies. The manufacture and marketing of drugs are subject to continuing FDA and foreign regulatory review and requirements that we update our regulatory filings. Later discovery of previously unknown problems with a product, manufacturer or facility, or our failure to update regulatory files, may result in restrictions, including withdrawal of the product from the market. Any of the

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following events, if they were to occur, could delay or preclude us from further developing, marketing or realizing full commercial use of our product candidates, which in turn would materially harm our business, financial condition and results of operations:

- failure to obtain or maintain requisite governmental approvals;
- failure to obtain approvals for clinically intended uses of our product candidates under development; or
- identification of serious and unanticipated adverse side effects in our product candidates under development.

Manufacturers of drugs also must comply with the applicable FDA good manufacturing practice regulations, which include production design controls, testing, quality control and quality assurance requirements as well as the corresponding maintenance of records and documentation. Compliance with current good manufacturing practices regulations is difficult and costly. Manufacturing facilities are subject to ongoing periodic inspection by the FDA and corresponding state agencies, including unannounced inspections, and must be licensed before they can be used for the commercial manufacture of our product candidates. We and/or our present or future suppliers and distributors may be unable to comply with the applicable good manufacturing practice regulations and other FDA regulatory requirements. We have not been subject to a good manufacturing regulation inspection by the FDA relating to our pharmaceutical systems. If we, our third-party collaborators or our respective suppliers do not achieve compliance for the product candidates we or they manufacture, the FDA may refuse or withdraw marketing clearance or require product recall, which may cause interruptions or delays in the manufacture and sale of our product candidates.

Our near-term revenues depend on collaboration agreements with other companies. These agreements subject us to obligations which must be fulfilled and require us to manage complex relationships with third parties. If we are unable to meet our obligations or manage our relationships with our collaborators under these agreements or enter into additional collaboration agreements or if our existing collaborations are terminated, our revenues may decrease

Our near-term revenues are based to a significant extent on collaborative arrangements with third parties, pursuant to which we receive payments based on our performance of research and development activities and the attainment of milestones set forth in the agreements. We may not be able to fulfill our obligations or attain milestones set forth in any specific agreement, which could cause our revenues to fluctuate or be less than anticipated and may expose us to liability for contractual breach. In addition, these agreements may require us to devote significant time and resources to communicating with and managing our relationship with such collaborators and resolving possible issues of contractual interpretation which may detract from time our management would otherwise devote to our managing our operations. In general, our collaboration agreements, including our agreements with Endo with respect to CHRONOGESIC and TRANSDUR-Sufentanil, Pain Therapeutics with respect to Remoxy and Voyager with respect to DURIN-Leuprolide (Memryte), may be terminated by the other party at will or upon specified conditions including, for example, if we fail to satisfy specified performance milestones or if we breach the terms of the agreement.

Our agreement with Endo for the development and commercialization of our CHRONOGESIC product candidate in the United States and Canada can be terminated by Endo starting in January 2006 in the event we have not commenced a specified clinical trial for the CHRONOGESIC product candidate by January 1, 2006, provided that Endo provides us written notice of termination prior to January 31, 2006. Due to our redesign of the system to address performance problems, we do not anticipate commencing the specified trial by January 1, 2006, and therefore Endo may elect to terminate this agreement.

If any of our collaborative agreements are terminated, our revenues will be reduced and our product candidates related to those agreements may not be commercialized.

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We depend to a large extent on third-party collaborators, and we do not have or have limited control over the development, sales, distribution and disclosure for our product candidates which are the subject of third-party collaborative or license agreements

Our future performance depends to a large extent on the ability of our third-party collaborators to successfully develop and obtain approvals for our product candidates. We have entered into agreements with Endo related to the development, promotion and distribution of our CHRONOGESIC and TRANSDUR-Sufentanil product candidates in the United States and Canada once such products are approved for commercialization. In addition, we have entered into agreements with Pain Therapeutics and Voyager under which we granted such third parties the right to develop, apply for regulatory approval for, market, promote or distribute Remoxy and DURIN-Leuprolide (Memryte), respectively, subject to payments to us in the form of product royalties and other payments. We have limited or no control over the expertise or resources that any collaborator may devote to the development, marketing or sale of these product candidates, or the timing of their activities. Any of our present or future collaborators may not perform their obligations as expected. These collaborators may breach or terminate their agreement with us or otherwise fail to conduct their collaborative activities successfully and in a timely manner. Further, our collaborators may elect not to develop or commercialize products arising out of our collaborative arrangements or not devote sufficient resources to the development, manufacture, marketing or sale of these products. If any of these events occur, we may not be able to develop our technologies or recognize revenue from the commercialization of our product candidates based on such collaborations. In addition, these third parties may have similar or competitive products to the ones which are the subject of their collaborations with us, or relationships with our competitors, which may reduce their interest in developing or selling our product candidates. We may not be able to control public disclosures made by some of our third-party collaborators, which could negatively impact our stock price.

We may develop our own sales force to market our SABER-Bupivacaine and to co-promote along with Endo our TRANSDUR-Sufentanil product candidates in the United States but we have limited sales experience and may not be able to do so effectively

We currently plan to develop our own sales force to market our SABER-Bupivacaine and to co-promote along with Endo our TRANSDUR-Sufentanil product candidates in the United States, if such product candidates are approved for marketing by the FDA. Developing a sales force will require substantial expenditures. DURECT has limited sales and marketing experience, and may not be able to effectively recruit, train or retain sales personnel. We may not be able to effectively sell our product candidates, if approved, and our failure to do so could materially harm our business.

We and our third-party collaborators may not effectively sell our product candidates

We and our third-party collaborators compete with many other companies that currently have extensive and well-funded marketing and sales operations. Our marketing and sales efforts and those of our third-party collaborations may be unable to compete successfully against these other companies. We and our third-party collaborators, if relevant, may be unable to establish a sufficient sales and marketing organization on a timely basis, if at all. We and our third-party collaborators, if relevant, may be unable to engage qualified distributors. Even if engaged, these distributors may:

- fail to satisfy financial or contractual obligations to us;
- fail to adequately market our products;
- cease operations with little or no notice to us;

offer, design, manufacture or promote competing product lines;

fail to maintain adequate inventory and thereby restrict use of our products; or

build up inventory in excess of demand thereby limiting future purchases or our products resulting in significant quarter-to-quarter variability in our sales.

The failure of us or our third-party collaborators to effectively develop, gain regulatory approval for sell and market our products will hurt our business and financial results.

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We rely heavily on third parties to support development, clinical testing and manufacturing of our product candidates

We rely on third-party contract research organizations, service providers and suppliers to provide critical services to support development, clinical testing, and manufacturing of our pharmaceutical systems. For example, we currently depend on third-party vendors to manage and monitor our clinical trials and to perform critical manufacturing steps for our pharmaceutical systems. We rely on third-parties to manufacture or perform manufacturing steps relating to our pharmaceutical systems or components. See We may not be able to manufacture sufficient quantities of our product candidates to support our clinical and commercial requirements at an acceptable cost, and we have limited manufacturing experience. We anticipate that we will continue to rely on these and other third-party contractors to support development, clinical testing, and manufacturing of our pharmaceutical systems. Failure of these contractors to provide the required services in a timely manner or on reasonable commercial terms could materially delay the development and approval of our product candidates, increase our expenses and materially harm our business, financial condition and results of operations.

Key components of our pharmaceutical systems are provided by limited numbers of suppliers, and supply shortages or loss of these suppliers could result in interruptions in supply or increased costs

Certain components and drug substances used in our pharmaceutical systems (including our SABER-Bupivacaine, TRANSDUR-Sufentanil, Remoxy, DURIN-Leuprolide (Memryte) and CHRONOGESIC product candidates) are currently purchased from a single or a limited number of outside sources. The reliance on a sole or limited number of suppliers could result in:

delays associated with redesigning a product candidate due to a failure to obtain a single source component;

an inability to obtain an adequate supply of required components; and

reduced control over pricing, quality and time delivery.

We have supply agreements in place for certain components of our pharmaceuticals systems, but do not have in place long term supply agreements with respect to all of the components of any of our pharmaceutical system candidates. Therefore the supply of a particular component could be terminated at any time without penalty to the supplier. In addition, we may not be able to procure required components or drugs from third-party suppliers at a quantity, quality and cost acceptable to us. Any interruption in the supply of single source components could cause us to seek alternative sources of supply or manufacture these components internally. Furthermore, in some cases, we are relying on our third-party collaborators to procure supply of necessary components. If the supply of any components for our pharmaceutical systems is interrupted, components from alternative suppliers may not be available in sufficient volumes or at acceptable quality levels within required timeframes, if at all, to meet our needs or those of our third-party collaborators. This could delay our ability to complete clinical trials and obtain approval for commercialization and marketing of our product candidates, causing us to lose sales, incur additional costs and delay new product introductions and could harm our reputation.

If we do not generate sufficient cash flow through increased revenues or raising additional capital, then we may not be able to meet our substantial debt obligations that become due in 2008

As of September 30, 2005, we had approximately $57.3 million in long-term convertible subordinated notes which mature in June 2008, $29,000 in non-current lease obligations, $875,000 in non-current bonds payable and $108,000 in other long-term liabilities. Our substantial indebtedness, which totals $58.3 million, has and will continue to impact us by:

making it more difficult to obtain additional financing; and

constraining our ability to react quickly in an unfavorable economic climate.

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Currently we are not generating positive cash flow. Adverse occurrences related to our product development efforts will adversely impact our ability to meet our obligations to repay the principal amounts on our convertible subordinated notes when due in June 2008. In addition, if the market price of our common stock on the due date of our notes is below $3.15 per share, the approximate equity conversion price of the notes, it will be highly unlikely that the holders of a large percentage of our outstanding convertible subordinated notes will convert such securities to equity in accordance with their existing terms. If we are unable to satisfy our debt service requirements, substantial liquidity problems could result. As of September 30, 2005 we had cash and investments valued at approximately $59.2 million. We expect to use substantially all of these assets to fund our on-going operations over the next few years. We may not generate sufficient cash from operations to repay our convertible subordinated notes or satisfy any other of these obligations when they become due and may have to raise additional financing from the sale of equity or debt securities or otherwise restructure our obligations in order to do so. There can be no assurance that any such financing or restructuring will be available to us on commercially acceptable terms, if at all. If we are unable to restructure our obligations, we may be forced to seek protection under applicable bankruptcy laws. Any restructure or bankruptcy could materially impair the value of our common stock.

We may be required to redeem our outstanding convertible subordinated notes before maturity, and we may not have sufficient funds to do so. The redemption rights in our outstanding convertible subordinated notes could discourage a potential acquirer

If a fundamental change occurs, we may be required to redeem all or part of the remaining $57.3 million in outstanding principal, plus any accrued but unpaid interest on our outstanding convertible promissory notes. A fundamental change is defined as:

> any transaction or event in connection with which all or substantially all of our common stock is exchanged for, converted into, acquired for or constitutes solely the right to receive consideration which is not all or substantially all common stock listed on a United States national securities exchange or approved for quotation on the NASDAQ National Market or any similar United States system of automated dissemination of quotations of securities prices, or,
>
> if for any reason, our common stock is no longer listed for trading on a United States national securities exchange nor approved for trading on the NASDAQ National Market.

If there is a fundamental change, we may not have enough funds to pay the redemption price for all tendered notes. In addition, any credit agreement or other agreements relating to our indebtedness may contain provisions prohibiting redemption of the notes under certain circumstances, or expressly prohibit our redemption of the notes upon a designated event or may provide that a designated event constitutes an event of default under that agreement. Our failure to redeem tendered notes would constitute an event of default under the indenture, which might also constitute a default under the terms of our other indebtedness. Any such default could cause us to seek to restructure our indebtedness or seek protection under applicable bankruptcy laws, either of which could materially impair the value of our common stock.

This redemption feature upon fundamental change could also discourage a potential acquirer. However, this redemption feature is not the result of management s knowledge of any specific effort to obtain control of us by means of a merger, tender offer or solicitation, or part of a plan by management to adopt a series of anti-takeover provisions. The term fundamental change is limited to specified transactions and may not include other events that might adversely affect our financial condition or business operations.

We have a history of operating losses, expect to continue to have losses in the future and may never achieve or maintain profitability

We have incurred significant operating losses since our inception in 1998 and, as of September 30, 2005, had an accumulated deficit of approximately $176.0 million. We expect to continue to incur significant operating losses

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over the next several years as we continue to incur costs for research and development, clinical trials and manufacturing. Our ability to achieve profitability depends upon our ability, alone or with others, to successfully complete the development of our proposed product candidates, obtain the required regulatory clearances and manufacture and market our proposed product candidates. Development of pharmaceutical systems is costly and requires significant investment. In addition, we may choose to license either additional drug delivery platform technology or rights to particular drugs or other appropriate technology for use in our pharmaceutical systems. The license fees for these technologies or rights would increase the costs of our pharmaceutical systems.

To date, we have not generated significant revenue from the commercial sale of our products and do not expect to receive significant revenue in the near future. Our current product revenues are from the sale of the ALZET product we acquired in April 2000 from ALZA and the sale of biodegradable polymers. We do not expect these product revenues to increase significantly in future periods. We do not anticipate commercialization and marketing of our product candidates in development in the near future, and therefore do not expect to generate sufficient revenues to cover expenses or achieve profitability in the near future.

We may have difficulty raising needed capital in the future

Our business currently does not generate sufficient revenues to meet our capital requirements and we do not expect that it will do so in the near future. We have expended and will continue to expend substantial funds to complete the research, development and clinical testing of our product candidates. We will require additional funds for these purposes, to establish additional clinical- and commercial-scale manufacturing arrangements and facilities and to provide for the marketing and distribution of our product candidates. Additional funds may not be available on acceptable terms, if at all. If adequate funds are unavailable from operations or additional sources of financing, we may have to delay, reduce the scope of or eliminate one or more of our research or development programs which would materially harm our business, financial condition and results of operations.

We believe that our cash, cash equivalents and investments, will be adequate to satisfy our capital needs for at least the next 12 months. However, our actual capital requirements will depend on many factors, including:

- continued progress and cost of our research and development programs;
- success in entering into collaboration agreements and meeting milestones under such agreements;
- progress with preclinical studies and clinical trials;
- the time and costs involved in obtaining regulatory clearance;
- costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- costs of developing sales, marketing and distribution channels and our ability to sell our product candidates;
- costs involved in establishing manufacturing capabilities for clinical and commercial quantities of our product candidates;

competing technological and market developments;

market acceptance of our product candidates; and

costs for recruiting and retaining employees and consultants.

We may consume available resources more rapidly than currently anticipated, resulting in the need for additional funding. We may seek to raise any necessary additional funds through equity or debt financings, convertible debt financings, collaborative arrangements with corporate partners or other sources, which may be dilutive to existing stockholders and may cause the price of our common stock to decline. In addition, in the event that additional funds are obtained through arrangements with collaborators or other sources, we may have to relinquish rights to some of our technologies, product candidates or products that we would otherwise seek to

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develop or commercialize ourselves. If adequate funds are not available, we may be required to significantly reduce or refocus our product development efforts, resulting in loss of sales, increased costs, and reduced revenues.

If we are unable to adequately protect or enforce our intellectual property rights or secure rights to third-party patents, we may lose valuable assets, experience reduced market share or incur costly litigation to protect our rights

Our success will depend in part on our ability to obtain patents, maintain trade secret protection and operate without infringing the proprietary rights of others. As of September 30, 2005, we held 27 issued U.S. patents and 35 issued foreign patents. In addition, we have 41 pending U.S. patent applications and have filed 54 patent applications under the Patent Cooperation Treaty, from which 105 national phase applications are currently pending in Europe, Australia, Japan, Canada, Mexico, New Zealand, Brazil, Israel, India, Hong Kong and China. Our patents expire at various dates starting in the year 2012. Under our agreement with ALZA, we must assign to ALZA any intellectual property rights relating to the DUROS system and its manufacture and any combination of the DUROS system with other components, active agents, features or processes. In addition, ALZA retains the right to enforce and defend against infringement actions relating to the DUROS system, and if ALZA exercises these rights, it will be entitled to the proceeds of these infringement actions.

The patent positions of pharmaceutical companies, including ours, are uncertain and involve complex legal and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, our patent applications or those of ALZA that are licensed to us may not issue into patents, and any issued patents may not provide protection against competitive technologies or may be held invalid if challenged or circumvented. Our competitors may also independently develop products similar to ours or design around or otherwise circumvent patents issued to us or licensed by us. In addition, the laws of some foreign countries may not protect our proprietary rights to the same extent as U.S. law.

We also rely upon trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. We require our employees, consultants, advisors and collaborators to execute appropriate confidentiality and assignment-of-inventions agreements with us. These agreements typically provide that all materials and confidential information developed or made known to the individual during the course of the individual s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances, and that all inventions arising out of the individual s relationship with us shall be our exclusive property. These agreements may be breached, and in some instances, we may not have an appropriate remedy available for breach of the agreements. Furthermore, our competitors may independently develop substantially equivalent proprietary information and techniques, reverse engineer our information and techniques, or otherwise gain access to our proprietary technology.

We may be unable to meaningfully protect our rights in trade secrets, technical know-how and other non-patented technology. We may have to resort to litigation to protect our intellectual property rights, or to determine their scope, validity or enforceability. Enforcing or defending our proprietary rights is expensive, could cause diversion of our resources and may not prove successful. Any failure to enforce or protect our rights could cause us to lose the ability to exclude others from using our technology to develop or sell competing products.

We may be sued by third parties which claim that our product candidates infringe on their intellectual property rights, particularly because there is substantial uncertainty about the validity and breadth of medical patents

We may be exposed to future litigation by third parties based on claims that our product candidates or activities infringe the intellectual property rights of others or that we have misappropriated the trade secrets of others. This risk is exacerbated by the fact that the validity and breadth of claims covered in medical technology

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patents and the breadth and scope of trade secret protection involve complex legal and factual questions for which important legal principles are unresolved. Any litigation or claims against us, whether or not valid, could result in substantial costs, could place a significant strain on our financial resources and could harm our reputation. We also may not have sufficient funds to litigate against parties with substantially greater resources. Intellectual property litigation or claims could force us to do one or more of the following, any of which could harm our business or financial results:

- cease selling, incorporating or using any of our product candidates that incorporate the challenged intellectual property, which would adversely affect our revenue;
- obtain a license from the holder of the infringed intellectual property right, which license may be costly or may not be available on reasonable terms, if at all; or
- redesign our product candidates, which would be costly and time-consuming.

We may be required to obtain rights to certain drugs

Some of the pharmaceutical systems that we are currently developing require the use of proprietary drugs to which we do not have commercial rights. For example, our research collaboration with the University of Maastricht has demonstrated that the use of a proprietary angiogenic factor in a pharmaceutical system can lead to elevated local concentration of the angiogenic factor in the pericardial sac of the heart, resulting in physical changes, including the growth of new blood vessels. We do not currently have a license to develop or commercialize a product candidate containing such proprietary angiogenic factor.

To complete the development and commercialization of pharmaceutical systems containing drugs to which we do not have commercial rights, we will be required to obtain rights to those drugs. We may not be able to do this at an acceptable cost, if at all. If we are not able to obtain required rights to commercialize certain drugs, we may not be able to complete the development of pharmaceutical systems which require use of those drugs. This could result in the cessation of certain development projects and the potential write-off of certain assets.

Technologies and businesses which we have acquired may be difficult to integrate, disrupt our business, dilute stockholder value or divert management attention. We may also acquire additional businesses or technologies in the future, which could have these same effects

We may acquire technologies, products or businesses to broaden the scope of our existing and planned product lines and technologies. Future acquisitions expose us to:

- increased costs associated with the acquisition and operation of the new businesses or technologies and the management of geographically dispersed operations;
- the risks associated with the assimilation of new technologies, operations, sites and personnel;

the diversion of resources from our existing business and technologies;

the inability to generate revenues to offset associated acquisition costs;

the requirement to maintain uniform standards, controls, and procedures; and

the impairment of relationships with employees and customers as a result of any integration of new management personnel.

Acquisitions may also result in the issuance of dilutive equity securities, the incurrence or assumption of debt or additional expenses associated with the amortization of acquired intangible assets or potential businesses. Past acquisitions, such as our acquisitions of IntraEAR, ALZET, SBS and APT, as well future acquisitions, may not generate any additional revenue or provide any benefit to our business.

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Our operating history makes evaluating our stock difficult

We have engaged primarily in research and development, licensing technology, raising capital and recruiting scientific and management personnel and, to a lesser extent, sales and marketing of products that we do not consider core to our business. We have no approved pharmaceutical system products. This history does not enable investors to fully assess our ability to successfully develop our product candidates, achieve market acceptance of our product candidates and respond to competition. Furthermore, we anticipate that our quarterly and annual results of operations will fluctuate for the foreseeable future. We believe that period-to-period comparisons of our operating results should not be relied upon as predictive of future performance. Our prospects must be considered in light of the risks, expenses and difficulties encountered by companies with no approved pharmaceutical products, particularly companies in new and rapidly evolving markets such as pharmaceuticals, drug delivery and biotechnology. To address these risks, we must, among other things, obtain regulatory approval for and commercialize our product candidates, which may not occur. We may not be successful in addressing these risks and difficulties. We may require additional funds to complete the development of our product candidates and to fund operating losses to be incurred in the next several years.

Some of our product candidates contain controlled substances, the making, use, sale, importation and distribution of which are subject to regulation by state, federal and foreign law enforcement and other regulatory agencies

Some of our product candidates currently under development contain, and our products in the future may contain, controlled substances which are subject to state, federal and foreign laws and regulations regarding their manufacture, use, sale, importation and distribution. Our TRANSDUR-Sufentanil patch, Remoxy and CHRONOGESIC product candidates and other product candidates we have under development contain opioids which are classified as Schedule II controlled substances under the regulations of the U.S. Drug Enforcement Agency. For our product candidates containing controlled substances, we and our suppliers, manufacturers, contractors, customers and distributors are required to obtain and maintain applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation and distribution of controlled substances. These regulations are extensive and include regulations governing manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, record keeping, reporting, handling, shipment and disposal. Failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing our product candidates containing controlled substances and subject us to enforcement action. In addition, because of their restrictive nature, these regulations could limit our commercialization of our product candidates containing controlled substances.

Write-offs related to the impairment of long-lived assets and other non-cash charges, as well as future deferred compensation expenses may adversely impact or delay our profitability

We may incur significant non-cash charges related to impairment write-downs of our long-lived assets, including goodwill and other intangible assets. In 2002, Statement of Financial Accounting Standards No. 142, *Goodwill and Other Intangible Assets* (SFAS 142) became effective and as a result, we ceased to amortize approximately $4.7 million of goodwill and assembled workforce on January 1, 2002.

However, we will continue to incur non-cash charges related to amortization of other intangible assets. We are required to perform periodic impairment reviews of our goodwill at least annually. To the extent these reviews conclude that the expected future cash flows generated from our business activities are not sufficient to recover the cost of our long-lived assets, we will be required to measure and record an impairment charge to write down these assets to their realizable values. We completed our last review during the fourth quarter of 2004 and determined that goodwill was not impaired as of December 31, 2004. However, there can be no assurance that upon completion of subsequent reviews a material impairment charge will not be recorded. If future periodic reviews determine that our assets are impaired and a write down is required, it will adversely impact or delay our profitability.

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To date, we have recorded deferred compensation expenses related to stock options grants, including stock options assumed in our acquisition of SBS, which will be amortized through 2006. In addition, deferred compensation expense related to option awards to non-employees will be calculated during the vesting period of the option based on the then-current price of our common stock, which could result in significant charges that adversely impact or delay our profitability. Furthermore, we have issued to ALZA common stock and a warrant to purchase common stock with an aggregate value of approximately $13.5 million, which will be amortized over time based on sales of our DUROS-based products and which will also adversely impact or delay our profitability.

We depend upon key personnel who may terminate their employment with us at any time, and we need to hire additional qualified personnel

Our success will depend to a significant degree upon the continued services of key management, technical and scientific personnel, including Felix Theeuwes, our Chairman and Chief Scientific Officer and James E. Brown, our President and Chief Executive Officer. Although we have obtained key man life insurance policies for each of Messrs. Theeuwes and Brown in the amount of $1.0 million, this insurance may not adequately compensate us for the loss of their services. In addition, our success will depend on our ability to attract and retain other highly skilled personnel. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all. Our management and other employees may voluntarily terminate their employment with us at any time. The loss of the services of key personnel, or the inability to attract and retain additional qualified personnel, could result in delays to product development or approval, loss of sales and diversion of management resources.

We may not successfully manage our growth

Our success will depend on the timely expansion of our operations and the effective management of growth, which will place a significant strain on our management and on our administrative, operational and financial resources. To manage such growth, we must expand our facilities, augment our operational, financial and management systems and hire, train and supervise additional qualified personnel. If we were unable to manage growth effectively our business would be harmed.

Our business involves environmental risks and risks related to handling regulated substances

In connection with our research and development activities and our manufacture of materials and product candidates, we are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. Although we believe that we have complied with the applicable laws, regulations and policies in all material respects and have not been required to correct any material noncompliance, we may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development involves the use, generation and disposal of hazardous materials, including but not limited to certain hazardous chemicals, solvents, agents and biohazardous materials. The extent of our use, generation and disposal of such substances has increased substantially since we started manufacturing and selling biodegradable polymers. Although we believe that our safety procedures for storing, handling and disposing of such materials comply with the standards prescribed by state and federal regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. We currently contract with third parties to dispose of these substances generated by us, and we rely on these third parties to properly dispose of these substances in compliance with applicable laws and regulations. If these third parties do not properly dispose of these substances in compliance with applicable laws and regulations, we may be subject to legal action by governmental agencies or private parties for improper disposal of these substances. The costs of defending such actions and the potential liability resulting from such actions are often very large. In the event we are subject to such legal action or we otherwise fail to comply with applicable laws and regulations governing the use, generation and disposal of hazardous materials and chemicals, we could be held liable for any damages that result, and any such liability could exceed our resources.

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Our agreement with ALZA limits our fields of operation for our DUROS-based pharmaceutical systems and gives ALZA a first right to negotiate to distribute selected products for us

Our agreement with ALZA gives us exclusive rights to develop, commercialize and manufacture products using ALZA s DUROS technology to deliver by catheter:

- drugs to the central nervous system to treat select nervous system disorders;
- drugs to the middle and inner ear;
- drugs to the pericardial sac of the heart; and
- select drugs into vascular grafts.

We also have the right to use the DUROS technology to deliver systemically and by catheter:

- sufentanil to treat chronic pain; and
- select cancer antigens.

We may not develop, manufacture or commercialize DUROS-based pharmaceutical systems outside of these specific fields without ALZA s prior approval. In addition, if we develop or commercialize any drug delivery technology for use in a manner similar to the DUROS technology in a field covered in our license agreement with ALZA, then we may lose our exclusive rights to use the DUROS technology in such field as well as the right to develop new product candidates using DUROS technology in such field. In order to maintain commercialization rights for our products on a worldwide basis, we must diligently develop our product candidates, procure required regulatory approvals and commercialize the product candidates in selected major market countries. If we fail to meet commercialization diligence requirements, we may lose rights for products in some or all countries, including the United States. These rights would revert to ALZA, which could then develop DUROS-based pharmaceutical products in such countries itself or license others to do so. In addition, in the event that our rights terminate with respect to any product or country, or this agreement terminates or expires in its entirety (except for termination by us due to a breach by ALZA), ALZA will have the exclusive right to use all of our data, rights and information relating to the products developed under the agreement as necessary for ALZA to commercialize these products, subject to the payment of a royalty to us based on the net sales of the products by ALZA.

Our agreement with ALZA gives us the right to perform development work and manufacture the DUROS pump component of our DUROS-based pharmaceutical systems. In the event of a change in our corporate control, including an acquisition of us, our right to manufacture and perform development work on the DUROS pump would terminate and ALZA would have the right to manufacture and develop DUROS systems for us so long as ALZA can meet our specification and supply requirements following such change in control.

Under the ALZA agreement, we must pay ALZA royalties on sales of DUROS-based pharmaceutical systems we commercialize and a percentage of any up-front license fees, milestone or special fees, payments or other consideration we receive, excluding research and

development funding. In addition, commencing upon the commercial sale of a product developed under the agreement, we are obligated to make minimum product payments to ALZA on a quarterly basis based on our good faith projections of our net product sales of the product. These minimum payments will be fully credited against the product royalty payments we must pay to ALZA.

ALZA may obtain from us, for its own behalf or on behalf of one of its affiliates, the exclusive right to develop and commercialize a product in a field of use exclusively licensed to us, provided that such product does not incorporate a drug in the same drug class and is not intended for the same therapeutic indication as a product which is then being developed or commercialized by us or for which we have made commitments to a third-party. In the event that ALZA or an affiliate commercializes such a product, ALZA or its affiliate will pay us a royalty on sales of such product at a specified rate.

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ALZA also has an exclusive option to distribute any DUROS-based pharmaceutical system we develop to deliver non-proprietary cancer antigens worldwide. The terms of any distribution arrangement have not been set and are to be negotiated in good faith between ALZA and us. ALZA s option to acquire distribution rights limits our ability to negotiate with other distributors for these products and may result in lower payments to us than if these rights were subject to competitive negotiations. We must allow ALZA an opportunity to negotiate in good faith for commercialization rights to our products developed under the agreement prior to granting these rights to a third-party. These rights do not apply to products that are subject to ALZA s option or products for which we have obtained funding or access to a proprietary drug from a third-party to whom we have granted commercialization rights prior to the commencement of human clinical trials.

ALZA has the right to terminate the agreement in the event that we breach a material obligation under the agreement and do not cure the breach in a timely manner. In addition, ALZA has the right to terminate the agreement if at any time prior to July 2006, we solicit for employment or hire, without ALZA s consent, a person who is or within the previous 180 days has been an employee of ALZA in the DUROS technology group.

We do not control ALZA s ability to develop and commercialize DUROS technology outside of fields licensed to us, and problems encountered by ALZA could result in negative publicity, loss of sales and delays in market acceptance of our DUROS-based pharmaceutical systems

ALZA retains complete rights to the DUROS technology for fields outside the specific fields licensed to us. Accordingly, ALZA may develop and commercialize DUROS-based products or license others to do so, so long as there is no conflict with the rights granted to us. ALZA received FDA approval to market its first DUROS-based product, VIADUR (leuprolide acetate implants) for the palliative treatment of advanced prostate cancer in March 2000. If ALZA or its commercialization partner, Bayer, fails to commercialize this product successfully, or encounters problems associated with this product, negative publicity could be created about all DUROS-based products, which could result in harm to our reputation and cause reduced sales of our DUROS-based product candidates. In addition, if any third party that may be licensed by ALZA fails to develop and commercialize DUROS-based products successfully, the success of all DUROS-based systems could be impeded, including ours, resulting in delay or loss of revenue or damage to our reputation, any one of which could harm our business.

Our corporate headquarters, manufacturing facilities and personnel are located in a geographical area that is seismically active

Our corporate headquarters, manufacturing facilities and personnel are located in a geographical area that is known to be seismically active and prone to earthquakes. Should such a natural disaster occur, our ability to conduct our business could be severely restricted, and our business and assets, including the results of our research and development efforts, could be destroyed.

RISKS RELATED TO OUR INDUSTRY

The market for our product candidates is new, rapidly changing and competitive, and new products or technologies developed by others could impair our ability to grow our business and remain competitive

The pharmaceutical industry is subject to rapid and substantial technological change. Developments by others may render our product candidates under development or technologies noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Technological competition in the industry from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase. Many of these entities have significantly greater research and development capabilities than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities

represent significant competition for us. Acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors financial, marketing, manufacturing and other resources.

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We are engaged in the development of novel therapeutic technologies. Our resources are limited and we may experience technical challenges inherent in such novel technologies. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these products may have an entirely different approach or means of accomplishing similar therapeutic effects than our product candidates. Our competitors may develop products that are safer, more effective or less costly than our product candidates and, therefore, present a serious competitive threat to our product offerings.

The widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our product candidates even if commercialized. Chronic and post-operative pain are currently being treated by oral medication, transdermal drug delivery systems, such as drug patches, and implantable drug delivery devices which will be competitive with our product candidates. These treatments are widely accepted in the medical community and have a long history of use. The established use of these competitive products may limit the potential for our product candidates to receive widespread acceptance if commercialized.

We could be exposed to significant product liability claims which could be time consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage

The testing, manufacture, marketing and sale of our product candidates involve an inherent risk that product liability claims will be asserted against us. Although we are insured against such risks up to an annual aggregate limit in connection with clinical trials and commercial sales of our product candidates, our present product liability insurance may be inadequate and may not fully cover the costs of any claim or any ultimate damages we might be required to pay. Product liability claims or other claims related to our product candidates, regardless of their outcome, could require us to spend significant time and money in litigation or to pay significant damages. Any successful product liability claim may prevent us from obtaining adequate product liability insurance in the future on commercially desirable or reasonable terms. In addition, product liability coverage may cease to be available in sufficient amounts or at an acceptable cost. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our pharmaceutical systems. A product liability claim could also significantly harm our reputation and delay market acceptance of our product candidates.

Acceptance of our product candidates in the marketplace is uncertain, and failure to achieve market acceptance will delay our ability to generate or grow revenues

Our future financial performance will depend upon the successful introduction and customer acceptance of our future products, including our SABER-Bupivacaine, TRANSDUR-Sufentanil, Remoxy, DURIN-Leuprolide (Memryte) and CHRONOGESIC product candidates. Even if approved for marketing, our product candidates may not achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including:

- the receipt of regulatory clearance of marketing claims for the uses that we are developing;
- the establishment and demonstration in the medical community of the safety and clinical efficacy of our products and their potential advantages over existing therapeutic products, including oral medication, transdermal drug delivery products such as drug patches, or external or implantable drug delivery products; and
- pricing and reimbursement policies of government and third-party payors such as insurance companies, health maintenance organizations and other health plan administrators.

Physicians, patients, payors or the medical community in general may be unwilling to accept, utilize or recommend any of our products. If we are unable to obtain regulatory approval, commercialize and market our future products when planned and achieve market acceptance, we will not achieve anticipated revenues.

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If users of our products are unable to obtain adequate reimbursement from third-party payors, or if new restrictive legislation is adopted, market acceptance of our products may be limited and we may not achieve anticipated revenues

The continuing efforts of government and insurance companies, health maintenance organizations and other payors of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and collaborative partners and the availability of capital. For example, in certain foreign markets, pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, recent federal and state government initiatives have been directed at lowering the total cost of health care, and the U.S. Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid systems. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of such proposals could materially harm our business, financial condition and results of operations.

The successful commercialization of our product candidates will depend in part on the extent to which appropriate reimbursement levels for the cost of our product candidates and related treatment are obtained by governmental authorities, private health insurers and other organizations, such as HMOs. Third-party payors are increasingly limiting payments or reimbursement for medical products and services. Also, the trend toward managed health care in the United States and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care or reduce government insurance programs, may limit reimbursement or payment for our products. The cost containment measures that health care payors and providers are instituting and the effect of any health care reform could materially harm our ability to operate profitably.

If we or our third-party collaborators are unable to train physicians to use our pharmaceutical systems to treat patients diseases or medical conditions, we may incur delays in market acceptance of our products

Broad use of our pharmaceutical systems will require extensive training of numerous physicians on the proper and safe use of our products. The time required to begin and complete training of physicians could delay introduction of our products and adversely affect market acceptance of our products. We or third parties selling our products may be unable to rapidly train physicians in numbers sufficient to generate adequate demand for our pharmaceutical systems. Any delay in training would materially delay the demand for our systems and harm our business and financial results. In addition, we may expend significant funds towards such training before any orders are placed for our products, which would increase our expenses and harm our financial results.

Legislative actions, potential new accounting pronouncements and higher insurance costs are likely to impact our future financial position or results of operations

Future changes in financial accounting standards, including proposed changes in accounting for employee stock-based awards, may cause adverse, unexpected fluctuations in the timing of the recognition of revenues or expenses and may affect our financial position or results of operations. New pronouncements and varying interpretations of pronouncements have occurred with frequency and may occur in the future and we may make changes in our accounting policies in the future. Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses. Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new SEC regulations, PCAOB pronouncements and Nasdaq National Market rules, are creating uncertainty for companies such as ours and insurance, accounting and auditing costs are increasing as a result of this uncertainty and other factors. We are committed to maintaining high standards of corporate governance and public disclosure. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities.

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In December 2004, the FASB issued Statement No. 123 (revised 2004, or SFAS 123R), Share-Based Payment, which was originally effective for annual or interim periods beginning after June 15, 2005. SFAS 123R supersedes APB Opinion No. 25, Accounting for Stock Issued to Employees, and will require companies to recognize compensation expense, using a fair-value based method, for costs related to share-based payments including stock options and stock issued under our employee stock purchase plans. In April 2005, the SEC issued a press release that revised the required date of adoption under SFAS 123R. We will be required to adopt SFAS 123R no later than the fiscal year that begins after June 15, 2005. Our adoption will be applied on a modified prospective basis and measured compensation expense will be recognized commencing on January 1, 2006. We expect that our adoption of SFAS 123R will have a material adverse impact on our consolidated results of operations.

In March 2005, the SEC issued SAB No. 107 regarding the interaction between SFAS 123R which was revised in December 2004, and certain SEC rules and regulations and provides the SEC s staff views regarding the valuation of share-based payment arrangements for public companies. We are evaluating the impact this guidance will have on our consolidated results of operations and financial position.

In May 2005, the FASB issued Statement No. 154, Accounting Changes and Error Corrections a replacement of APB Opinion No. 20 and FASB Statement No. 3 . SFAS 154 changes the requirements for the accounting for and reporting of a change in accounting principle, and applies to all voluntary changes in accounting principle. It also applies to changes required by an accounting pronouncement in the unusual instance that the pronouncement does not include specific transition provisions. This statement requires retrospective application to prior periods financial statements of changes in accounting principle, unless it is impracticable to determine either the period-specific effects or the cumulative effect of the change. SFAS 154 is effective for accounting changes made in fiscal years beginning after December 15, 2005. We do not expect that adoption of this statement will have a material impact on our consolidated results of operations.

RISKS RELATED TO OUR COMMON STOCK

Investors may experience substantial dilution of their investment

In the past, we have issued and have assumed, pursuant to the SBS acquisition, options and warrants to acquire common stock. To the extent these outstanding options are ultimately exercised, there will be dilution to investors. In addition, conversion of some or all of the remaining $57.3 million aggregate principal amount of convertible subordinated notes that we issued in June and July 2003 will dilute the ownership interests of investors. Investors may experience further dilution of their investment if we raise capital through the sale of additional equity securities or convertible debt securities. Any sales in the public market of the common stock issuable upon such conversion could adversely affect prevailing market prices for our common stock.

We may choose to purchase a portion of our convertible subordinated notes in exchange for shares of our common stock in the open market. These transactions could dilute existing stockholders and increase the volatility of our stock

To the extent we are able to do so on terms favorable to us, we may choose to purchase a portion of our outstanding 6.25% Convertible Subordinated Notes due June 2008 from time to time in privately negotiated transactions under Section 3(a)(9) of the Securities Act of 1933. On July 21, 2005, we entered into an agreement for such a transaction for notes with an aggregate principal amount of up to $5.0 million. The issuance of shares of our common stock in such transactions will dilute our existing investors. To the extent such shares are resold, such transactions may increase the volatility of our stock.

The price of our common stock may be volatile

The stock markets in general, and the markets for pharmaceutical stocks in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. These broad market fluctuations may adversely affect the trading price of our common stock.

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Price declines in our common stock could result from general market and economic conditions and a variety of other factors, including:

- failure of our third-party collaborators (such as Endo Pharmaceuticals, Pain Therapeutics or Voyager Pharmaceuticals) to develop and commercialize successfully the respective pharmaceutical systems they are developing;
- adverse results or delays in our clinical trials of SABER-Bupivacaine, TRANSDUR-Sufentanil, Remoxy, DURIN-Leuprolide (Memryte), CHRONOGESIC or other product candidates;
- announcements of FDA non-approval of our product candidates, or delays in the FDA or other foreign regulatory agency review process;
- adverse actions taken by regulatory agencies with respect to our product candidates or our or our third-party collaborator s clinical trials, manufacturing processes or sales and marketing activities;
- announcements of technological innovations, patents or new products by our competitors;
- regulatory developments in the United States and foreign countries;
- any lawsuit involving us or our product candidates;
- announcements concerning our competitors, or the biotechnology or pharmaceutical industries in general;
- developments concerning our strategic alliances or acquisitions;
- actual or anticipated variations in our operating results;
- changes in recommendations by securities analysts or lack of analyst coverage;
- deviations in our operating results from the estimates of analysts;
- sales of our common stock by our executive officers, directors and five percent stockholders or sales of substantial amounts of common stock;
- changes in accounting principles; and
- loss of any of our key scientific or management personnel.

In the past, following periods of volatility in the market price of a particular company s securities, litigation has often been brought against that company. If litigation of this type is brought against us, it could be extremely expensive and divert management s attention and our company s resources.

Our trading volume is relatively low and may contribute to its volatility

The average daily trading volume of our common stock for the three months ending September 30, 2005, was 373,333 shares. The limited trading volume of our stock may contribute to its volatility, and an active trading market in our stock might not continue. Pursuant to a Purchase Agreement with Morgan Stanley & Co., Incorporated, we filed a registration statement on August 29, 2003 with the SEC on Form S-3 to register an aggregate of $60.0 million in convertible subordinated notes and the shares of common stock issuable upon conversion of the notes for resale. The registration statement was declared effective by the SEC on November 3, 2003. The convertible subordinated notes are convertible into shares of our common stock at a conversion rate of 317.4603 shares per $1,000 principal amount of notes, subject to adjustment and will bear interest at a rate of 6.25% per annum. So long as this registration is effective, shares covered thereunder are tradable without limitation. If substantial amounts of our common stock issued upon conversion of our promissory notes or otherwise were to be sold in the public market, the market price of our common stock could fall. In addition, the existence of our convertible subordinated notes may encourage short selling by market participants. The market price of our common stock may fluctuate significantly in response to factors which are beyond our control. The stock market in general has recently experienced extreme price and volume fluctuations. In addition, the market

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prices of securities of technology and pharmaceutical companies have also been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to the operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our common stock, which could cause a decline in the value of our investors stock.

We have broad discretion over the use of our cash and investments, and their investment may not always yield a favorable return

Our management has broad discretion over how our cash and investments are used and may from time to time invest in ways with which our stockholders may not agree and that do not yield favorable returns.

Executive officers, directors and entities affiliated with them have substantial control over us, which could delay or prevent a change in our corporate control favored by our other stockholders

Our directors, executive officers and principal stockholders, together with their affiliates have substantial control over us. The interests of these stockholders may differ from the interests of other stockholders. As a result, these stockholders, if acting together, would have the ability to exercise control over all corporate actions requiring stockholder approval irrespective of how our other stockholders may vote, including:

- the election of directors;
- the amendment of charter documents;
- the approval of certain mergers and other significant corporate transactions, including a sale of substantially all of our assets; or
- the defeat of any non-negotiated takeover attempt that might otherwise benefit the public stockholders.

Our certificate of incorporation, our bylaws, Delaware law and our stockholder rights plan contain provisions that could discourage another company from acquiring us

Provisions of Delaware law, our certificate of incorporation, bylaws and stockholder rights plan may discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions include:

- authorizing the issuance of blank check preferred stock without any need for action by stockholders;
- providing for a dividend on our common stock, commonly referred to as a poison pill , which can be triggered after a person or group acquires 17.5% or more of common stock;

providing for a classified board of directors with staggered terms;

requiring supermajority stockholder voting to effect certain amendments to our certificate of incorporation and bylaws;

eliminating the ability of stockholders to call special meetings of stockholders;

prohibiting stockholder action by written consent; and

establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

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CAUTIONARY NOTE REGARDING FORWARD LOOKING INFORMATION

All statements included or incorporated by reference in this prospectus, other than statements of historical facts, that address activities, events or developments that we intend, expect, project, believe or anticipate will or may occur in the future are forward looking statements. Such statements are typically characterized by terminology such as believe, anticipate, should, intend, plan, will, expect, estimate, proje strategy, and similar expressions. These statements are based on assumptions and assessments made by our management in light of its experience and its perception of historical trends, current conditions, expected future developments and other factors our management believes to be appropriate. These forward looking statements are subject to a number of risks and uncertainties, including those risks described or incorporated by reference in this prospectus under Risk Factors above. Any such forward looking statements are not guarantees of future performance and actual results, developments and business decisions may differ from those contemplated by such forward looking statements. We disclaim any duty to update any forward looking statements. You should also carefully consider other information set forth in reports or other documents that we file with the Securities and Exchange Commission.

USE OF PROCEEDS

Unless otherwise indicated in a prospectus supplement, the net proceeds from the sale of securities offered by this prospectus will be used for general corporate purposes, including clinical trials, research and development activities, capital expenditures, facilities expansion and to meet working capital needs. We may also use all or a portion of the proceeds from the sale of securities offered by this prospectus to purchase, exchange or induce conversion of some or all of our 6.25% convertible notes due June 2008 in open market or privately negotiated transactions. We expect from time to time to evaluate the acquisition of businesses, products and technologies for which a portion of the net proceeds may be used, although we currently are not planning or negotiating any such transactions. Pending such uses, we may invest the net proceeds in investment-grade interest-bearing securities. We will not receive any proceeds from the sale of the shares of our common stock by the selling stockholders.

The amounts actually expended for each purpose may vary significantly depending upon numerous factors, including the amount and timing of the proceeds from this offering and progress with the commercial development of our products as well as our clinical development programs. Expenditures will also depend upon the establishment of collaborative arrangements with other companies, the availability of additional financing and other factors. Investors will be relying on the judgment of our management regarding the application of the proceeds of any sale of securities.

DESCRIPTION OF CAPITAL STOCK

This section describes the general terms and provisions of the shares of our common stock, $0.0001 par value per share and preferred stock, $0.0001 par value per share. This description is only a summary. Our certificate of incorporation and our bylaws have been filed as exhibits to our periodic reports filed with the SEC, which are incorporated by reference into this prospectus. You should read our certificate of incorporation and our bylaws for additional information before you buy any of our securities. See Where You Can Find More Information .

Common Stock

General. We are authorized to issue up to 110,000,000 shares of common stock. As of October 11, 2005, there were 53,289,445 shares of common stock issued and outstanding.

Voting Rights. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose.

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Dividends. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably dividends, if any, as may be declared by our board of directors out of funds legally available therefor. We have not declared any dividends and have no current plans to do so.

Other Rights. Upon our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding. Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are, and the common stock offered, when issued, will be, fully paid and nonassessable.

Transfer Agent and Registrar for Common Stock

The transfer agent and registrar for our Common Stock is Computershare. Its offices are located at 250 Royall Street, Canton, MA 02021, and its telephone number is (781) 575-3452.

Preferred Stock

General. We are authorized to issue up to 10,000,000 shares of preferred stock. As of October 11, 2005, no shares of preferred stock were issued and outstanding. Our board of directors has the authority, without further action by our stockholders, to issue from time to time the preferred stock in one or more series, and to fix the number of shares, designations, preferences, powers, and other rights and qualifications, limitations or restrictions as our board of directors may authorize, including:

- the distinctive designation of each series and the number of shares that will constitute the series;
- the purchase price;
- the voting rights, if any, of shares of the series and the terms and conditions of the voting rights;
- the dividend rate on the shares of the series, the dates on which dividends are payable, any restriction, limitation or condition upon the payment of dividends, whether dividends will be cumulative, and the dates from and after which dividends shall accumulate;
- the prices at which, and the terms and conditions on which, the shares of the series may be redeemed, if the shares are redeemable;
- the procedures for any auction or remarketing, if any;
- the terms and conditions of a sinking or purchase fund for the purchase or redemption of shares of the series, if such a fund is provided;

any preferential amount payable upon shares of the series in the event of the liquidation, dissolution or winding up of, or upon the distribution of any of our assets; and

any listing of the preferred stock on any securities exchange or market;

preemption rights, if any;

restrictions on transfer, sale or other assignment, if any;

the prices or rates of conversion or exchange at which, and the terms and conditions on which, the shares of the series may be converted or exchanged into other securities, if the shares are convertible or exchangeable; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

When we issues shares of preferred stock, the shares will be fully paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

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Delaware General Corporation Law (DGCL) provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to holders of common stock or adversely affect the rights and powers, including voting rights, of the holders of common stock. The issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company, which could depress the market price of our common stock.

Series A Participating Preferred Stock. Of the 10,000,000 shares of preferred stock currently authorized, we have designated 100,000 shares as series A participating preferred stock. As of October 11, 2005, no shares of series A participating preferred stock were issued and outstanding.

Voting Rights. The holders of our series A participating preferred stock are entitled to 1,000 votes, subject to certain adjustments, for each share held of record on all matters submitted to a vote of the stockholders. Except as otherwise provided, holders of shares of series A participating preferred stock and the holders of shares of common stock shall vote together as one class on all matters submitted to a vote of the stockholders.

Dividends. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of series A participating preferred stock are entitled to receive ratably dividends, if any, as may be declared by our board of directors out of funds legally available therefor, to be paid on a quarterly basis in an amount per share equal to, subject to certain adjustments, 1,000 times the aggregate per share amount of all cash dividends and 1,000 times the aggregate per share amount of all non-cash dividends or other distributions other than a dividend payable in shares of common stock or a subdivision of the outstanding shares of common stock. We will not declare any dividend on, make any distribution on or redeem or purchase or otherwise acquire for consideration any shares of common stock after the first issuance of a share or fraction of a share of series A participating preferred stock unless we concurrently declare a dividend on the series A participating preferred stock. When dividends payable to holders of series A participating preferred stock are in arrears, we will not take certain actions until such all accrued and unpaid dividends and distributions on shares of series A participating preferred stock are paid in full. We have not declared any dividends and have no plans to do so.

Other Rights. Upon our liquidation, dissolution or winding up, no distribution shall be made to the holders of shares ranking junior to the series A participating preferred stock unless the holders of series A participating preferred stock have received an amount equal to the accrued and unpaid dividends and distributions, whether or not declared, to the date of such payment plus an amount equal to the greater of (i) $1,000 per share, or an adjusted amount if we do not have sufficient assets, and (ii) 1,000 times the aggregate per share amount to be distributed to the holders of common stock, subject to certain adjustments. Upon a consolidation, merger, combination or other transaction in which shares of our common stock are exchanged for or changed into other stock or securities, cash and/or any other property, each share of series A participating preferred stock shall be exchanged or changed in an amount equal to 1,000 times the aggregate amount of stock, securities, cash and/or any other property into which or for which each share of common stock is changed or exchanged, subject to certain adjustments. Holders of series A participating preferred stock have no redemption rights. All outstanding shares of series A participating preferred stock, when issued, will be fully paid and nonassessable.

Stockholder Rights Plan

On July 6, 2001, our board of directors adopted a stockholder rights plan. The stockholder rights plan was adopted to give our board of directors increased power to negotiate in our best interests and to discourage appropriation of control of us at a price that is unfair to our stockholders. It is not intended to prevent fair offers for acquisition of control determined by our board of directors to be in the best interest of us and out

stockholder, nor is it intended to prevent a person or group from obtaining representation on or control of our board of directors through a proxy contest, or to relieve our board of directors of its fiduciary duty to consider any proposal for our acquisition in good faith.

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The material provisions of the rights plan are summarized below. However, since the terms of our rights agreement are complex, this summary may not contain all the information that is important to you. For more information, you should obtain a copy of the agreement, which is filed as an exhibit with the SEC. See Where You Can Find More Information for information on how to obtain a copy.

Under the rights agreement, we will issue one right with respect to each share of common stock that is issued prior to the distribution date described below. Except as set forth below, each right, when exercisable, entitles the holder to purchase from us one one-thousandth of a share of our series A participating preferred stock at a price of $120.00, subject to adjustment. The rights trade in tandem with the common stock until, and become exercisable following, a distribution date. Our board of directors retains the right to amend the stockholder rights plan in any respect until 10 days following our announcement of the occurrence of any such triggering event, as defined below, leading to a distribution. Until a right is exercised, the holder of the right, as such, will have no rights as a stockholder of ours and will not have the right to vote or to receive dividends.

In general, the rights separate from the common stock and a distribution date will occur upon the earlier of:

- the close of business on the tenth day (or such later date as may be determined by a majority of our board of directors) following a public announcement that a person or group of affiliated or associated persons has acquired, or obtained the right to acquire, beneficial ownership of 17.5% or more of the outstanding common stock; or

- the close of business on the tenth day (or such later date as may be determined by a majority of our board of directors) following the commencement of a tender offer or exchange offer, the consummation of which would result in the beneficial ownership by a person or group of 17.5% or more of the outstanding Common Shares.

If a person or group acquires 17.5% or more of our common stock, all rightholders except the buyer will be entitled to acquire our common stock at a discount and, under certain circumstances, to acquire shares of the acquiring company at a discount. Also, in the event our board of directors may authorize the exchange of all or part of the then outstanding and exercisable rights for shares of our common stock at a rate of one share of our common stock per right if the buyer has not acquired 50% or more of our common stock.

Our board of directors may authorize the redemption of the rights, at a price of $0.01 per right, at any time before a person or group acquires 17.5% or more of our common stock. The rights will expire on July 6, 2011.

ADDITIONAL INFORMATION CONCERNING OUR CAPITAL STOCK

Anti-Takeover Effects of Our Certificate of Incorporation and Bylaws

Our certificate of incorporation and by-laws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions:

authorizing the issuance of blank check preferred stock without any need for action by stockholders;

providing for a classified board of directors with staggered terms;

requiring supermajority stockholder voting to effect certain amendments to our certificate of incorporation and by-laws;

eliminating the ability of stockholders to call special meetings of stockholders;

prohibiting stockholder action by written consent; and

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establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

These provisions could discourage, delay or prevent certain types of transactions involving an actual or potential change in control of us, including transactions in which stockholders might otherwise receive a premium for their shares over current market prices.

Anti-Takeover Effects of Provisions of Delaware Law

We are subject to the provisions of Section 203 of the DGCL. In general, the statute prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date that person became an interested stockholder, unless the business combination was approved in a prescribed manner. A business combination includes a merger, asset sale or other transaction resulting in a financial benefit to an interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns, or, within the three years prior to the determination of interested stockholder status, owned, 15% or more of our outstanding voting stock.

Section 203 makes it more difficult for an interested stockholder to effect various business combinations with a corporation for a three-year period. This statute could prohibit or delay mergers or other takeover or change in control attempts not approved in advance by our board of directors, and as a result could discourage attempts to acquire us, which could depress the market price of our common stock.

Limitation of Liability and Indemnification

To the fullest extent permitted by the Delaware law, our certificate of incorporation provides that directors shall not be personally liable to us or any of our stockholders for monetary damages for breach of fiduciary duty as a director. However, this provision does not eliminate the duty of care, and in appropriate circumstances, equitable remedies such as injunctive or other forms of nonmonetary relief that will remain available under Delaware law. In addition, each director will continue to be subject to liability for (i) breach of the directors duty of loyalty to us or our stockholders, (ii) acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) violating Section 174 of the DGCL, or (iv) any transaction from which the director derived an improper personal benefit. The provision also does not affect a director s responsibilities under any other law, such as the federal securities laws or state or federal environmental laws.

Our bylaws provide that we shall, to the maximum extent and in the manner permitted by the Delaware law, indemnify each of our directors and officers against expenses (including attorneys fees), judgments, fines, settlements and other amounts actually and reasonably incurred in connection with any proceeding, arising by reason of the fact that such person is or was an agent of our company. Our bylaws also provide that we shall have the power to, to the maximum extent and in the manner permitted by the Delaware law, indemnify each of our employees and agents against expenses (including attorneys fees), judgments, fines, settlements and other amounts actually and reasonably incurred in connection with any proceeding, arising by reason of the fact that such person is or was an agent of our company. Our bylaws provide that expenses incurred in defending any such action or proceeding shall be paid in advance of the final disposition of such action or proceeding upon the receipt of an undertaking by or on behalf of the indemnified party to repay such amount if it shall be ultimately determined that the indemnified party is not entitled to be indemnified as authorized by our bylaws. The indemnification provided by our bylaws shall not be deemed exclusive of any other rights to which those seeking indemnification may have been entitled under any bylaw, agreement, vote of shareholders or disinterested directors or otherwise, to the extent that such additional rights to indemnification are authorized in our certificate of incorporation.

We also maintain liability insurance for our officers and directors and have entered into indemnification agreements with them.

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SELLING STOCKHOLDERS

Below is information with respect to the number of shares of our common stock owned by the selling stockholders as of October 11, 2005. Except as described below, the selling stockholders do not have, or have had, any position, office or other material relationship with us or any of our affiliates beyond their investment in, or receipt of, our securities. See Plan of Distribution for additional information about the selling stockholders and the manner in which the selling stockholders may dispose of their shares.

Percentage ownership for each stockholder is based on 53,289,445 shares of common stock outstanding at October 11, 2005, together with options owned by such stockholder. Beneficial ownership is determined in accordance with the rules of the SEC, and includes voting and investment power with respect to the shares. Beneficial ownership also includes shares of stock subject to options exercisable within 60 days of October 11, 2005. Shares of common stock subject to outstanding options are deemed outstanding for computing the percentage of ownership of the person holding such options, but are not deemed outstanding for computing the percentage ownership of any other person.

Except pursuant to applicable community property laws or as indicated in the footnotes to this table, to our knowledge, each stockholder identified in the table possesses sole voting and investment power with respect to all shares of common stock shown as beneficially owned by such stockholder.

We are registering 347,256 shares of our common stock for resale by the selling stockholders identified in this prospectus. Our registration of these shares does not necessarily mean that the selling stockholders will sell any or all of the shares covered by this prospectus.

The number of shares of common stock that may actually be sold by the selling stockholders will be determined by the selling stockholders. Because each selling stockholder may sell all, some or none of the shares of common stock which it holds, and because the offering contemplated by this prospectus is not currently being underwritten, no estimate can be given as to the number of shares of common stock that will be held by each selling stockholder upon termination of the offering. The information set forth in the following table regarding the beneficial ownership after resale of shares is based on the premise that the selling stockholder will sell all of the shares of common stock owned by that selling stockholder and covered by this prospectus.

	Ownership Before Offering			Ownership After Offering	
Name and address(1)	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned	Number of Shares Offered	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
James E. Brown(2)	2,913,450	5.44%	300,000	2,613,450	4.88%
Tai Wah Chan(3)	194,121	*	25,000(4)	169,121	*
Jonathan Heuer(5)	22,256	*	22,256	0	*

* Less than one percent.

(1) Except as otherwise indicated, the address of the persons above is our address appearing on page 2 of this prospectus.

(2) Includes 217,450 shares issuable upon exercise of options exercisable within 60 days of October 11, 2005. Dr. Brown is our Chief Executive Officer and a member of our Board of Directors.

(3) Includes 131,750 shares issuable upon exercise of options exercisable within 60 days of October 11, 2005. Dr. Chan is our Vice President, Pharmaceutical Research and Development.
(4) Includes shares of common stock to be sold by such holder pursuant to a prospectus supplement, which shares will be issued immediately prior to the sale as a result of the exercise of options.
(5) Mr. Heuer is the husband of Jean I Liu, our Senior Vice President, General Counsel and Corporate Secretary.

Generally, only selling stockholders identified in the foregoing table who beneficially own the securities set forth opposite their respective names may sell offered securities under the registration statement of which this prospectus forms a part. We may from time to time include additional selling stockholders in an amendment to this registration statement or a supplement to this prospectus.

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PLAN OF DISTRIBUTION

We may sell the securities being offered by this prospectus separately or together through any of the following methods:

- to or through one or more underwriters or dealers in a public offering and sale by them;
- directly to investors;
- through agents;
- to holders of our 6.25% convertible promissory notes due June 2008 in transactions to repurchase, exchange or induce conversion of such notes; or
- through block trades in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction.

We may sell the securities from time to time in one or more transactions at a fixed price or prices, which may be changed from time to time:

- at market prices prevailing at the times of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We will describe the method of distribution of the securities in the applicable prospectus supplement. We may also determine the price or other terms of the securities offered under this prospectus by use of an electronic auction. We will describe how any auction will determine the price or any other terms, how potential investors may participate in the auction and the nature of the obligations of the underwriter, dealer or agent in the applicable prospectus supplement.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers (as their agents in connection with the sale of the securities). In addition, underwriters may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they act as agent. These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions, or profits on resale received by the underwriters, dealers or agents may be treated as underwriting discounts and commissions. The prospectus supplement will identify any such underwriter, dealer or agent, and describe any compensation received by them from us. Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement. Any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

We may sell the securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

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Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us and the underwriters, dealers and agents.

We may grant underwriters who participate in the distribution of the securities an option to purchase additional securities to cover over-allotments, if any, in connection with the distribution. Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the common stock in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the common stock originally sold by the dealer is purchased in a covering transaction to cover short positions. Those activities may cause the price of the common stock to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters who are qualified market makers on the Nasdaq National Market may engage in passive market making transactions in the common stock on the Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker s bid, however, the passive market maker s bid must then be lowered when certain purchase limits are exceeded.

Underwriters or agents and their associates may be customers of, engage in transactions with or perform services for us in the ordinary course of business and any such relationships will be described in the applicable prospectus supplement.

Selling Stockholders

The selling stockholders, or their pledgees, donees, transferees, or any of their successors in interest selling shares received from a named selling stockholder as a gift, partnership distribution or other non-sale-related transfer after the date of this prospectus (all of whom may be selling stockholders) may sell the common stock offered by this prospectus from time to time on any stock exchange or automated interdealer quotation system on which the common stock is listed or quoted at the time of sale, in the over-the-counter market, in privately negotiated transactions or otherwise, at fixed prices that may be changed, at market prices prevailing at the time of sale, at prices related to prevailing market prices or at prices otherwise negotiated. The selling stockholders may sell the common stock by one or more of the following methods, without limitation:

Block trades in which the broker or dealer so engaged will attempt to sell the common stock as agent but may position and resell a portion of the block as principal to facilitate the transaction;

An exchange distribution in accordance with the rules of any stock exchange on which the common stock is listed;

Ordinary brokerage transactions and transactions in which the broker solicits purchases;

Privately negotiated transactions;

In connection with short sales of company shares;

Through the distribution of common stock by any selling stockholder to its partners, members or stockholders;

By pledge to secure debts of other obligations;

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In connection with the writing of non-traded and exchange-traded call options, in hedge transactions and in settlement of other transactions in standardized or over-the-counter options;

Purchases by a broker-dealer as principal and resale by the broker-dealer for its account; or

In a combination of any of the above.

These transactions may include crosses, which are transactions in which the same broker acts as an agent on both sides of the trade. The selling stockholders may also transfer the common stock by gift. We do not know of any arrangements by the selling stockholders for the sale of any of the common stock.

The selling stockholders may engage brokers and dealers, and any brokers or dealers may arrange for other brokers or dealers to participate in effecting sales of the common stock. These brokers or dealers may act as principals, or as an agent of a selling stockholder. Broker-dealers may agree with a selling stockholder to sell a specified number of the stocks at a stipulated price per share. If the broker-dealer is unable to sell common stock acting as agent for a selling stockholder, it may purchase as principal any unsold shares at the stipulated price. Broker-dealers who acquire common stock as principals may thereafter resell the shares from time to time in transactions in any stock exchange or automated interdealer quotation system on which the common stock is then listed, at prices and on terms then prevailing at the time of sale, at prices related to the then-current market price or in negotiated transactions. Broker-dealers may use block transactions and sales to and through broker-dealers, including transactions of the nature described above. The selling stockholders may also sell the common stock in accordance with Rule 144 or Rule 144A under the Securities Act, rather than pursuant to this prospectus. In order to comply with the securities laws of some states, if applicable, the shares of common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers.

From time to time, the selling stockholders may pledge, hypothecate or grant a security interest in some or all of the shares owned by them. The pledgees, secured parties or person to whom the shares have been hypothecated will, upon foreclosure in the event of default, be deemed to be selling stockholders. The number of a selling stockholder s shares offered under this prospectus will decrease as and when it takes such actions. The plan of distribution for that selling stockholder s shares will otherwise remain unchanged. In addition, a selling stockholder may, from time to time, sell the shares short, and, in those instances, this prospectus may be delivered in connection with the short sales and the shares offered under this prospectus may be used to cover short sales.

To the extent required under the Securities Act, the aggregate amount of selling stockholder s shares being offered and the terms of the offering, the names of any agents, brokers, dealers or underwriters, any applicable commission and other material facts with respect to a particular offer will be set forth in an accompanying prospectus supplement or a post-effective amendment to the registration statement of which this prospectus is a part, as appropriate. Any underwriters, dealers, brokers or agents participating in the distribution of the common stock may receive compensation in the form of underwriting discounts, concessions, commissions or fees from a selling stockholder and/or purchasers of selling stockholder s shares, for whom they may act (which compensation as to a particular broker-dealer might be less than or in excess of customary commissions). Neither we nor the selling stockholders can presently estimate the amount of any such compensation.

The selling stockholders and any underwriters, brokers, dealers or agents that participate in the distribution of the common stock may be deemed to be underwriters within the meaning of the Securities Act, and any discounts, concessions, commissions or fees received by them and any profit on the resale of the securities sold by them may be deemed to be underwriting discounts and commissions. If a selling stockholder is deemed to be an underwriter, the selling stockholder may be subject to certain statutory liabilities including, but not limited to Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Exchange Act. Selling stockholders who are deemed underwriters within the meaning of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act. The SEC staff is of a view that selling stockholders who are registered broker-dealers or affiliates of registered broker-dealers may be underwriters under the Securities Act. We will not pay any compensation or give any discounts or commissions to any underwriter in connection with the securities being offered by this

prospectus.

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A selling stockholder may enter into hedging transactions with broker-dealers and the broker-dealers may engage in short sales of the common stock in the course of hedging the positions they assume with that selling stockholder, including, without limitation, in connection with distributions of the common stock by those broker-dealers. A selling stockholder may enter into option or other transactions with broker-dealers, who may then resell or otherwise transfer those common stock. A selling stockholder may also loan or pledge the common stock offered hereby to a broker-dealer and the broker-dealer may sell the common stock offered by this prospectus so loaned or upon a default may sell or otherwise transfer the pledged common stock offered by this prospectus.

The selling stockholders and other persons participating in the sale or distribution of the common stock will be subject to applicable provisions of the Exchange Act, and the rules and regulations under the Exchange Act, including Regulation M. This regulation may limit the timing of purchases and sales of any of the common stock by the selling stockholders and any other person. The anti-manipulation rules under the Exchange Act may apply to sales of common stock in the market and to the activities of the selling stockholders and their respective affiliates. Regulation M may restrict the ability of any person engaged in the distribution of the common stock to engage in market-making activities with respect to the particular common stock being distributed for a period of up to five business days before the distribution. These restrictions may affect the marketability of the common stock and the ability of any person or entity to engage in market-making activities with respect to the common stock.

We have agreed to indemnify the selling stockholders and any brokers, dealers and agents who may be deemed to be underwriters, if any, of the common stock offered by this prospectus, against specified liabilities, including liabilities under the Securities Act. The selling stockholders have agreed to indemnify us against specified liabilities.

We have agreed with the selling stockholders to keep this registration statement effective until the earliest date on which (i) all of the shares of common stock have been disposed of pursuant to the prospectus and (ii) all of the shares of common stock are eligible for resale under Rule 144 under the Securities Act without restrictions as to volume.

We cannot assure you that the selling stockholders will sell all or any portion of the common stock offered by this prospectus. In addition, we cannot assure you that the selling stockholders will not transfer the shares of our common stock by other means not described in this prospectus.

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon by Heller Ehrman LLP of Menlo Park, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements and schedule included in our Annual Report on Form 10-K for the year ended December 31, 2004, and management s assessment of the effectiveness of our internal controls over financial reporting as of December 31, 2004, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and schedule and management s assessment are incorporated by reference in reliance on Ernst & Young LLP s reports, given on their authority as experts in accounting and auditing.

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WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission, or the SEC. You may read and copy these reports, proxy statements and other information at the SEC s public reference rooms at 450 Fifth Street, N.W., Washington, D.C., 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. Our SEC filings are also available at the SEC s web site at www.sec.gov and our website at www.durect.com. We have not incorporated by reference into this prospectus the information contained on our website and you should not consider it to be part of this prospectus. In addition, you can read and copy our SEC filings at the office of the National Association of Securities Dealers, Inc. at 1735 K Street, Washington, D.C. 20006.

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

- our annual report on Form 10-K for the fiscal year ended December 31, 2004, filed with the SEC on March 14, 2005;
- our quarterly report on Form 10-Q for the quarter ended March 31, 2005, filed with the SEC on May 6, 2005;
- our quarterly report on Form 10-Q for the quarter ended June 30, 2005, filed with the SEC on August 4, 2005, as amended by Amendment No. 1 to Form 10-Q filed with the SEC on August 9, 2005;
- our quarterly report on Form 10-Q for the quarter ended September 30, 2005, filed with the SEC on October 13, 2005;
- our definitive proxy statement dated April 28, 2005 for our annual stockholders meeting on June 22, 2005; and
- our current reports on Form 8-K, filed with the SEC on January 13, 2005, January 25, 2005, January 28, 2005, February 10, 2005, February 16, 2005; March 14, 2005, April 11, 2005, April 18, 2005, June 20, 2005, July 11, 2005, July 22, 2005, August 10, 2005 September 9, 2005, September 19, 2005 and September 21, 2005 (except for information concerning financial results contained in such current reports on Form 8-K);
- the description of our common stock in our Registration Statements on Form 8-A filed with the SEC on July 10, 2001, as amended by Amendment No. 1 to Form 8-A filed with the SEC on June 24, 2003.

All documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended after the date of this registration statement and prior to the effectiveness of this registration statement, shall be deemed to be incorporated by reference.

We will provide to you at no cost a copy of any and all of the information incorporated by reference into the registration statement of which this prospectus is a part. You may make a request for copies of this information in writing or by telephone. Requests should be directed to:

DURECT Corporation

Attention: Schond L. Greenway, Executive Director, Investor Relations and Strategic Planning

10240 Bubb Road

Cupertino, CA 95014

(408) 777-1417

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PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other expenses of issuance and distribution

The following table sets forth all expenses, other than the underwriting discounts and commissions, payable by the registrant in connection with the sale of the common stock being registered. All the amounts shown are estimates except for the registration fee.

Securities and Exchange Commission Registration Fee	$ 8,827.50
Nasdaq National Market Listing Fee	*
Legal Fees and Expenses	*
Accountants Fees and Expenses	*
Printing Expenses	*
Transfer Agent Fees and Expenses	*
Miscellaneous	*
Total	$ *

* To be filed by amendment

Item 15. Indemnification of Directors and Officers

Our Amended Bylaws provide generally for indemnification of our officers, directors, agents and employees to the extent authorized by the DGCL. Pursuant to Section 145 of the DGCL, a corporation generally has the power to indemnify its present and former directors, officers, employees and agents against expenses incurred by them in connection with any suit to which they are, or are threatened to be made, a party by reason of their serving in such positions so long as they acted in good faith and in a manner they reasonably believed to be in, or not opposed to, the best interests of a corporation, and with respect to any criminal action, they had no reasonable cause to believe their conduct was unlawful. With respect to suits by or in the right of a corporation, however, indemnification is not available if such person is adjudged to be liable for negligence or misconduct in the performance of his duty to the corporation unless the court determines that indemnification is appropriate. In addition, a corporation has the power to purchase and maintain insurance for such person. The statute also expressly provides that the power to indemnify that it authorizes is not exclusive of any rights granted under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise.

As permitted by Section 102 of the DGCL, our stockholders have approved and incorporated provisions into Article XIII of our Amended and Restated Certificate of Incorporation and Article VI of our Amended Bylaws eliminating a director s personal liability for monetary damages to us and our stockholders arising from a breach of a director s fiduciary duty, except for liability under Section 174 of the DGCL or liability for any breach of the director s duty of loyalty to us or its stockholders, for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law or for any transaction in which the director derived an improper personal benefit. DURECT has also entered into agreements with its directors and certain of its officers that will require DURECT, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors to the fullest extent not prohibited by law.

Under Section 145 of the DGCL, we have broad powers to indemnify our directors and officers against liabilities they may incur in such capacities, including liabilities under the Securities Act of 1933, as amended.

We have entered into indemnification agreements with each of our officers and directors in which we agree to indemnify and hold harmless the officer or director to the fullest extent permitted by applicable law in connection with any threatened, pending or completed action, suit or proceeding, or any inquiry or investigation not initiated by the officer or director, by reason of the fact that such person is or was a director, officer, employee, agent or fiduciary of ours, or is or was serving at our request as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise,

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against any and all expenses, judgments, penalties, fines and settlement amounts actually and reasonably incurred by such officer or director or on his or her behalf (including mandatory advancement of expenses), if such person acted in good faith and in a manner which such person believed to be or not opposed to our best interests. The indemnification agreements set forth procedures that apply in the event of a claim for indemnification thereunder.

We also maintain insurance to protect ourselves and our directors, officers, employees and agents against expenses, liabilities and losses incurred by such persons in connection with their service in the foregoing capacities.

Item 16. Exhibits and Financial Statement Schedules

(a) The following exhibits are filed herewith or incorporated herein by reference:

Exhibit Number	Description
1.1	Form of Underwriting Agreement *
3.1	Amended and Restated Certificate of Incorporation of the Company (1)
3.2	Amended and Restated Bylaws of the Company (1)
3.3	Certificate of Designation of Rights Preferences and Privileges of Series A Participating Preferred Stock
4.1	Form of Common Stock Certificate (1)
4.2	Preferred Shares Rights Agreement, dated as of July 6, 2001, between the Company and EquiServe Trust Company, N.A. including the Certificate of Designation, the form of the Rights Certificate and the Summary of Rights attached thereto as Exhibits A, B and C, respectively (2)
5.1	Opinion of Heller Ehrman LLP *
23.1	Consent of independent registered public accounting firm
23.2	Consent of Counsel (included in Exhibit 5.1)
24.1	Power of Attorney of certain directors and officers of DURECT Corporation (see page II-4 of this Form S-3)

* To be filed by amendment or by a Current Report on Form 8-K and incorporated herein by reference.

(1) Filed as an exhibit to our Registration Statement on Form S-1, as amended (File No. 333-35316), originally filed with the SEC on April 20, 2000, and incorporated herein by reference.

(2) Incorporated by reference to our Registration Statement on Form 8-A (File No. 000-31615) filed with the Securities and Exchange Commission on July 10, 2001.

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of

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prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment 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.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(b) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant s annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan s annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the Registration Statement 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.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered 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 of 1933 and will be governed by the final adjudication of such issue.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cupertino, State of California, on the 13th day of October, 2005.

DURECT Corporation.

By: /s/ JAMES E. BROWN
James E. Brown

President, Chief Executive Officer and a Director

POWER OF ATTORNEY

We, the undersigned officers and directors of DURECT Corporation, and each of us, do hereby constitute and appoint each and any of James E. Brown and Felix Theeuwes, our true and lawful attorney and agent, with full power of substitution and resubstitution, to do any and all acts and things in our name and behalf in any and all capacities and to execute any and all instruments for us in our names, in connection with this registration statement or any registration statement for the same offering that is to be effective upon filing under the Securities Act of 1933, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, including specifically, but without limitation, power and authority to sign for us or any of us in our names in the capacities indicated below, any and all amendments (including post-effective amendments) hereto or any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act; and we hereby ratify and confirm all that said attorney and agent, or his substitute, shall do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and as of the dates indicated.

Signature	Title	Date
/s/ JAMES E. BROWN **James E. Brown**	President, Chief Executive Officer and Director (Principal Executive Officer)	October 13, 2005
/s/ FELIX THEEUWES **Felix Theeuwes**	Chairman of the Board and Chief Scientific Officer	October 13, 2005
/s/ JIAN LI **Jian Li**	Vice President, Finance and Corporate Controller (Principal Financial and	October 13, 2005

	Accounting Officer)	
/s/ SIMON X. BENITO	Director	October 13, 2005
Simon X. Benito		
/s/ MICHAEL D. CASEY	Director	October 13, 2005
Michael D. Casey		
/s/ DAVID R. HOFFMANN	Director	October 13, 2005
David R. Hoffmann		
/s/ ARMAND P. NEUKERMANS	Director	October 13, 2005
Armand P. Neukermans		
/s/ JON S. SAXE	Director	October 13, 2005
Jon S. Saxe		

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