DURECT CORP
Form S-3/A
October 31, 2003
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As filed with the Securities and Exchange Commission on October 31, 2003

Registration No. 333-108398

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

AMENDMENT NO. 1

TO THE

FORM S-3

REGISTRATION STATEMENT

Under

THE SECURITIES ACT OF 1933

DURECT CORPORATION

(Exact name of registrant as specified in charter)

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

10240 Bubb Road

Cupertino, CA 95014

(408) 777-1417

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

James E. Brown

Chief Executive Officer

10240 Bubb Road

Cupertino, CA 95014

(408) 777-1417

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

COPIES TO:

Mark B. Weeks

Stephen B. Thau

Heller Ehrman White & McAuliffe LLP

2775 Sand Hill Road

Menlo Park, CA 94025

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. ¨

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

Subject To Completion, Dated October 31, 2003

PRELIMINARY PROSPECTUS

DURECT CORPORATION

$60,000,000 principal amount 6.25% Convertible Notes due 2008 and

Common Stock Issuable Upon Conversion of the Notes

The securities offered by this prospectus involve a high degree of risk. You should carefully consider the Risk Factors beginning on page 5 in determining whether to purchase the DURECT 6.25% Convertible Notes (the Notes) or the common stock.

This prospectus covers resales from time to time by selling securityholders of our 6.25% Convertible Notes due 2008 (the Notes) held by certain selling securityholders and 19,047,618 shares of our common stock issuable upon conversion of the Notes and held by certain securityholders, plus such indeterminate number of shares of common stock as may become issuable upon conversation of the Notes by reason of adjustment of the conversion price and as additional interest in certain circumstances. The Notes and the common stock may be sold from time to time by or on behalf of the selling securityholders named in this prospectus or in supplements to this prospectus.

The selling securityholders identified on page 39 of this prospectus are offering these Notes and shares of common stock. The selling securityholders may sell all or a portion of the Notes from time to time in market transactions, in negotiated transactions or otherwise, and at prices and at terms which will be determined by the then prevailing market price for the Notes or at negotiated prices directly or through a broker or brokers, who may act as agent or as principal or by a combination of such methods of sale. The selling securityholders may also sell all or a portion of the shares of common stock from time to time on the over-the-counter market in regular brokerage transactions, in transactions directly with market makers or in certain privately negotiated transactions. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution beginning on page 22. We will not receive any portion of the proceeds from the sale of these Notes or shares of common stock.

The selling securityholders may be deemed to be underwriters, as such term is defined in the Securities Act of 1933, as amended.

DURECT Corporation s common stock is quoted on the Nasdaq National Market under the symbol DRRX. The Notes are not listed on any national securities exchange or on the Nasdaq Stock Market.

On October 27, 2003, the last sale price of the common stock on the Nasdaq National Market was $2.25 per share.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of the securities or passed on the adequacy or accuracy of the disclosures in this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2003

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We have not authorized any dealer, salesperson or other person to give any information or represent anything not contained in this prospectus. You should not rely on any unauthorized information. This prospectus does not offer to sell or buy any shares in any jurisdiction in which it is unlawful. The information in this prospectus is current as of the date on the cover.

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SUMMARY

DURECT Corporation

DURECT Corporation is pioneering the treatment of chronic diseases and conditions by developing and commercializing pharmaceutical systems to deliver the right drug to the right site in the right amount at the right time. These capabilities can enable new drug therapies or optimize existing ones based on a broad range of compounds, including small molecule pharmaceuticals as well as biotechnology molecules such as proteins, peptides and genes. We focus on the development of pharmaceutical products for the treatment of chronic diseases including pain, cardiovascular diseases, central nervous system disorders and asthma and the development of pharmaceutical products incorporating biotechnology agents. We are developing these pharmaceutical system products based on our solid foundation of four proprietary drug delivery technology platforms. These platforms are the DUROS®, SABER, MICRODUR and DURIN technology platforms.

Our lead product in development is the CHRONOGESIC® (sufentanil) Pain Therapy System, an osmotic implant that continuously delivers sufentanil, an opioid medication, for three months. This product is designed to treat chronic pain and is based on the DUROS® implant technology for which we hold an exclusive license from ALZA Corporation, a subsidiary of Johnson & Johnson, to develop and commercialize products in selected fields. In 2001, we successfully completed a Phase II clinical trial, a pharmacokinetic trial and a pilot Phase III clinical trial for the CHRONOGESIC product. We also completed construction of a manufacturing facility designed to manufacture the CHRONOGESIC product for our Phase III clinical trials and to meet initial commercial demand for our product if approved by the FDA.

In 2002, we announced positive results from our pilot Phase III clinical trial, validated our aseptic manufacturing facility and used the facility to manufacture clinical supplies for our initial pivotal Phase III clinical trial. We also conducted ongoing animal toxicological studies and other development activities that are necessary to support regulatory approval of the product in the U.S. and abroad. We initiated our first pivotal Phase III clinical trial for the CHRONOGESIC product in June 2002.

In August 2002, the FDA requested that we delay enrolling new patients in our Phase III clinical trial initiated in June 2002 until the clinical trial protocol is revised and approved by the FDA to provide for additional patient monitoring and data collection. These requested protocol changes were not in response to any observed patient safety or adverse event. We subsequently discontinued all patients from the clinical trial at our discretion in September 2002, and the clinical trial is currently on temporary hold. We intend to revise the existing clinical trial protocol to provide additional monitoring measures and data collection requested by the FDA. Independently from the revisions to the protocol, we started to implement some necessary design and manufacturing enhancements to the CHRONOGESIC product in October 2002.

In November 2002, we entered into a development, commercialization and supply license agreement with Endo Pharmaceuticals Holdings Inc. (Endo) under which the companies will collaborate on the development and commercialization of our CHRONOGESIC product for the U.S. and Canada. Once a specified clinical trial for the CHRONOGESIC product is restarted, Endo will fund 50% of the ongoing development costs and will reimburse us for a portion of our prior development costs for the product upon the achievement of certain milestones. Milestone payments made by Endo under this agreement could total up to $52 million. In addition, under the agreement, Endo has licensed exclusive promotional rights to the CHRONOGESIC product in the U.S. and Canada. Endo will be responsible for marketing, sales and distribution, including providing specialty sales representatives dedicated to supplying technical and training support for CHRONOGESIC therapy and will pay for all product launch costs. We will be responsible for the manufacture of the CHRONOGESIC product. We will share profits from the commercialization of the product in the U.S. and Canada with Endo based on the financial performance of the CHRONOGESIC product. Based on our projected financial performance of the product in the U.S. and Canada, we anticipate that our share of such profits from commercialization of the product will be 50%.

In the first nine months of 2003, we continued to conduct in-vitro and animal studies, implement and evaluate design and manufacturing enhancements and revise clinical trial protocols for the CHRONOGESIC product. On October 16, 2003, we announced that we have received data from a preclinical animal test with our CHRONOGESIC (sufentanil) Pain Therapy Product which indicate that a small number of units (less than 2% in total) utilizing the new system design under evaluation by the Company experienced a premature shutdown (stop in delivery of drug). In parallel track with the CHRONOGESIC development program using the current system design, we have been exploring additional mechanisms to prevent any premature shutdown, and have already generated feasibility data relating to these mechanisms. We are currently investigating the impact of these new data on the timing of the development program, but we expect that this will delay the restart of the product s phase III clinical program previously anticipated to begin during the second half of 2003.

NOTE: CHRONOGESIC®, IntraEAR®, ALZET®, SABER , DURIN and MICRODUR are trademarks of DURECT Corporation. LACTEL® is a trademark of Birmingham Polymers, Inc., a wholly owned subsidiary of DURECT Corporation. DUROS® is a trademark of ALZA Corporation, a subsidiary of Johnson & Johnson. Other trademarks referred to belong to their respective owners.

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We also develop other pharmaceutical products using our SABER delivery system. The SABER delivery system is a patented, biodegradable controlled-release technology that can be formulated for parenteral, oral, dermal or other route of administration of active agents for human pharmaceutical and veterinary applications. In June 2003, we commenced a clinical study of our post-operative pain relief depot product, a sustained release injectible using the SABER delivery system and a local anesthetic. This product is designed to be administered around a surgical site after surgery for post-operative pain relief and is intended to provide local analgesia for up to three days, which we believe coincides with the greatest need for post surgical pain control in most patients. Bupivacaine, the active agent for the product, is currently FDA-approved for use in hospitals as a local anesthetic. One dose of our post-operative pain relief product is intended to provide up to 72 hours of regional pain relief. Currently, there are more than 20 million surgical procedures performed annually in the United States for which this product could be potentially utilized. Our initial human clinical study has been initiated in the normal, healthy volunteers in Europe. The objectives of the clinical study are to determine the safety and tolerability of the SABER delivery system and the SABER-bupivacaine combination and to determine the sensory effects of the SABER-bupivacaine combination administered subcutaneously.

During the first nine months of 2003, we also continued to make technical progress on our collaborative research and development projects with our strategic partners, such as Pain Therapeutics, Inc., BioPartners, GmbH, Voyager Pharmaceutical Corporation and others. Under these collaborative agreements, we perform research and development activities to develop products utilizing our drug delivery technologies and recognize collaborative research and development revenue on reimbursement payments of expenses and milestone payments from our partners. Depending on the agreement, we may also have royalty, distribution, or other rights once products are commercialized under the agreement. We intend to enter into additional collaborative partnering arrangements in the future.

We currently generate product revenues from the sale of:

ALZET® osmotic pumps for animal research use, and

LACTEL® biodegradable polymers through our wholly owned subsidiary, Birmingham Polymers, Inc. (BPI).

Because we consider our core business to be developing and commercializing pharmaceutical systems, we do not intend to significantly increase our investments in or efforts to sell or market any of our existing product lines. In addition, we may discontinue activities that have an immaterial impact on our business. However, we expect that we will continue to make efforts to increase our revenue related to collaborative research and development by entering into additional research and development agreements with third party partners to develop products based on our drug delivery technologies.

Since our inception in 1998, we have had a history of operating losses. At June 30, 2003, we had an accumulated deficit of $124.6 million and our net losses were $11.0 million and $19.7 million for the six months ended June 30, 2003 and 2002, respectively. These losses have resulted primarily from costs incurred to research and develop our products and to a lesser extent, from selling, general and administrative costs associated with our operations and product sales. We expect our research and development expenses to modestly increase in the future as we continue to expand our clinical trials and research and development activities. We anticipate that we will support our research and development activities within our existing corporate infrastructure, so we expect our general and administrative expenses to continue at current levels in the near future. We also expect to incur additional non-cash expenses relating to amortization of intangible assets and stock-based compensation. We do not anticipate revenues from our pharmaceutical systems, should they be approved, for at least several years. Therefore, we expect to incur continuing losses and negative cash flow from operations for the foreseeable future.

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Our principal executive offices are located at 10240 Bubb Road, Cupertino, CA 95014 and our telephone number is (408) 777-1417. As used in this prospectus, we, us, our and DURECT refer to DURECT Corporation, a Delaware corporation, and its wholly-owned subsidiary.

Terms of the Notes

This prospectus covers the resale of $60,000,000 aggregate principal amount of the Notes and 19,047,618 of our shares of common stock, plus an indeterminate number of additional shares of common stock that may be issued from time to time upon conversion of the Notes as a result of antidilution adjustments and as additional interest, in circumstances described in the prospectus.

We issued and sold $60,000,000 aggregate principal amount of the Notes on June 18, 2003, in a private offering to Morgan Stanley & Co. Incorporated (the Initial Purchaser). We were told by the Initial Purchaser that the Notes were resold in transactions which were exempt from the registration requirements of the Securities Act of 1933, as amended (the Securities Act) to persons reasonably believed by the Initial Purchaser to be qualified institutional buyers (as defined in Rule 144A under the Securities Act).

Shares of our common stock may be offered by the selling securityholders following the conversion of the Notes.

The following is a brief summary of the terms of the Notes. For a more complete description of the Notes, you should read the section entitled Description of the Notes beginning on page 23 of this prospectus.

Securities Offered	$60,000,000 principal amount of 6.25% Convertible Notes due 2008.
Maturity Date	June 15, 2008.
Interest	6.25% per annum on the principal amount, payable semi-annually in arrears in cash on June 15 and December 15 of each year, beginning December 15, 2003.
Conversion	You may convert the Notes into shares of our common stock at a conversion rate of 317.4603 shares per $1,000 principal amount of Notes, subject to adjustment, prior to the close of business on the final maturity date.
Redemption	We may not redeem any of the Notes at our option prior to their maturity date.
Designated Event	If a designated event (as described under Description of Notes Redemption at Option of the Holder) occurs prior to maturity, you may require us to purchase all or part of your Notes at a redemption price equal to 100% of their principal amount, plus accrued and unpaid interest.
Use of Proceeds	We will not receive any proceeds from the sale of the Notes of the shares of common stock offered by this prospectus.
Registration Rights	We entered into a registration rights agreement with the Initial Purchaser in which we agreed to file the shelf registration statement of which this prospectus is a part with the SEC covering the resale of

the Notes and the underlying common stock within 90 days after the closing date. We will use our best efforts to cause the shelf registration statement to be declared effective within 180 days of the date of filing and will use our best efforts to keep the shelf registration statement effective

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	until the date that there are no longer any registrable securities, as defined in Description of Notes Registration Rights of the Noteholders.
DTC Eligibility	The Notes were issued in book-entry form and are represented by one or more permanent certificates deposited with a custodian for and registered in the name of a nominee of The Depository Trust Company (DTC) in New York, New York. Beneficial interests in any such securities are shown on, and transfers are effected only through record maintained by DTC and its direct and indirect participants, and any such interest may not be exchanged for certificates securities. See Description of Notes Form, Denomination and Registration Global Note, Book-Entry Form.
Trading	The Notes are not currently listed and we do not intend to list the Notes on any national securities exchange. Although the Notes are currently eligible for trading in PORTAL, Notes resold pursuant to the registration statement of which this prospectus is a part will no longer be eligible for trading in PORTAL.
Absence of a Public Market	The Notes are securities for which there is currently no public market. An active or liquid market may not develop for the Notes. See Plan of Distribution.
NASDAQ National Market Symbol	DRRX.

RECENT DEVELOPMENTS

On June 18, 2003, we completed the private placement of the Notes more fully described in this prospectus. In connection with the private placement of the Notes, we entered into a Registration Rights Agreement more fully described in this prospectus, under which we are required to file the registration statement with the SEC, of which this prospectus is a part, for resale by September 16, 2003 (90 days after the issue date) and cause the registration statement to be declared effective by the SEC by December 15, 2003 (180 days after the issue date).

On August 15, 2003, we completed an acquisition of Absorbable Polymer Technologies, Inc. (APT) pursuant to an Agreement and Plan of Merger by and among the Company, Absorbable Polymer Technologies, Inc. and Birmingham Polymers, Inc. In connection with the acquisition, we issued an aggregate of 485,122 shares of our common stock and agreed to issue additional shares of our common stock or cash in connection with the first, second and third anniversaries of the closing of the merger.

On October 16, 2003, we announced that we have received data from a preclinical animal test with our CHRONOGESIC (sufentanil) Pain Therapy Product which indicate that a small number of units (less than 2% in total) utilizing the new system design under evaluation by the Company experienced a premature shutdown (stop in delivery of drug). In parallel track with the CHRONOGESIC development program using the current system design, we have been exploring additional mechanisms to prevent any premature shutdown, and have already generated feasibility data relating to these mechanisms. We are currently investigating the impact of these new data on the timing of the development program, but we expect that this will delay the restart of the product s phase III clinical program previously anticipated to begin during the second half of 2003.

RISK FACTORS

Prospective purchasers of the common stock offered by this prospectus should carefully consider the following Risk Factors in addition to the other information appearing in or incorporated by reference into this prospectus.

Factors that May Affect Future Results

In addition to the other information in this Registration Statement on Form S-3, the following factors should be considered carefully in evaluating our business and prospects:

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We have not completed development of any of our pharmaceutical systems, and we cannot be certain that our pharmaceutical systems will be able to be commercialized

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

selecting and developing drug delivery platform technology to deliver the proper dose of drug over the desired period of time;

selecting and developing catheter technology, if appropriate, to deliver the drug to a specific location within the body;

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; and

demonstrating the drug formulation will be stable for commercially reasonable time periods.

The time frame necessary to achieve these developmental milestones for any individual product is long and uncertain, and we may not successfully complete these milestones for any of our products in development. We have not yet completed development of any pharmaceutical systems, and DURECT has limited experience in developing such products. We have not finalized the system design of our lead product, CHRONOGESIC, and must still complete necessary design changes and enhancements to the product prior to continuing clinical trials for the product. In addition, even after we complete the final design of the product, the product 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 have not selected the drug dosages nor finalized the system design of any other pharmaceutical system including those based on our SABER, DURIN and MICRODUR delivery platforms, and we may not be able to complete the design of any additional products. We are continuing testing and development of our products and may explore possible design changes to address issues of safety, manufacturing efficiency and performance. We may not be able to complete development of any products that will be safe and effective and that will have a commercially reasonable treatment and storage period. If we are unable to complete development of our CHRONOGESIC product or other products, we will not be able to earn revenue from them, which would materially harm our business.

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

Before we can obtain government approval to sell any of our pharmaceutical systems, we 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. As of September 30, 2003, for our lead product, CHRONOGESIC, we have completed an initial Phase I clinical trial using an external pump to test the safety of continuous chronic infusion of sufentanil, a Phase II clinical trial, a pilot Phase III clinical trial and a pharmacokinetic trial. We are currently in the preclinical or research stages with respect to all our other products 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 CHRONOGESIC product. These studies include laboratory performance studies and safety testing, pivotal Phase III and other clinical trials and animal toxicological studies necessary to support regulatory approval of the product 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 of our product. In addition, we plan to conduct extensive and costly clinical trials and animal studies for our other potential products. We may not be permitted to begin or continue our planned clinical trials for our potential products or, if our trials are permitted, our potential products 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 products, including CHRONOGESIC, which we have not planned or anticipated that could delay commercialization of such products and harm our business and financial conditions.

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We initiated our first pivotal Phase III clinical trial for the CHRONOGESIC product in June 2002. In August 2002, the FDA requested that we delay enrolling new patients in our Phase III clinical study initiated in June 2002 until the clinical trial protocol is revised by us and approved by the FDA to provide for additional patient monitoring and data collection. These requested protocol changes were not in response to any observed patient safety or adverse event. We subsequently discontinued all patients from the clinical trial at our discretion in September 2002, and the clinical trial is currently on temporary hold. We intend to revise the existing clinical trial protocol to provide additional monitoring measures and data collection requested by the FDA. Independently from the revisions to the protocol, we are implementing some necessary design and manufacturing enhancements to the CHRONOGESIC product. On October 16, 2003, we announced that we have received data from a preclinical animal test with our CHRONOGESIC (sufentanil) Pain Therapy Product which indicate that a small number of units (less than 2% in total) utilizing the new system design under evaluation by the Company experienced a premature shutdown (stop in delivery of drug). In parallel track with the CHRONOGESIC development program using the current system design, we have been exploring additional mechanisms to prevent any premature shutdown, and have already generated feasibility data relating to these mechanisms. We are currently investigating the impact of these new data on the timing of the development program, but we expect that this will delay the restart of the product s phase III clinical program previously anticipated to begin during the second half of 2003.

We expect our pivotal Phase III trials for CHRONOGESIC collectively to include over 900 patients. 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 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 enroll the number of patients we expect in the time frame we expect, our clinical trials may not provide the data necessary to support regulatory approval for the products for which they were conducted. Additionally, we 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 may fail to complete and submit a new drug application as scheduled. Even if we are able to submit a new drug application as scheduled, the Food and Drug Administration may not clear our 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 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 under development could delay or prevent regulatory clearance of the potential product, resulting in delays to the commercialization of our products, and could materially harm our business. Our clinical trials may not demonstrate the sufficient levels of safety and efficacy necessary to obtain the requisite regulatory approvals for our products, and thus our products may not be approved for marketing.

Failure to obtain product approvals or comply with ongoing governmental regulations could delay or limit introduction of our new products and result in failure to achieve anticipated revenues

The manufacture and marketing of our products 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 must obtain clearance or approval from applicable regulatory authorities before we can market or sell our products in the U.S. or abroad. Before receiving approval or clearance to market a product in the U.S. or in any other country, we will have to demonstrate to the satisfaction of applicable regulatory agencies that the product is safe and effective on the patient population and for the diseases that will be treated. 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 may encounter delays or rejections based

upon administrative action or interpretations of current rules and regulations. For example, in August 2002, the FDA requested that we delay enrolling new patients in our Phase III clinical study for the CHRONOGESIC product initiated in June 2002 until the clinical trial protocol is amended and approved by the FDA to provide for additional patient monitoring and data collection. We will not be able to enroll patients in our clinical trials for the CHRONOGESIC product until the FDA approves our amendments to the existing clinical trial protocol to provide additional monitoring measures and data collection requested by the FDA. We may not be able to timely reach agreement with the FDA on such protocol amendments or on the required data we must collect to continue with our clinical trials or eventually commercialize our product.

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We 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 may encounter similar delays in foreign countries. Sales of our products outside the U.S. 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 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 fail to obtain timely clearance or approval for our products, we will not be able to market and sell our products, which will limit our ability to generate revenue.

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 following events, if they were to occur, could delay or preclude us from further developing, marketing or realizing full commercial use of our products, 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 products under development; or
- identification of serious and unanticipated adverse side effects in our products 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 products. 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 do not achieve compliance for the products we 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 products.

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 June 30, 2003, had an accumulated deficit of approximately $124.6 million. We expect to continue to incur significant operating losses 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 products, obtain the required regulatory clearances and manufacture and market our proposed products. 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. All revenues to date are from the sale of products we acquired in October 1999 in connection with the acquisition of substantially all of the assets of IntraEAR, Inc., the ALZET product we acquired in April 2000 from ALZA and the sale of biodegradable polymers through our wholly owned subsidiary, BPI, and collaborative and contract research and development revenues from our collaborations with third parties and those of our former wholly owned subsidiary, Southern BioSystems, Inc. (SBS), now merged into DURECT. We do not expect the product revenues to increase significantly in future periods. We do not anticipate commercialization and marketing of our products 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.

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Our near-term revenues depend on collaborations with other companies. If we are unable to meet milestones under these agreements or enter into additional collaboration agreements, 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 attain milestones set forth in any specific agreement, which could cause our revenues to fluctuate or be less than anticipated. In general, our collaboration agreements may be terminated by the other party upon specified conditions including if we breach the terms of the agreement. If the agreements are terminated, our revenues will be reduced and our products related to those agreements may not be commercialized. We have limited or no control over the resources that any collaborator may devote to our products. 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 commercialize our products based on such collaborations.

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 products. 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 products. 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 products;

costs involved in establishing manufacturing capabilities for clinical and commercial quantities of our products;

competing technological and market developments;

market acceptance of our products; and

costs for recruiting and retaining employees and consultants.

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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 collaborative partners or other sources, we may have to relinquish rights to some of our technologies, product candidates or products under development that we would otherwise seek to 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.

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 $60.0 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. See Liquidity and Capital Resources . 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 not be able to manufacture sufficient quantities of our products to support our clinical and commercial requirements at an acceptable cost, and we have limited manufacturing experience

We must manufacture our products in clinical and commercial quantities, either directly or through third parties, in compliance with regulatory requirements and at an acceptable cost. The manufacture of our DUROS-based pharmaceutical systems is a complex process. Although we have completed development of an initial manufacturing process for our CHRONOGESIC product, we are currently pursuing necessary enhancements of such manufacturing process to satisfy regulatory requirements, improve product performance and quality, increase efficiencies and lower cost. If we fail to timely complete such necessary manufacturing process enhancements, we will not be able to timely produce product for our clinical trials and commercialization of our CHRONOGESIC product. In the future, we will continue to consider ways to optimize our manufacturing process and to explore possible changes to improve product performance and quality, increase efficiencies and lower costs. We have not yet completed development of the manufacturing process for any products other than CHRONOGESIC. If we fail to develop manufacturing processes to permit us to manufacture a product at an acceptable cost, then we may not be able to commercialize that product.

We completed construction of a manufacturing facility for our DUROS-based pharmaceutical systems in May 2001 in accordance with our initial plans, and we expect that this facility will be capable of manufacturing supplies for our Phase III and other clinical trials required for regulatory approval and commercial launch of our CHRONOGESIC product and for our other DUROS-based products on a pilot scale. As of September 30, 2003, we have completed validating and qualifying our manufacturing facility from which we will manufacture supplies of the CHRONOGESIC product for our Phase III and other clinical trials once all necessary product design and manufacturing process enhancements have been finalized and implemented.

In order to manufacture clinical and commercial supplies of our pharmaceutical systems, we must attain and maintain compliance with applicable federal, state and foreign regulatory standards relating to manufacture of pharmaceutical products which are rigorous, complex and subject to varying interpretations. Furthermore, our new facility will be subject to government audits to determine compliance with good manufacturing practices regulations, and we may be unable to pass inspection with the applicable regulatory agencies or may be asked to undertake corrective measures which may be costly and cause delay.

If we are unable to manufacture product in a timely manner or at an acceptable cost, quality or performance level, and attain and maintain compliance with applicable regulations, we could experience a delay in our clinical trials and the commercial sale of our DUROS-based pharmaceutical systems. 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 our clinical trials and commercial launch. We may also choose to subcontract with third party contractors to perform manufacturing steps of 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 products. 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 products to third parties which have not been approved by ALZA. If we cannot manufacture product in time to meet our clinical or commercial requirements or at an acceptable cost, our operating results will be harmed.

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In April 2000, we acquired the ALZET product and related assets from ALZA. We manufacture subassemblies of the ALZET product at our Vacaville facility. We currently rely on ALZA to perform the coating process for the manufacture of the ALZET product, but we will be required to perform this process ourselves starting April 2004 or sooner. We have limited experience manufacturing this product, and we may not be able to successfully or consistently manufacture this product at an acceptable cost, if at all.

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

In April 1998, we entered into a development and commercialization agreement with ALZA Corporation, which was amended and restated in April 1999, April 2000 and October 2002. ALZA was acquired by Johnson & Johnson in June 2001 and has since operated as a wholly owned subsidiary. 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 products using DUROS technology in such field. In order to maintain commercialization rights for our products on a worldwide basis, we must diligently develop our products, procure required regulatory approvals and commercialize the products 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 U.S. 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.

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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.

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 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 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. For example, in October 1999, we acquired substantially all of the assets of IntraEAR, Inc., in April 2000 we acquired the ALZET product and related assets from ALZA, in April 2001, we completed the acquisition of SBS and in August 2003, we acquired APT. These and our 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.

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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.

Our limited operating history makes evaluating our stock difficult

Investors can only evaluate our business based on a limited operating history. We were incorporated in February 1998 and have engaged primarily in research and development, licensing technology, raising capital and recruiting scientific and management personnel. This short history may not be adequate to enable investors to fully assess our ability to successfully develop our products, achieve market acceptance of our products 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 at an early stage of development, 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 products, 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 products and to fund operating losses to be incurred in the next several years.

Acceptance of our products 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 CHRONOGESIC product. Even if approved for marketing, our products 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.

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.

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Our ability to commercialize our products successfully will depend in part on the extent to which appropriate reimbursement levels for the cost of our products 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.

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 products. 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.

We do not own the trademark DUROS and any competitive advantage we derive from the name may be impaired by third-party use

ALZA owns the trademark DUROS. Because ALZA is also developing and marketing DUROS-based systems, and may license third parties to do so, there may be confusion in the market between ALZA, its potential licensees and us, and this confusion could impair the competitive advantage, if any, we derive from use of the DUROS name. In addition, any actions taken by ALZA or its potential licensees that negatively impact the trademark DUROS could negatively impact our reputation and result in reduced sales of our DUROS-based pharmaceutical systems.

We may be sued by third parties which claim that our products 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 products 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 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. In addition, 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 products 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 products, which would be costly and time-consuming.

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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, 2003, we held 16 issued U.S. patents and 6 issued foreign patents. In addition, we have 36 pending U.S. patent applications and have filed 34 patent applications under the Patent Cooperation Treaty, from which 69 national phase applications are currently pending in Europe, Australia, Japan, Canada, Mexico, New Zealand, Brazil 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 rely heavily on third parties to support development, clinical testing and manufacturing of our products

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 perform blood plasma assays in connection with our clinical trials for CHRONOGESIC, to perform quality control services related to components of our DUROS-based pharmaceutical systems, and to supply us with molded rubber components of our DUROS-based pharmaceutical systems. In the past, we relied on Chesapeake Biological Labs, Inc. to perform the final manufacturing steps of our CHRONOGESIC product, and we may choose to rely on a third party manufacturer again. See We may not be able to manufacture sufficient quantities of our products 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 products, increase our expenses and materially harm our business, financial condition and results of operations.

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Key components of our DUROS-based 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 DUROS-based pharmaceutical systems 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 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 a supply agreement with Mallinckrodt, Inc. for our sufentanil requirements for our CHRONOGESIC product, which expires in September 2004. Additionally, we have a supply agreement with a third party vendor to supply us with titanium components of our DUROS-based pharmaceutical systems until April 2004. Other than these agreements, we do not have long-term agreements with any of our suppliers, and therefore the supply of a particular component could be terminated at any time without penalty to the supplier. Any interruption in the supply of single source components could cause us to seek alternative sources of supply or manufacture these components internally. 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. This could delay our ability to complete clinical trials and obtain approval for commercialization and marketing of our products, causing us to lose sales, incur additional costs and delay new product introductions and could harm our reputation.

We will not control sales and distribution for our pharmaceutical systems

We recently entered into an agreement with Endo Pharmaceuticals Inc. related to the promotion and distribution of our CHRONOGESIC product in the U.S. and Canada once it is approved for commercialization. In addition, we have entered into several agreements with third party companies under which we will collaborate with such companies to develop select pharmaceutical system products and such third parties will have the right to promote and distribute the resulting developed products subject to payments to us in the form of product royalties and other payments. These agreements make us dependent on third parties to sell and distribute our pharmaceutical systems. These third parties may have similar or more established relationships with our competitors, which may reduce their interest in selling our products. Other than these agreements with third party companies, we have yet to establish marketing, sales or distribution capabilities for our pharmaceutical system products.

We 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 may be unable to establish a sufficient sales and marketing organization on a timely basis, if at all. We 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; or

offer, design, manufacture or promote competing product lines.

If we fail to develop sales, marketing and distribution channels, we would experience delays in product sales and incur increased costs, which would harm our financial results.

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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 products involve an inherent risk that product liability claims will be asserted against us. Although we are insured against such risks up to a $10.0 million annual aggregate limit in connection with clinical trials and commercial sales of our products, 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 products, 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 products.

If we 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.

Some of our products 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 products 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 CHRONOGESIC, spinal opioid and oral opiate products under development contain opioids which are classified as Schedule II controlled substances under the regulations of the U.S. Drug Enforcement Agency. For our products 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 products containing controlled substances and subject us to enforcement action. In addition, because of their restrictive nature, these regulations could limit our commercialization of our products 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.

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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 initial review during the second quarter of 2002. We concluded that our goodwill was fairly stated as of January 1, 2002 and no accounting change adjustment was required. We performed the annual assessment in the fourth quarter of 2002 and determined that goodwill was not impaired. 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.

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 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, James E. Brown, our President and Chief Executive Officer and Thomas A. Schreck, our Chief Financial Officer. Although we have obtained key man life insurance policies for each of Messrs. Theeuwes, Brown and Schreck 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.

The market for our products 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 products 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.

We are a new enterprise and are engaged in the development of novel therapeutic technologies. As a result, 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 products. Our competitors may develop products that are safer, more effective or less costly than our products and, therefore, present a serious competitive threat to our product offerings.

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The widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our products even if commercialized. Chronic pain can also be treated by oral medication, transdermal drug delivery systems, such as drug patches, or with other implantable drug delivery devices. 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 products to receive widespread acceptance if commercialized.

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 products, 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 through our subsidiary Birmingham Polymers, Inc. 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.

Our stock price may fluctuate, and your investment in the Notes or our common stock issuable upon conversion of the Notes could decline in value

The average daily trading volume of our common stock for the three months ending September 30, 2003, was 399,363 shares. The limited trading volume of our stock may contribute to its volatility, and an active trading market in our stock might not develop or continue. In accordance with our Common Stock Purchase Agreement with Endo Pharmaceuticals Inc. (Endo), we filed a registration statement on Form S-3 with the SEC on August 29, 2003 to register 1,533,742 shares of our common stock issued to Endo for resale. The registration statement was declared effective by the SEC on September 26, 2003. Pursuant to a Registration Rights Agreement with the initial purchaser, we have agreed to file the shelf registration statement of which this prospectus is a part with the SEC covering the resale of the Notes and our common stock issuable upon conversion of the Notes. Once registered, such shares of common stock become tradable without limitation. If substantial amounts of our common stock 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 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. In addition, because the Notes are convertible into shares of our common stock, volatility or depressed prices for our common stock could have a similar effect on the trading price of the Notes.

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The Notes are unsecured and, therefore, are effectively subordinated to any of our secured debt and are effectively subordinated to all liabilities of our subsidiaries

The Notes are not secured by any of our assets or those of our subsidiaries. As a result, the Notes are effectively subordinated to any secured debt we currently have, or may incur. In any liquidation, dissolution, bankruptcy or other similar proceeding, the holders of our secured debt may assert rights against the secured assets in order to receive full payment of their debt before the assets may be used to pay the holders of the Notes. In addition, as debt of DURECT, the Notes are effectively subordinated to all debt and other liabilities, including trade payables, of our subsidiaries.

We may not have the ability to raise the funds necessary to finance the designated event redemption option

If a designated event, as described under the heading Description of the Notes Redemption at the Option of the Holder, occurs prior to maturity, we may be required to redeem all of part of the Notes. 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.

No public market exists for the Notes, and the resale of the Notes is subject to significant restrictions as well as uncertainties regarding the existence of any trading market for the Notes

Until the registration statement of which this prospectus is a part is declared effective, the Notes and the shares of common stock issuable upon conversion of the Notes may only be offered or sold if:

- an applicable exemption from the registration requirements of the Securities Act and applicable state laws applies to the circumstances of the sale, or
- a registration statement covering the resale of these securities is filed and declared effective.

Although the Notes are currently traded on PORTAL, the Notes resold pursuant to the registration statement of which this prospectus is a part will no longer be eligible for trading on PORTAL. There can be no assurance as to: (1) the liquidity of any market for the Notes, (2) the ability of the holders to sell their Notes or (3) the prices at which holders of the Notes would be able to sell their Notes. The Notes could trade at prices higher or lower than their initial purchase prices depending on many factors, including, among other things, prevailing interest rates, our operating results, the price of our common stock and the market for similar securities. Historically, the market for convertible debt has been subject to disruptions that have caused volatility in prices. It is possible that the market for the Notes will be subject to disruptions which may have a negative effect on the holders of the Notes, regardless of our prospects or financial performance.

We do not intend to apply for listing of the Notes on any securities exchange of for quotation on the Nasdaq National Market.

The redemption rights in the Notes triggered by a fundamental change could discourage a potential acquirer

The redemption rights in the Notes triggered by a fundamental change, as described under the heading Description of the Notes Redemption at the Option of the Holder, could 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. Our obligation to offer to redeem the Notes upon a fundamental change would not necessarily afford you protection in the event of a highly leveraged transaction, reorganization, merger or similar transaction involving us.

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

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

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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 by-laws;
- 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.

USE OF PROCEEDS

The proceeds from the sale of the Notes and the common stock offered by this prospectus are solely for the account of the selling securityholders. We will not receive any proceeds from the sale of the Notes or the common stock offered by this prospectus.

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of earnings to fixed charges for each of the periods indicated (in thousands):

Six Months Ended June 30,	Year Ended December 31,				Period from inception (February 6, 1998) to December 31,
2003	2002	2001	2000	1999	1998
$	$	$	$	$	$

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For purposes of computing the ratio of earnings to fixed charges, earnings consist of net loss plus fixed charges. Fixed charges consist of interest charges, amortization of debt expense and discount or premium related to indebtedness, whether expensed or capitalized, and that portion of rental payments under operating leases we believe to be representative of interest. Earnings were insufficient to cover fixed charges for these periods. The amount of the coverage deficiency was $1,279, $7,947, $18,485, $43,803 and $35,782 for the period from inception (February 6, 1998) to December 31, 1998, the years ended December 31, 1999, 2000, 2001 and 2002, respectively, and $10,147 for the six months ended June 30, 2003.

PLAN OF DISTRIBUTION

We are registering the resale of the Notes and the shares of common stock issuable upon conversion of the Notes on behalf of the selling securityholders. We are required to use our best efforts keep this registration statement on Form S-3 effective until the date that there are no longer any registrable securities. All costs, expenses and fees in connection with the registration of the shares offered by this prospectus will be borne by us. Brokerage commissions and similar selling expenses, if any, attributable to the sale of the Notes or the shares of common stock will be borne by the selling securityholders.

Sales of Notes and shares of common stock may be effected by selling securityholders from time to time in one or more of the following types of transactions (which may include block transactions):

- on any national securities exchange or quotation service on which the Notes or shares of common stock may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions otherwise than on such exchanges or services or in the over-the-counter market;
- through the writing of options, whether the options are listed on an option exchange or otherwise; or
- through the settlement of short sales.

In addition, any Notes or shares of common stock that qualify for resale pursuant to Rule 144 or Rule 144A of the Securities Act may be sold under Rule 144 or Rule 144A of the Securities Act rather than pursuant to this prospectus.

The selling securityholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. The selling securityholders may effect such transactions by selling shares directly to purchasers or to or through broker-dealers, which may act as agents or principals. Such broker-dealers may receive compensation in the form of discounts, concessions, or commissions from the selling securityholders and/or the purchasers of shares for whom such broker-dealers may act as agents or to whom they sell as principal, or both (which compensation as to a particular broker-dealer might be in excess of customary commissions). In effecting sales, broker-dealers or agents engaged by the selling securityholders may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the selling securityholders in amounts to be negotiated immediately prior to the sale.

The selling securityholders and any broker-dealers that act in connection with the sale of the common stock may be deemed to be underwriters within the meaning of Section 2(11) of the Securities Act of 1933, and any commission received by them and any profit on the resale of the shares of common stock as principal might be deemed to be underwriting discounts and commissions under the Securities Act of 1933. The selling securityholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares against some liabilities, including liabilities arising under the Securities Act of 1933. Liabilities under the federal securities laws cannot be waived.

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The selling securityholders will be subject to prospectus delivery requirements under the Securities Act of 1933. In the event of a distribution of shares by a selling stockholder, the selling stockholder, any selling broker or dealer and any affiliated purchasers may be subject to Regulation M under the Securities Exchange Act of 1934, which would generally prohibit these persons from bidding for or purchasing any security that is the subject of the distribution until his or her participation in that distribution is completed. In addition, Regulation M generally prohibits any stabilizing bid or stabilizing purchase for the purpose of pegging, fixing or stabilizing the price of common stock in connection with this offering.

If we are notified by a selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, a supplement to this prospectus will be filed, if required, pursuant to Rule 424(b) under the Act, disclosing (i) the name of each such selling stockholder and of the participating broker-dealer(s), (ii) the number of shares involved, (iii) the price at which such shares were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus and (vi) other facts material to the transaction. Unless otherwise permitted by law, if the Notes or shares of common stock are to be sold be pledgees, donees or transferees of, or other successors in interest to the selling securityholders, then we must distribute a prospectus supplement and/or file an amendment to this registration statement under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling securityholders to include the pledgee, transferee or other successors in interest as selling securityholders under this prospectus

DESCRIPTION OF THE NOTES

The Notes were issued under an indenture dated as of June 18, 2003, between DURECT, as issuer, and The Bank of New York, as trustee. The Notes and the shares issuable upon conversion of the Notes are covered by a registration rights agreement. See Where You Can Find More Information for information on how to obtain a copy of the indenture and the registration rights agreement

The following description is a summary of the material provisions of the Notes, the indenture and the registration rights agreement. It does not purport to be complete. This summary is subject to and is qualified by reference to all the provisions of the indenture, including the definitions of certain terms used in the indenture, and to all provisions of the registration rights agreement. Wherever particular provisions or defined terms of the indenture or form of note are referred to, these provisions or defined terms are incorporated in this prospectus by reference. We urge you to read the indenture because it, and not this description, defines your rights as a holder of the Notes.

As used in this Description of the Notes section, references to DURECT, we, our or us refer solely to DURECT Corporation and not to our subsidiaries, unless the context otherwise requires.

General

The Notes are senior unsecured indebtedness of DURECT and rank on a parity with all of our other existing and future senior unsecured debt and prior to all of our subordinated debt. The Notes are convertible into common stock as described under Conversion of Notes.

The Notes are limited to $60,000,000 aggregate principal amount. The Notes are issued only in denominations of $1,000 and multiples of $1,000. The Notes will mature on June 15, 2008 unless earlier converted or redeemed.

Neither we nor any of our subsidiaries are subject to any financial covenants under the indenture. In addition, neither we nor any of our subsidiaries are restricted under the indenture from paying dividends, incurring debt, or issuing or repurchasing our securities.

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You are not afforded protection under the indenture in the event of a highly leveraged transaction or a change in control of DURECT except to the extent described below under Redemption at Option of the Holder.

The Notes bear interest at a rate of 6.25% per annum. Interest is calculated on the basis of a 360-day year consisting of twelve 30-day months and accrues from June 18, 2003, or from the most recent date to which interest has been paid or duly provided for. We will pay interest on June 15 and December 15 of each year, beginning December 15, 2003, to record holders at the close of business on the preceding June 1 and December 1, as the case may be, except interest payable upon redemption will be paid to the person to whom principal is payable, unless the redemption date is an interest payment date.

We will maintain an office in the Borough of Manhattan, The City of New York, where we will pay the principal and premium, if any, on the Notes and you may present the Notes for conversion, registration of transfer or exchange for other denominations, which shall initially be an office or agency of the trustee. This office is initially the office or agency of the trustee in the City of New York. We may pay interest by check mailed to your address as it appears in the note register, provided that if you are a holder with an aggregate principal amount in excess of $2.0 million, you shall be paid, at your written election, by wire transfer in immediately available funds.

However, payments to The Depository Trust Company, New York, New York, which we refer to as DTC, will be made by wire transfer of immediately available funds to the account of DTC or its nominee.

Conversion of Notes

You may convert any of your Notes, in whole or in part, into common stock prior to the close of business on the final maturity date of the Notes, subject to prior redemption of the Notes.

The number of shares of common stock you will receive upon conversion of your Notes will be determined by multiplying the number of $1,000 principal amount Notes you convert by the conversion rate on the date of conversion. You may convert your Notes in part so long as such part is $1,000 principal amount or an integral multiple of $1,000.

If you have submitted your Notes for redemption upon a designated event, you may convert your Notes only if you withdraw your redemption election. Upon conversion of Notes, a holder will not receive any cash payment of interest (unless such conversion occurs between a regular record date and the interest payment date to which it relates). Our delivery to the holder of the full number of shares of our common stock into which the note is convertible, together with any cash payment for such holder s fractional shares, or cash or a combination of cash and shares of our common stock in lieu thereof, will be deemed to satisfy our obligation to pay:

the principal amount of the note; and

accrued but unpaid interest attributable to the period from the most recent interest payment date to the conversion date.

As a result, accrued but unpaid interest to the conversion date is deemed to be paid in full rather than cancelled, extinguished or forfeited.

Notwithstanding the preceding paragraph, if Notes are converted after a record date but prior to the next succeeding interest payment date, holders of such Notes at the close of business on the record date will receive the interest payable on such Notes on the corresponding interest payment date notwithstanding the conversion. Such Notes, upon surrender for conversion, must be accompanied by funds equal to the amount of interest payable on the Notes so converted; provided that no such payment need be made if (1) we have specified a purchase date following a designated event that is during such period or (2) only to the extent of overdue interest, any overdue interest exists at the time of conversion with respect to such note.

The initial conversion rate for the Notes is 317.4603 shares of common stock per $1,000 principal amount of Notes, subject to adjustment as described below. We will not issue fractional shares of common stock upon conversion of Notes. Instead, we will pay cash equal to the closing price of the common stock on the trading day prior to the conversion date. Except as described below, you will not receive any accrued interest or dividends upon conversion.

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To convert your Note into common stock you must:

- complete and manually sign the conversion notice on the back of the Note or facsimile of the conversion notice and deliver this notice to the conversion agent;
- surrender the Note to the conversion agent;
- if required, furnish appropriate endorsements and transfer documents;
- if required, pay all transfer or similar taxes; and
- if required, pay funds equal to interest payable on the next interest payment date.

The date you comply with these requirements is the conversion date under the indenture.

We will adjust the conversion rate if any of the following events occurs:

(1) we issue common stock as a dividend or distribution on our common stock;

(2) we issue to all holders of common stock certain rights or warrants to purchase our common stock;

(3) we subdivide or combine our common stock;

(4) we distribute to all holders of our common stock shares of our capital stock, evidences of indebtedness or assets, including securities but excluding:

- rights or warrants specified above;
- dividends or distributions specified above; and
- cash distributions.

If we distribute capital stock of, or similar equity interests in, a subsidiary or other business unit of ours, the conversion rate will be adjusted based on the market value of the securities so distributed relative to the market value of our common stock, in each case based on the average closing sales prices of those securities for the 10 trading days commencing on and including the fifth trading day after the date on which ex-dividend trading commences for such distribution on the NASDAQ National Market or such other national or regional exchange or market on which the securities are then listed or quoted.

(5) we distribute cash, excluding any dividend or distribution in connection with our liquidation, dissolution or winding up or any quarterly cash dividend on our common stock to the extent that the aggregate cash dividend per share of common stock in any quarter does not exceed the greater of:

the amount per share of common stock of the next preceding quarterly cash dividend on the common stock to the extent that the preceding quarterly dividend did not require an adjustment of the conversion rate pursuant to this clause, as adjusted to reflect subdivisions or combinations of the common stock; and

1.25% of the average closing sale prices of the common stock during the ten trading days immediately prior to the declaration date of the dividend, calculated at the time of the declaration of each distribution during such quarter.

If an adjustment is required to be made under this clause as a result of a distribution that is a quarterly dividend, the adjustment would be based upon the amount by which the distribution exceeds the amount of the quarterly cash dividend permitted to be excluded pursuant to this clause. If an adjustment is required to be made under this clause as a result of a distribution that is not a quarterly dividend, the adjustment would be based upon the full amount of the distribution;

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(6) we or one of our subsidiaries makes a payment in respect of a tender offer or exchange offer for our common stock to the extent that the cash and value of any other consideration included in the payment per share of common stock exceeds the current market price per share of common stock on the trading day next succeeding the last date on which tenders or exchanges may be made pursuant to such tender or exchange offer; and

(7) someone other than us or one of our subsidiaries makes a payment in respect of a tender offer or exchange offer in which, as of the closing date of the offer, our board of directors is not recommending rejection of the offer. The adjustment referred to in this clause will only be made if:

the tender offer or exchange offer is for an amount that increases the offeror s ownership of common stock to more than 25% of the total shares of common stock outstanding; and

the cash and value of any other consideration included in the payment per share of common stock exceeds the closing sale price per share of common stock on the trading day next succeeding the last date on which tenders or exchanges may be made pursuant to the tender or exchange offer.

However, the adjustment referred to in this clause will generally not be made if as of the closing of the offer, the offering documents disclose a plan or an intention to cause us to engage in a consolidation or merger or a sale of all or substantially all of our assets.

To the extent that we have a rights plan in effect upon conversion of the Notes into common stock, you will receive, in addition to the common stock, the rights under the rights plan unless the rights have separated from the common stock at the time of conversion, in which case the conversion rate will be adjusted as if we distributed to all holders of our common stock, shares of our capital stock, evidences of indebtedness or assets as described above, subject to readjustment in the event of the expiration, termination or redemption of such rights.

In the event of:

any reclassification of our common stock;

a consolidation, merger or combination involving us; or

a sale or conveyance to another person or entity of all or substantially all of our property and assets;

in which holders of our common stock would be entitled to receive stock, other securities, other property, assets or cash for their common stock, upon conversion of your Notes you will be entitled to receive the same type of consideration that you would have been entitled to receive if you had converted the Notes into our common stock immediately prior to any of these events.

You may in certain situations be deemed to have received a distribution subject to United States federal income tax as a dividend in the event of any taxable distribution to holders of common stock or in certain other situations requiring a conversion rate adjustment. See United States Federal Income Tax Considerations.

We may, from time to time, increase the conversion rate if our board of directors has made a determination that this increase would be in our best interests. Any such determination by our board will be conclusive. In addition, we may increase the conversion rate if our board of directors deems it advisable to avoid or diminish any income tax to holders of common stock resulting from any stock or rights distribution. See United States Federal Income Tax Considerations.

We will not be required to make an adjustment in the conversion rate unless the adjustment would require a change of at least 1% in the conversion rate. However, we will carry forward any adjustments that are less than 1% of the conversion rate. Except as described above in this section, we will not adjust the conversion rate for any issuance of our common stock or convertible or exchangeable securities or rights to purchase our common stock or convertible or exchangeable securities.

Optional Redemption by DURECT

We may not redeem the Notes in whole or in part at our option prior to their maturity date.

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Redemption at Option of the Holder

If a designated event occurs at any time prior to the maturity of the Notes, you may require us to redeem your Notes, in whole or in part, on a redemption date specified by us that is not less than 20 nor more than 35 business days after the date of our notice of the designated event. The Notes will be redeemable in integral multiples of $1,000 principal amount.

We will redeem the Notes at a price equal to 100% of the principal amount to be redeemed, plus accrued and unpaid interest, if any, to, but excluding, the redemption date. If the redemption date falls after a record date and on or prior to the corresponding interest payment date, we will pay the full amount of accrued and unpaid interest, if any, and liquidated damages, if any, on such interest payment date to the holder of record at the close of business on the corresponding record date.

We will mail to all record holders a notice of a designated event within 10 days after it has occurred. We are also required to deliver to the trustee a copy of the designated event notice. If you elect to redeem your Notes, you must deliver to us or our designated agent, on or before the redemption date specified in our designated event notice, your redemption notice and any Notes to be redeemed, duly endorsed for transfer.

The redemption notice from the holder must state:

- if certificated Notes have been issued, the note certificate numbers (or, if your Notes are not certificated, your redemption notice must comply with appropriate DTC procedures);
- the portion of the principal amount of Notes to be redeemed, which must be in $1,000 multiples; and
- that the Notes are to be redeemed by us pursuant to the applicable provisions of the Notes and the indenture.

You may withdraw any written redemption notice by delivering a written notice of withdrawal to the paying agent prior to the close of business on the redemption date. The withdrawal notice must state:

- the principal amount of the withdrawn Notes;
- if certificated Notes have been issued, the certificate numbers of the withdrawn Notes (or, if your Notes are not certificated, your withdrawal notice must comply with appropriate DTC procedures); and
- the principal amount, if any, that remains subject to the redemption notice.

Payment of the repurchase price for a Note for which a repurchase notice has been delivered and not withdrawn is conditioned upon book-entry transfer or delivery of the Note, together with necessary endorsements, to the paying agent at its corporate trust office in the Borough of Manhattan, The City of New York, or any other office of its paying agent, at any time after delivery of the redemption notice. Payment of the

redemption price for the Note will be made promptly following the later of the redemption date and the time of book-entry transfer or delivery of the Note. If the paying agent holds money sufficient to pay the redemption price of the Note on the business day following the redemption date, then, on and after the date:

The Note will cease to be outstanding;

Interest will cease to accrue; and

All other rights of the holder will terminate, other than the right to receive the redemption price upon delivery of the Note.

This will be the case whether or not book-entry transfer of the Note has been made or the Note has been delivered to the paying agent.

A designated event will be deemed to have occurred upon a fundamental change or a termination of trading.

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A fundamental change is any transaction or event (whether by means of an exchange offer, liquidation, tender offer, consolidation, merger, combination, reclassification, recapitalization or otherwise) 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 that:

- is listed on, or immediately after the transaction or event will be listed on, a United States national securities exchange, or
- is approved, or immediately after the transaction or event will be approved, for quotation on the NASDAQ National Market or any similar United States system of automated dissemination of quotations of securities prices.

A termination of trading will be deemed to have occurred if our common stock (or other common stock into which the Notes are then convertible) is neither listed for trading on a United States national securities exchange nor approved for trading on the NASDAQ National Market.

We will comply with any applicable provisions of Rule 13e-4 and any other tender offer rules under the Exchange Act in the event of a designated event.

These designated event redemption rights could discourage a potential acquirer of DURECT. However, this designated event 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 designated event is limited to specified transactions and may not include other events that might adversely affect our financial condition or business operations. Our obligation to offer to redeem the Notes upon a designated event would not necessarily afford you protection in the event of a highly leveraged transaction, reorganization, merger or similar transaction involving us.

We may be unable to redeem the Notes upon a designated event. If a designated event were to occur, we may not have enough funds to pay the redemption price for all tendered Notes. Any future credit agreements 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. If a designated event occurs at a time when we are prohibited from purchasing or redeeming Notes, we could seek the consent of our lenders to redeem the Notes or attempt to refinance this debt. If we do not obtain consent, we would not be permitted to purchase or redeem the Notes. Our failure to redeem tendered Notes would constitute an event of default under the indenture, which might constitute a default under the terms of our other indebtedness.

Merger and Sale of Assets by DURECT

The indenture provides that we may not consolidate with or merge with or into any other person or convey, transfer or lease its properties and assets substantially as an entirety to another person, unless among other items:

- we are the surviving person, or the resulting, surviving or transferee person, if other than us, is organized and existing under the laws of the United States, any state thereof or the District of Columbia;

the successor person assumes, by supplemental indenture satisfactory in form and substance to the trustee, all of our obligations under the Notes and the indenture;

after giving effect to such transaction, there is no event of default, and no event which, after notice or passage of time or both, would become an event of default; and

we have delivered to the trustee an officers certificate and an opinion of counsel each stating that such consolidation, merger, sale, conveyance, transfer or lease complies with these requirements.

When such a person assumes our obligations in such circumstances, subject to certain exceptions, we shall be discharged from all obligations under the Notes and the indenture.

Events of Default; Notice and Waiver

The following are events of default under the indenture:

we fail to pay principal or premium, if any, when due upon redemption or otherwise on the Notes;

we fail to pay any interest or liquidated damages, if any, on the Notes, when due and such failure continues for a period of 30 days;

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we fail to provide notice of the occurrence of a designated event on a timely basis;

we fail to perform or observe any of the covenants in the indenture for 60 days after written notice to us from the trustee (or to us and the trustee from the holders of at least 25% in principal amount of the outstanding Notes); or

certain events involving our bankruptcy, insolvency or reorganization.

The trustee may withhold notice to the holders of the Notes of any default, except defaults in payment of principal, premium, interest or liquidated damages, if any, on the Notes. However, the trustee must consider it to be in the interest of the holders of the Notes to withhold this notice.

If an event of default occurs and continues, the trustee or the holders of at least 25% in principal amount of the outstanding Notes may declare the principal, premium, if any, and accrued and unpaid interest, if any, and liquidated damages, if any, on the outstanding Notes to be immediately due and payable. In case of certain events of bankruptcy or insolvency involving us, the principal, premium, if any, accrued and unpaid interest, if any, and liquidated damages, if any, on the Notes will automatically become due and payable. However, if we cure all defaults, except the nonpayment of principal, premium, if any, interest or liquidated damages, if any, that became due as a result of the acceleration, and meet certain other conditions, with certain exceptions, this declaration may be cancelled and the holders of a majority of the principal amount of outstanding Notes may waive these past defaults.

Payments of principal, premium, if any, or interest on the Notes that are not made when due will accrue interest from the required payment date at the annual rate of 1% above the then applicable interest rate for the Notes.

The holders of a majority of outstanding Notes will have the right to direct the time, method and place of any proceedings for any remedy available to the trustee, subject to limitations specified in the indenture.

No holder of the Notes may pursue any remedy under the indenture, except in the case of a default in the payment of principal, premium, if any, or interest, if any, or liquidated damages, if any, on the Notes, unless:

the holder has given the trustee written notice of an event of default;

the holders of at least 25% in principal amount of outstanding Notes make a written request, and offer reasonable indemnity, to the trustee to pursue the remedy;

the trustee does not receive an inconsistent direction from the holders of a majority in principal amount of the Notes;

the holder or holders have offered reasonable security or indemnity to the trustee against any costs, liability or expense of the trustee; and

the trustee fails to comply with the request within 60 days after receipt of the request and offer of indemnity.

Modification and Waiver

The consent of the holders of a majority in principal amount of the outstanding Notes is required to modify or amend the indenture. However, a modification or amendment requires the consent of the holder of each outstanding Note if it would:

extend the fixed maturity of any Note;

reduce the rate or extend the time for payment of interest of any Note;

reduce the principal amount or premium of any Note;

reduce any amount payable upon redemption of any Note;

adversely change our obligation to redeem any Notes on a redemption date;

adversely change our obligation to redeem any Note upon a designated event;

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impair the right of a holder to institute suit for payment on any Note;

change the currency in which any Note is payable;

impair the right of a holder to convert any Note or reduce the number of common shares or any other property receivable upon conversion;

reduce the quorum or voting requirements under the indenture; or

subject to specified exceptions, modify certain of the provisions of the indenture relating to modification or waiver of provisions of the indenture.

We are permitted to modify certain provisions of the indenture without the consent of the holders of the Notes.

Form, Denomination and Registration

The Notes are issued:

in fully registered form;

without interest coupons; and

in denominations of $1,000 principal amount and integral multiples of $1,000.

Global Note, Book-Entry Form

The Notes are evidenced by one or more global Notes. We have deposited the global note or Notes with DTC and registered the global Notes in the name of Cede & Co. as DTC s nominee. Except as set forth below, a global note may be transferred, in whole or in part, only to another nominee of DTC or to a successor of DTC or its nominee.

Beneficial interests in a global note may be held through organizations that are participants in DTC (called participants). Transfers between participants will be effected in the ordinary way in accordance with DTC rules and will be settled in clearing house funds. The laws of some states require that certain persons take physical delivery of securities in definitive form. As a result, the ability to transfer beneficial interests in the global note to such persons may be limited.

Beneficial interests in a global note held by DTC may be held only through participants, or certain banks, brokers, dealers, trust companies and other parties that clear through or maintain a custodial relationship with a participant, either directly or indirectly (called indirect participants). So long as Cede & Co., as the nominee of DTC, is the registered owner of a global note, Cede & Co. for all purposes will be considered the sole holder of such global note. Except as provided below, owners of beneficial interests in a global note will:

not be entitled to have certificates registered in their names;

not receive physical delivery of certificates in definitive registered form; and

not be considered holders of the global note.

We will pay interest on and the redemption price of a global Note to Cede & Co., as the registered owner of the global note, by wire transfer of immediately available funds on each interest payment date or the redemption date, as the case may be. Neither we, the trustee nor any paying agent will be responsible or liable:

for the records relating to, or payments made on account of, beneficial ownership interests in a global Note; or

for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

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Neither we, the trustee, registrar, paying agent nor conversion agent will have any responsibility for the performance by DTC or its participants or indirect participants of their respective obligations under the rules and procedures governing their operations. DTC has advised us that it will take any action permitted to be taken by a holder of Notes, including the presentation of Notes for conversion, only at the direction of one or more participants to whose account with DTC interests in the global Note are credited, and only in respect of the principal amount of the Notes represented by the global note as to which the participant or participants has or have given such direction.

DTC has advised us that it is:

a limited purpose trust company organized under the laws of the State of New York, and a member of the Federal Reserve System;

a clearing corporation within the meaning of the Uniform Commercial Code; and

a clearing agency registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC was created to hold securities for its participants and to facilitate the clearance and settlement of securities transactions between participants through electronic book-entry changes to the accounts of its participants. Participants include securities brokers, dealers, banks, trust companies and clearing corporations and other organizations. Some of the participants or their representatives, together with other entities, own DTC. Indirect access to the DTC system is available to others such as banks, brokers, dealers and trust companies that clear through or maintain a custodial relationship with a participant, either directly or indirectly.

DTC has agreed to the foregoing procedures to facilitate transfers of interests in a global note among participants. However, DTC is under no obligation to perform or continue to perform these procedures, and may discontinue these procedures at any time. We will issue Notes in definitive certificate form only if:

DTC notifies us that it is unwilling or unable to continue as depositary or DTC ceases to be a clearing agency registered under the Securities and Exchange Act of 1934, as amended, and a successor depositary is not appointed by us within 90 days;

an event of default shall have occurred and the maturity of the Notes shall have been accelerated in accordance with the terms of the Notes and any holder shall have requested in writing the issuance of definitive certificated Notes; or

we have determined in our sole discretion that the Notes shall no longer be represented by global Notes.

Registration Rights of the Noteholders

We entered into a registration rights agreement with the initial purchaser in which we agreed to file the shelf registration statement of which this prospectus is a part with the SEC covering resale of the registrable securities within 90 days after the closing date. We will use our best efforts to cause the shelf registration statement to become effective within 180 days of the closing date. We will use our best efforts to keep the shelf registration statement effective until the date there are no longer any registrable securities.

When we use the term registrable securities in this section, we are referring to the Notes and the common stock issuable upon conversion of the Notes until the earlier of:

the sale pursuant to Rule 144 under the Securities Act or the shelf registration statement of all registrable securities; and

the expiration of the holding period applicable to such securities held by persons that are not affiliates of DURECT under Rule 144(k) under the Securities Act or any successor provision.

We may suspend the use of the prospectus under certain circumstances relating to pending corporate developments, public filings with the SEC and similar events. Any suspension period shall not:

exceed 30 days in any three-month period; or

an aggregate of 90 days for all periods in any 12-month period.

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Notwithstanding the foregoing, we will be permitted to suspend the use of the prospectus for up to 60 days in any 3-month period under certain circumstances relating to possible acquisitions, financings or other similar transactions.

We will pay predetermined liquidated damages on any interest payment date if the shelf registration statement is not timely filed or made effective or if the prospectus is unavailable for periods in excess of those permitted above:

- on the Notes at an annual rate equal to 0.5% of the aggregate principal amount of the Notes outstanding until the registration statement is filed or made effective or during the additional period the prospectus is unavailable; and
- on the common stock that has been converted, at an annual rate equal to 0.5% of an amount equal to $1,000 divided by the conversion rate in effect during such periods.

A holder who elects to sell registrable securities pursuant to the shelf registration statement will be required to:

- be named as a selling stockholder in the related prospectus;
- deliver a prospectus to purchasers; and
- be subject to the provisions of the registration rights agreement, including indemnification provisions.

Under the registration rights agreement we will:

- pay all expenses with respect to the shelf registration statement;
- provide each registered holder copies of the prospectus;
- notify holders when the shelf registration statement has become effective; and
- take other reasonable actions as are required to permit unrestricted resales of the registrable securities in accordance with the terms and conditions of the registration rights agreement.

The plan of distribution of the shelf registration statement will permit resales of registrable securities by selling security holders through brokers and dealers.

This summary of the registration rights agreement is not complete. This summary is subject to, and is qualified in its entirety by reference to, all the provisions of the registration rights agreement.

Rule 144A Information Request

We will furnish to the holders or beneficial holders of the Notes or the underlying common stock and prospective purchasers, upon their request, the information required under Rule 144A(d)(4) under the Securities Act until such time as such securities are no longer restricted securities within the meaning of Rule 144 under the Securities Act, assuming these securities have not been owned by an affiliate of ours.

Information Concerning the Trustee

We have appointed The Bank of New York, the trustee under the indenture, as paying agent, conversion agent, note registrar and custodian for the Notes.

The trustee or its affiliates may provide banking and other services to us in the ordinary course of their business. The indenture contains certain limitations on the rights of the trustee, if it or any of its affiliates is then our creditor, to obtain payment of claims in certain cases or to realize on certain property received on any claim as security or otherwise. The trustee and its affiliates will be permitted to engage in other transactions with us. However, if the trustee or any affiliate continues to have any conflicting interest and a default occurs with respect to the Notes, the trustee must eliminate such conflict or resign.

Governing Law

The Notes and the indenture shall be governed by, and construed in accordance with, the laws of the State of New York.

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DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 110,000,000 shares of common stock, $0.0001 par value, and 10,000,000 shares of undesignated preferred stock, $0.0001 par value. As of October 24, 2003, there were 51,106,435 shares of common stock outstanding and warrants to purchase 1,000,770 shares of common stock outstanding.

Common Stock

The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Subject to preferential rights with respect to any outstanding preferred stock, holders of common stock are entitled to receive ratably such dividends as may be declared by the board of directors out of funds legally available therefor. In the event of our liquidation, dissolution or winding up, the holders of common stock are entitled to share ratably in all assets remaining after payment of liabilities and satisfaction of preferential rights of any outstanding preferred stock. The common stock has no preemptive or conversion rights or other subscription rights. There are no sinking fund provisions applicable to the common stock. The outstanding shares of common stock are, and the shares of common stock to be issued upon completion of this offering will be, fully paid and non-assessable.

Preferred Stock

Our board of directors is authorized to issue preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof, including dividend rights, dividend rates, conversion rights, voting rights, terms of redemption, redemption prices, liquidation preferences and the number of shares constituting any series or the designation of such series, without further vote or action by the stockholders.

The issuance of preferred stock may have the effect of delaying, deferring or preventing a change in our control without further action by the stockholders. The issuance of preferred stock with voting and conversion rights may adversely affect the voting power of the holders of common stock, including voting rights, of the holders of common stock. In certain circumstances, such issuance could have the effect of decreasing the market price of the common stock.

Options

As of October 24, 2003, options to purchase a total of 5,810,171 shares of common stock were outstanding with a weighted-average exercise price of $4.67 per share. Up to 3,420,861 additional shares of common stock may be subject to options granted in the future under the 2000 stock plan and the 2000 directors stock option plan.

Warrants

As of October 24, 2003, we had an outstanding warrant for the purchase of 1,000,000 shares of common stock at an exercise price of $12.00 per share. This warrant expires on October 3, 2004. We also had an additional outstanding warrant for the purchase of an aggregate of 770 shares of common stock at an exercise price of $8.50 per share. This warrant expires on May 11, 2011.

Registration Rights

In accordance with our Common Stock Purchase Agreement with Endo Pharmaceuticals, Inc. (Endo) and an Agreement and Plan of Merger by and among us, Absorbable Polymer Technologies, Inc. and Birmingham Polymers, Inc., we filed a registration statement on Form S-3 with the SEC on August 29, 2003 to register 2,261,425 shares of our common stock for resale. The registration statement was declared effective by the SEC on September 26, 2003.

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Stockholder Rights Plan

Our board of directors has 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.

The stockholder rights plan involved the distribution of one preferred share purchase right as a dividend on each outstanding share of our common stock to all holders of record on July 20, 2001. Each right will entitle the holder to purchase one one-thousandth of a share of our Series A participating preferred stock at an exercise price of $120.00 per one one-thousandth of a share of preferred stock. The rights trade in tandem with the common stock until, and become exercisable following, the occurrence of certain triggering events. 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.

Effect of Certain Certificate of Incorporation and Bylaw Provisions

Our certificate of incorporation and bylaws to provide, among other things, that our directors will be elected without the application of cumulative voting. In addition, any action required or permitted to be taken by our stockholders may be taken only at a duly called annual or special meeting of the stockholders. Our bylaws also contain procedures, including advance notice procedures with regard to the nomination, other than by or at the direction of the board of directors, of candidates for election as directors. The foregoing provisions could have the effect of making it more difficult for a third party to effect a change in the control of our board of directors. In addition, these provisions could have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, a majority of our outstanding voting stock.

Certain Anti-Takeover Effects of Provisions of Our Certificate of Incorporation and Bylaws and Of Delaware Law General

General. Certain provisions of Delaware law and our certificate of incorporation and bylaws could have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from acquiring, control of us. Such provisions could limit the price that certain investors might be willing to pay in the future for shares of our common stock. These provisions of Delaware law and our certificate of incorporation and bylaws may also have the effect of discouraging or preventing certain types of transactions involving an actual or threatened change in our control, including unsolicited takeover attempts, even though such a transaction may offer our stockholders the opportunity to sell their stock at a price above the prevailing market price.

Delaware Takeover Statute. We are subject to the business combination provisions of Section 203 of the Delaware General Corporation Law. In general, those provisions prohibit a publicly-held Delaware corporation from engaging in various business combination transactions with any interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless:

the transaction is approved by the board of directors prior to the date the interested stockholder obtained interested stockholder status;

upon consummation of the transaction that resulted in the stockholder s becoming an interested stockholder, the stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding those shares owned by (a) persons who are directors and also officers and (b) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to the date the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

A business combination is defined to include mergers, asset sales and other transactions resulting in financial benefit to a stockholder. In general, an interested stockholder is a person who, together with affiliates and associates, owns, or within three years, did own, 15% or more of a corporation s voting stock. The statute could prohibit or delay mergers or other takeover or change in control attempts with respect to us and, accordingly, may discourage attempts to acquire us.

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Certificate of Incorporation and Bylaws. Our certificate of incorporation provides that any action to be taken by our stockholders must be effected at an annual or special stockholder meeting and may not be taken by written consent. Our bylaws provide that special meetings of our stockholders may be called by the board of directors, the Chairman of the board or by our President. Our bylaws also require advance written notice by a stockholder of a proposal or director nomination that such stockholder desires to present at an annual or special stockholders meeting. No business other than that stated in the notice may be transacted at any special meeting. These provisions will delay consideration of a stockholder proposal until the next annual meeting unless a special meeting is called by the board of directors.

Our bylaws provide that the authorized number of directors may be changed by an amendment to the bylaws adopted by the board of directors or by the stockholders. Vacancies on the board of directors may be filled either by holders of a majority our voting stock or a majority of directors in office, although less than a quorum. Our certificate of incorporation also provides for a staggered board of directors. Under a staggered board of directors, each director is designated to one of three categories. Each year the directors positions in one of the three categories are subject to election so that it would take three years to replace the entire board, absent resignation or premature expiration of a director s term, which may have the effect of deterring a hostile takeover or delaying or preventing changes in our control or management.

Limitations on Liability and Indemnification of Officers and Directors

Our certificate of incorporation limits the liability of directors to the fullest extent permitted by the Delaware law. In addition, the certificate of incorporation and bylaws provide that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. We have entered into separate indemnification agreements with its directors and executive officers that provide these persons indemnification protection in the event the certificate of incorporation is subsequently amended.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is EquiServe Trust Company, N.A. EquiServe is located at 150 Royall Street, Canton, Massachusetts 02021, and its telephone number is (877) 282-1169.

UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS

This section summarizes the material U.S. federal income tax considerations relating to the purchase, ownership and disposition of the Notes and the shares of common stock into which the Notes may be converted. This summary is based on the Internal Revenue Code of 1986, as amended (the Code), existing and proposed Treasury Regulations, administrative pronouncements and judicial decisions, each as available on the date hereof. All of the foregoing are subject to change, possibly with retroactive effect or different interpretations. In such event, the federal income tax consequences of purchasing, owning or disposing of the Notes, or the common stock acquired upon conversion of the Notes, could differ from those described in this summary. This summary generally applies only to U.S. holders (as defined below) that purchase the Notes in the initial offering at their issue price and hold the Notes, or common stock acquired upon conversion of the Notes, as capital assets. The summary does not address any aspect of state, local or foreign tax law, nor does it address U.S. federal, estate and gift tax law.

For purposes of this summary, U.S. holders are beneficial owners of the Notes or the common stock that, for U.S. federal income tax purposes, are:

a citizen or resident of the United States;

a corporation created or organized under the laws of the United States or any State thereof (including the District of Columbia);

an estate if its income is subject to U.S. federal income taxation regardless of its source; or

a trust if such trust validly elects to be treated as a United States person for U.S. federal income tax purposes or if (1) a court within the United States is able to exercise primary supervision over its administration and (2) one or more United States persons have the authority to control all of the substantial decisions of such trust.

A non-U.S. holder is a holder that is not a U.S. holder.

This summary generally does not address federal income tax considerations that may be relevant to particular investors, such as:

financial institutions;

insurance companies;

partnerships or other entities classified as partnerships for U.S. federal income tax purposes;

real estate investment trusts;

regulated investment companies;

dealers or traders in securities or currencies;

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tax-exempt entities;

persons that will hold the Notes or common stock as part of a hedging or conversion transaction or as a position in a straddle for U.S. federal income tax purposes;

U.S. holders that have a functional currency other than the United States dollar; and

persons subject to the alternative minimum tax.

YOU SHOULD CONSULT YOUR OWN TAX ADVISOR REGARDING THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO YOUR PARTICULAR SITUATION AND THE CONSEQUENCES OF FEDERAL ESTATE OR GIFT TAX LAWS, FOREIGN, STATE, OR LOCAL LAWS AND TAX TREATIES.

U.S. Holders

Taxation of Interest

U.S. holders will be required to recognize as ordinary income any interest paid or accrued on the Notes in accordance with their regular method of tax accounting for U.S. federal income tax purposes. It is expected that the Notes will be issued without original issue discount for U.S. federal income tax purposes; however, if the stated redemption price at maturity of the Notes (generally, the sum of all payments required under the Notes other than payments of stated interest unconditionally payable at least annually at a single fixed rate) exceeds their issue price by more than a de minimus amount, a U.S. holder will be required to include such excess in gross income as original issue discount, as it accrues, using a constant-yield method.

We may be required to make additional payments to holders of the Notes if we do not file or cause to become effective a registration statement, as described under Description of Notes Registration Rights of the Noteholders, or if there is an event of default under the Notes. The original issue discount rules allow contingent payments such as these to be disregarded in determining whether a Note has original issue discount if the contingency is remote. We believe that the possibility is remote that we will make the additional payments described above. Our determination in this regard is binding on U.S. holders unless they disclose their contrary position.

Sale, Exchange or Redemption of the Notes

A U.S. holder will generally recognize capital gain or loss if the holder disposes of a Note in a sale, redemption or exchange other than a conversion of the Note into common stock. The holder s gain or loss will equal the difference between the proceeds received by the holder and the holder s adjusted tax basis in the Note. The proceeds received by the holder will include the amount of any cash and the fair market value of any other property received for the Note. The holder s tax basis in the Note generally will equal the amount the holder paid for the Note. The portion of any proceeds that is attributable to accrued interest will not be taken into account in computing the holder s capital gain or loss. Instead, that portion will be recognized as ordinary interest income to the extent that the holder has not previously included the accrued interest in income. The gain or loss recognized by a holder on a disposition of the Note will be long-term capital gain or loss if the holder held the Note

for more than one year. Long-term capital gains of non-corporate taxpayers are taxed at lower rates than those applicable to ordinary income. The deductibility of capital losses is subject to limitation. The registration of the Notes will not constitute a taxable exchange for U.S. federal income tax purposes and, thus, a U.S. holder will not recognize any gain or loss upon such registration.

Conversion of the Notes into Common Stock

A U.S. holder generally will not recognize any income, gain or loss on converting a Note into common stock, except that the fair market value of common stock received with respect to accrued interest will be taxed as a payment of interest as described under U.S. Holders Taxation of Interest, above. If the holder receives cash in lieu of a fractional share of common stock, however, the holder would be treated as if such holder received the fractional share and then the fractional share was redeemed for the cash. The holder would recognize capital gain or loss equal to the difference between the cash received and that portion of such holder s tax basis in the common stock attributable to the fractional share. The holder s aggregate tax basis in the common stock will equal the holder s adjusted tax basis in the Note, increased, for a cash method holder, by the amount of income recognized with respect to accrued interest, and decreased by the portion of tax basis allocable to the fractional share. The holder s holding period for the common stock will include the period during which such holder held the Note, except that the holding period of any common stock received with respect to accrued interest will commence on the day after the date of conversion.

Constructive Dividends

If at any time the conversion rate of the Notes is increased, such increase may be deemed to be the payment of a constructive taxable dividend, for U.S. federal income tax purposes, to the holders of the Notes. For example, an increase in the conversion rate in the event of distributions of our debt instruments, or our assets, or an increase in the event of an extraordinary cash dividend, generally may result in deemed dividend treatment to the holders of the Notes.

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Dividends

If, after a U.S. holder converts a Note into common stock, we make a distribution in respect of that stock, the distribution will be treated as a dividend to the extent it is paid from our current or accumulated earnings and profits. Under recently enacted 2003 federal tax legislation, qualified dividend income (generally, dividends received from a domestic U.S. corporation or qualified foreign corporation if a stock holding period requirement is satisfied and certain limitations do not apply) received by individual U.S. holders in tax years beginning prior to 2009 is taxable at the same rate as net capital gain; otherwise, dividends are taxable to U.S. holders as ordinary income. If the distribution exceeds our current and accumulated profits, the excess will be treated first as a tax-free return of the holder s investment, up to the holder s tax basis in the common stock. Any remaining excess will be treated as capital gain. If the U.S. holder is a U.S. corporation, it generally would be able to claim a dividends received deduction equal to a portion of any dividends received, subject to customary limitations and conditions.

Sale or Exchange of Common Stock

A U.S. holder will generally recognize capital gain or loss on a sale or exchange of common stock. The holder s gain or loss will equal the difference between the proceeds received by the holder and the holder s adjusted tax basis in the stock. The proceeds received by the holder will include the amount of any cash and the fair market value of any other property received for the stock. The gain or loss recognized by a holder on a sale or exchange of stock will be long-term capital gain or loss if the holder held the shares for more than one year. The registration of the common stock issuable upon conversion of the Notes will not constitute a taxable exchange for U.S. federal income tax purposes and, thus, a U.S. holder will not recognize any gain or loss upon such registration.

Non-U.S. Holders

Taxation of Interest

Payments of interest to non-U.S. holders generally are subject to U.S. federal income tax at a rate of 30%, collected by means of withholding by the payor. Payments of interest on the Notes to most non-U.S. holders, however, will qualify as portfolio interest, and thus will be exempt from the withholding tax, if the holders certify their nonresident status as described below. The portfolio interest exemption will not apply to payments of interest to a non-U.S. holder that:

owns, directly or indirectly (taking into account certain constructive ownership rules), at least 10% of our voting stock, or

is a controlled foreign corporation that is related to us.

Even if the portfolio interest exemption does not apply, the 30% withholding tax might not apply, or might apply at a reduced rate, under the terms of an income tax treaty between the United States and the non-U.S. holder s country of residence. The portfolio interest exemption, entitlement to treaty benefits and several of the special rules for non-U.S. holders described below apply only if the holder certifies its nonresident status. A non-U.S. holder can meet this certification requirement in the manner described under Backup Withholding and Information Reporting, below.

Sale, Exchange or Redemption of Notes

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

- the gain is effectively connected with the conduct by the non-U.S. holder of a U.S. trade or business;
- the non-U.S. holder was a citizen or resident of the United States and is subject to special rules that apply to expatriates;
- the non-U.S. holder is an individual present in the United States for 183 days or more in the taxable year of such sale or exchange and certain other conditions are met; or
- the rules of the Foreign Investment in Real Property Tax Act (FIRPTA) (described below) treat the gain as effectively connected with a U.S. trade or business.

The FIRPTA rules may apply to a sale, exchange or other disposition of Notes if we are, or have been within the shorter of the five-year period preceding such sale, exchange or disposition and the period the non-U.S. holder held the Notes, a U.S. real property holding corporation (USRPHC). In general, we would be a USRPHC if the fair market value of our interests in U.S. real estate equal or exceed 50% of the fair market value of our assets. We do not believe that we are a USRPHC or that we will become one in the future.

Conversion of the Notes

A non-U.S. holder generally will not recognize any income, gain or loss on converting a Note into common stock, except that the fair market value of common stock received with respect to accrued interest will be taxed as a payment of interest as described under Non-U.S. Holders Taxation of Interest, above. If the holder receives cash in lieu of a fractional share of common stock, however, the holder would be treated as if such holder received the fractional share and then the fractional share was redeemed for the cash. Any gain recognized as a result of the holder s receipt of cash in lieu of a fractional share of common stock would also generally not be subject to U.S. federal income tax. See Non-U.S. Holders Sale or Exchange of Common Stock, below.

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Dividends

Dividends (including any constructive dividends resulting from certain adjustments to the conversion rate, see U.S. Holders Constructive Dividends, above) paid to a non-U.S. holder on common stock received on conversion of a Note generally will be subject to U.S. withholding tax at a 30% rate. The withholding tax might not apply, however, or might apply at a reduced rate, under the terms of a tax treaty between the United States and the non-U.S. holder s country of residence. A non-U.S. holder must demonstrate its entitlement to treaty benefits by certifying its nonresident status as described under Backup Withholding and Information Reporting, below.

Sale or Exchange of Common Stock

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

- the gain is effectively connected with the conduct by the non-U.S. holder of a U.S. trade or business;
- the non-U.S. holder was a citizen or resident of the United States and is subject to special rules that apply to expatriates;
- the non-U.S. holder is an individual present in the United States for 183 days or more in the taxable year of such sale or exchange and certain other conditions are met; or
- the FIRPTA rules treat the gain as effectively connected with a U.S. trade or business.

Income or Gains Effectively Connected With a U.S. Trade or Business

The preceding discussion of the tax consequences of the purchase, ownership or disposition of Notes or common stock by a non-U.S. holder assumes that the holder is not engaged in a U.S. trade or business. If any interest on Notes, dividends on common stock or gain from the sale, exchange or other disposition of Notes or common stock is effectively connected with a U.S. trade or business conducted by the non-U.S. holder, then the income or gain will be subject to U.S. federal income tax in the same manner as if derived by a U.S. holder. If the non-U.S. holder is eligible for the benefits of a tax treaty between the United States and the holder s country of residence, any effectively connected income or gain will generally be subject to U.S. federal income tax only if it is also attributable to a permanent establishment maintained by the holder in the United States. Payments of interest or dividends that are effectively connected with a U.S. trade or business, and therefore included in the gross income of a non-U.S. holder, will not be subject to the 30% withholding tax. To claim this exemption from withholding, the holder must certify its qualification by filing Internal Revenue Service (IRS) Form W-8ECI. If the non-U.S. holder is a corporation, that portion of its earnings and profits that are effectively connected with its U.S. trade or business generally would be subject to a branch profits tax. The branch profits tax rate is generally 30%, although an applicable tax treaty might provide for a lower rate.

Backup Withholding and Information Reporting

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

Payments of interest or dividends to non-corporate U.S. holders of Notes or common stock will generally be subject to information reporting, and will be subject to backup withholding unless the holder provides us or our paying agent with a correct taxpayer identification number.

The information reporting and backup withholding rules do not apply to payments that are subject to the 30% (or lower treaty rate) withholding tax on dividends or interest paid to nonresidents, or to payments that are exempt from that tax by application of a tax treaty or special exception. Therefore, payments of dividends on common stock or interest on Notes to non-U.S. holders generally will not be subject to information reporting or backup withholding assuming appropriate certification requirements are satisfied. A non-U.S. holder can meet this certification requirement by providing a completed IRS Form W-8BEN or appropriate substitute form to us or our paying agent. If the holder holds the Notes through a financial institution or other agent acting on the holder s behalf, the holder will be required to provide appropriate documentation to the agent. The holder s agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries.

Payments made to U.S. holders by a broker upon a sale of Notes or common stock generally will be subject to information reporting and backup withholding. If, however, the sale is made through a foreign office of a U.S. broker, the sale will be subject to information reporting but not backup withholding. If the sale is made through a foreign office of a foreign broker, the sale will

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generally not be subject to either information reporting or backup withholding. This exception may not apply, however, if the foreign broker is owned or controlled by U.S. persons, or is engaged in a U.S. trade or business.

Payments made to a non-U.S. holder by a broker upon a sale of Notes or common stock will not be subject to information reporting or backup withholding provided the holder certifies its foreign status. Any amounts withheld from a payment to a holder of Notes or common stock under the backup withholding rules can be credited against any U.S. federal income tax liability of the holder and may entitle the holder to a refund, provided the required information is furnished to the IRS.

Tax Disclosure Authorization

Notwithstanding anything herein to the contrary, investors (and each employee, representative or other agent of the investors) may disclose to any and all persons, without limitation of any kind, the U.S. federal income tax treatment and tax structure of the offering and all materials of any kind (including opinions or other tax analyses) that are provided to the investors relating to such tax treatment and tax structure. For this purpose, tax structure is limited to facts relevant to the U.S. federal income tax treatment of the offering and does not include information relating to the identity of the issuer, its affiliates, agents or advisors.

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

SELLING SECURITYHOLDERS

The Notes were originally issued to and resold by Morgan Stanley & Co. Incorporated in transactions exempt from the registration requirements of the Securities Act to persons reasonably believed by them to qualified institutional buyers, as defined by Rule 144A under the Securities Act. The selling securityholders may from time to time offer and sell pursuant to this prospectus any or all of the Notes and the common stock into which the Notes are convertible. When we refer to the selling securityholders in this prospectus, we mean those persons listed in the table below, as well as their transferees, pledgees, donees or successors.

The table below sets forth the name of each selling securityholder, the principal amount of Notes at maturity that each selling securityholder may offer pursuant to this prospectus and the number of shares of common stock into which the Notes are convertible. Unless set forth below, none of the selling securityholders has had within the past three years any material relationship with us or any of our predecessors or affiliates.

We have prepared the table based on information given to us by the selling securityholders on or before October 24, 2003. Because the selling securityholders may offer, pursuant to this prospectus, all or some portion of the Notes or common stock listed below, no estimate can be given as to the amount of Notes or common stock that will be held by the selling securityholders upon consummation of any sales. In addition, the selling securityholders listed in the table may have sold or transferred, in transactions exempt from the registration requirements of the Securities Act, some or all of their Notes since the date as of which the information in the table is presented.

Information about the selling stockholders may change over time. Any changed information given to us by the selling securityholders will be set forth in prospectus supplements if and when necessary.

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Selling Securityholder	Principal Amount of Notes Beneficially Owned and Offered	Percentage of Outstanding Notes	Common Stock Issuable Upon Conversion of the Notes that May be Sold(1)	Percentage of Shares of Common Stock Outstanding(2)
AIG DKR SoundShore Opportunity Holding Fund Ltd.	$ 2,500,000	4.2%	793,650	1.5%
Alexandra Global Master Fund, L.T.D	$ 4,000,000	6.7%	1,269,841	2.4%
Arbitex Master Fund, L.P.	$ 5,000,000	8.3%	1,587,301	3.0%
Argent Classic Convertible Arbitrage Fund, L.P.	$ 1,400,000	2.3%	444,444	*
Argent Classic Convertible Arbitrage Fund II, L.P.	$ 400,000	*	126,984	*
BNP Paribos Equity Strategies, SNC	$ 1,373,000	2.2%	435,872	*(3)
Citadel Equity Fund Ltd.	$ 2,910,000	4.9%	923,809	1.8%
Citadel Jackson Investment Fund Ltd.	$ 310,000	*	98,412	*
Clinton Multistrategy Master Fund, Ltd.	$ 1,690,000	2.8%	536,507	1.0%
Clinton Riverside Convertible Portfolio Limited	$ 1,610,000	2.7%	511,111	1.0%
CooperNeff Convertible Strategies (Cayman) Master Fund, L.P.	$ 1,353,000	2.3%	429,523	*
DBAG London	$ 2,000,000	3.3%	634,920	1.2%
Highbridge International LLC	$ 2,000,000	3.3%	634,920	1.2%
KD Convertible Arbitrage Fund L.P.	$ 1,000,000	1.7%	317,460	*
Lyxor/Convertible Arbitrage Fund, Ltd.	$ 84,000	*	26,666	*
Morgan Stanley & Co. Incorporated(4)	$ 5,905,000	9.8%	1,874,603	7.2%(5)
PRS Convertible Arbitrage Master Fund L.P.	$ 500,000	*	158,730	*
Sagamore Hill Hub Fund Ltd.	$ 8,895,000	14.8%	2,823,809	5.2%
Singlehead U.S. Convertible Arbitrage Fund	$ 246,000	*	78,095	*
Salomon Brothers Asset Management, Inc.	$ 825,000	1.4%	261,904	*(6)
Sturgeon Limited	$ 194,000	*	61,587	*
Sutton Brook Capital Portfolio LP	$ 2,500,000	4.2%	793,650	1.5%
Xavex Convertible Arbitrage 10 Fund	$ 400,000	*	126,984	*
Unnamed securityholders or any future transferees, pledgees, donees or successors of or from any such unnamed securityholder	$ 12,905,000	21.5%	4,096,825	7.4%

* Less than one percent (1%).

(1) Assumes conversion of all of the securityholder s Notes at a conversion rate of 317.4603 shares of common stock per $1,000 principal amount of the Notes. This conversion rate is subject to adjustment as described under Description of the Notes Conversion Rights. As a result, the number of shares of common stock issuable upon conversion of the Notes may increase in the future. Excludes shares of common stock that may be issued by us upon the repurchase of the Notes.

(2) Calculated based on Rule 13d-3(d)(i) of the Exchange Act, using 51,106,435 shares of our common stock outstanding as of the close of business on October 24, 2003. In calculating this amount for each holder, we treated as outstanding the number of shares of common stock issuable upon conversion of all of that holder s Notes, but we did not assume conversion of any other holder s Notes.

(3) Includes 11,465 shares of our common stock owned by BNP Paribos Equity Strategies, SNC.

(4) Morgan Stanley & Co. Incorporated and/or its affiliates have performed financial advisory and investment banking services for us within the past three years.

(5) Includes 716 shares of our common stock owned by Morgan Stanley & Co. Incorporated.

(6) Salomon Brothers Asset Management, Inc. acts as discretionary investment advisor with respect to the following accounts that hold the indicated principal amounts of Notes: Salomon Brothers Archer Investors Ltd. ($527,000) and Salomon Brothers Archer Investors L.P. ($298,000).

Generally, only selling securityholders 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 securityholders in an amendment to this registration statement or a supplement to this prospectus.

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LEGAL MATTERS

The validity of the issuance of the Notes and the common stock offered by this prospectus will be passed upon by Heller Ehrman White & McAuliffe LLP, Menlo Park, California, counsel to DURECT Corporation. Mark B. Weeks, a shareholder of Heller Ehrman White & McAuliffe LLP, is our Secretary.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our consolidated financial statements and schedule included in our Annual Report on Form 10-K for the year ended December 31, 2002, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and schedule are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commissions. Certain information in the registration statements has been omitted from this prospectus in accordance with the rules of the SEC. We file proxy statements and annual, quarterly and special reports and other information with the SEC. You can inspect and copy the registration statement as well as the reports, proxy statements and other information we have filed with the SEC at the public reference room maintained by the SEC at 450 Fifth Street, N.W., Washington, D.C. 20549, and at the SEC Regional Offices located at Citicorp Center, 500 West Madison Street, Suite 1400, Chicago, Illinois 60661-2511 and the Woolworth Building, 233 Broadway Street, New York, New York 10004. You can call the SEC at 1-800-732-0330 for further information about the public reference rooms. We are also required to file electronic versions of these documents with the SEC, which may be accessed from the SEC s World Wide Web site at http://www.sec.gov. Reports, proxy and information statements and other information concerning DURECT Corporation may be inspected at The Nasdaq Stock Market at 1735 K Street, N.W., Washington, D.C. 20006.

The SEC allows us to incorporate by reference certain of our publicly-filed documents into this prospectus, which means that information included in those documents is considered part of this prospectus. Information that we file with the SEC after the date of this prospectus will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, until the selling securityholders have sold all the registrable securities.

The following documents filed with the SEC are incorporated by reference in this prospectus:

1. Our Annual Report on Form 10-K for the year ended December 31, 2002 (File No. 000-31615).

2. Our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2003 and for the quarter ended June 30, 2003 (File No. 000-31615).

3. Our definitive Proxy Statement dated April 16, 2003, filed in connection with our June 4, 2003 Annual Meeting of Stockholders (File No. 000-31615).

4. Our Current Reports on Form 8-K filed with the SEC on April 28, 2003, June 12, 2003, June 13, 2003, July 14, 2003, July 24, 2003, September 2, 2003, September 23, 2003, October 9, 2003 and October 17, 2003 (File No. 000-31615).

5. The description of our common stock in our Registration Statements on Form 8-A filed with the SEC on September 22, 2000, July 10, 2001 and June 24, 2003 (File No. 000-31615).

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.

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We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference, other than exhibits to those documents. You should direct any requests for documents to Thomas A. Schreck, at 10240 Bubb Road, Cupertino, CA 95014, telephone: (408) 777-1417.

FORWARD-LOOKING STATEMENTS

This prospectus contains or incorporates by reference certain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, including those identified by the words believes, expects, may, will, should, seeks, pro forma anticipates and similar expressions. These forward-looking statements include, among others, statements regarding:

- the trends we see in our business and the markets in which we operate;
- the features, functionality and market acceptance of our products (including products under development); and
- our expectations for our future operating results and cash flows.

These statements are subject to risks and uncertainties, including those set forth in the Risk Factors section beginning on page 5, and actual results could differ materially from those expressed or implied in these statements. All forward-looking statements included in this prospectus are made as of the date hereof. We assume no obligation to update any such forward-looking statement or reason why actual results might differ except as required by the Exchange Act. You should carefully review the section entitled Risk Factors and our subsequent filings with the SEC.

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PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The following table sets forth the costs and expenses payable by the Registrant in connection with the sale and distribution of the common stock being registered. Selling commissions and brokerage fees and any applicable transfer taxes and fees and disbursements of counsel for the selling securityholders are payable individually by the selling securityholders. All amounts shown are estimates except the SEC registration fee.

	Amount to be Paid
SEC registration fee	$ 4,793.33
Nasdaq National Market(1)	$ 22,500
Legal fees and expenses	$ 118,000
Accounting fees and expenses	$ 10,000
Transfer Agent fees and expenses	$ 10,000
Printing expenses	$ 20,000
Miscellaneous expenses	$ 2,500
Total	$ 187,793.33

(1) Nasdaq National Market bills companies for the listing of additional shares on a quarterly basis, and the amount billed is determined by the change in the company s total shares outstanding from one quarter to the next. The total amount billable in one quarter is capped at $22,500. Since all of the Notes are convertible on the same basis, solely for the purpose of estimating the expenses payable by DURECT in connection with issuance and distribution of the Notes and underlying common stock, we have assumed the conversion of all Notes into shares of DURECT common stock during one quarter.

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 General Corporation Law of the State of Delaware (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.

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Item 16. Exhibits.

Exhibit Number	Description of Document
3.1	Amended and Restated Certificate of Incorporation of the Company (1).
3.2	Amended and Restated Bylaws of the Company (1).
4.4	Indenture by and between DURECT Corporation and The Bank of New York as trustee dated as of June 18, 2003 (2).
4.5	Registration Right Agreement among DURECT Corporation as issuer and Morgan Stanley & Co. Incorporated as initial purchaser dated as of June 18, 2003 (2).
5.1	Opinion of Heller Ehrman White & McAuliffe LLP.
10.35	Convertible Note Purchase Agreement by and between DURECT Corporation and Morgan Stanley & Co. Incorporated dated as of June 12, 2003 (2).
12.1	Computation of Ratio of Earnings to Fixed Charge (3).
23.1	Consent of Ernst & Young LLP, Independent Auditors (see page II-5).
23.2	Consent of Heller Ehrman White & McAuliffe LLP (included in Exhibit 5.1).
24.1	Power of Attorney (3).
25.1	Statement of Eligibility of Trustee on Form T-1 (3).

(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) Filed as an exhibit to our Registration Statement on Form 10-Q (File No. 000-31615), filed with the SEC on August 8, 2003 and incorporated herein by reference.
(3) Filed as an exhibit to our Registration Statement on Form S-3 (File No. 333-108398), originally filed with the SEC on August 29, 2003, and incorporated herein by reference.

Item 17. Undertakings.

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, as amended;

(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 prospectus filed with the Securities and Exchange 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.

(4) 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.

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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 referred to in Item 15 above 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 against the Registrant 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, 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 amendment no. 1 to the registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cupertino, State of California, on October 31, 2003.

DURECT CORPORATION

By: /s/ James E. Brown

James E. Brown
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this amendment no. 1 to the registration statement has been signed by the following persons in the capacities indicated on this 31st day of October 2003:

Signature	Title
/s/ James E. Brown	President, Chief Executive Officer and Director
James E. Brown	(Principal Executive Officer)
*	Chairman and Chief Scientific Officer
Felix Theeuwes	
*	Chief Financial Officer and Director
Thomas A. Schreck	(Principal Financial and Accounting Officer)
*	Director
John L. Doyle	
*	Director
David Hoffman	
*	Director
Armand P. Neukermans	
*	Director
Albert L. Zesiger	

*By: /s/ James E. Brown

James E. Brown

Attorney-In-Fact

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CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the reference to our firm under the caption Experts in Amendment No. 1 to the Registration Statement (Form S-3 No. 333-108398) and related Prospectus of DURECT Corporation for the registration of $60,000,000 principal amount of DURECT Corporation 6.25% Convertible Notes due 2008 and the shares of its common stock issuable upon conversion thereof and to the incorporation by reference therein of our report dated January 24, 2003, with respect to the consolidated financial statements and schedule of DURECT Corporation included in its Annual Report (Form 10-K) for the year ended December 31, 2002, filed with the Securities and Exchange Commission.

/s/ ERNST & YOUNG LLP

Palo Alto, California

October 30, 2003

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DURECT Corporation

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