DURECT CORP
Form S-3/A
September 24, 2003
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As filed with the Securities and Exchange Commission on September 24, 2003

Registration No. 333-108396

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

Ughetta T. Manzone

VENTURE LAW GROUP

A Professional Corporation

2800 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. ¨

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered	Proposed maximum offering price per unit(1)	Proposed maximum aggregate offering price(1)	Amount of registration fee(2)
Common Stock, par value $0.0001	2,018,864	$2.77	$5,592,253.28	$452.41

(1) Estimated solely for the purpose of computing the amount of the registration fee based on the average of the high and low prices of our common stock as reported on the Nasdaq National Market on September 19, 2003 pursuant to Rule 457(c).
(2) $452.80 previously paid.

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

Subject To Completion, Dated September 24, 2003

PROSPECTUS

2,018,864 shares of Common Stock

DURECT CORPORATION

The common stock offered by this prospectus involve a high degree of risk. You should carefully consider the Risk Factors beginning on page 4 in determining whether to purchase the common stock.

The selling stockholders identified on page 21 of this prospectus are offering these shares of common stock. The shares of common stock were issued to Endo Pharmaceuticals Inc. on November 8, 2002, in connection with a development, commercialization and supply license agreement and to James P. English and Charlotte P. English on August 15, 2003 pursuant to an Agreement and Plan of Merger by and among DURECT Corporation, Absorbable Polymer Technologies, Inc. and Birmingham Polymers, Inc. For additional information concerning these agreements, you should refer to the section entitled Issuance of Common Stock to Selling Stockholders. The Selling Stockholders may sell 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 on page 20. We will not receive any portion of the proceeds from the sale of these shares.

The selling stockholders 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.

On September 19, 2003, the last sale price of the common stock on the Nasdaq National Market was $2.81 per share.

	Price to Public	Underwriting Discounts and Commissions	Proceeds to Selling Stockholders
Per Share	See Text Above	See Text Above	See Text Above
Total			

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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THE COMPANY

Overview

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 an aseptic 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%.

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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In the first six 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. We anticipate that we will restart the clinical program to support regulatory approval of the product in the U.S. and outside the U.S. by the end of 2003.

We also develop other pharmaceutical products using our patented 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 six 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,

LACTEL® biodegradable polymers through our wholly owned subsidiary, BPI, and

IntraEAR® catheters, which have been used by physicians to treat inner ear disorders.

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.

RECENT DEVELOPMENTS

On June 18, 2003, we completed a private placement of an aggregate of $50.0 million in convertible subordinated notes. The notes bear interest at a fixed rate of 6.25% per annum and are due on June 15, 2008. The notes are convertible at the option of the note holders into our common stock at a conversion rate of 317.4603 shares per $1,000 principal amount of the notes, subject to adjustment in certain circumstances. Interest on the notes is payable semi-annually in arrears in June and December. We received net proceeds of approximately $47.2 million after deducting underwriting fees of $2.5 million and related expenses of $300,000. On July 14, 2003, we received approximately $9.5 million in net proceeds from the sale of an additional $10.0 million of convertible subordinated notes. These additional notes bear the same terms as the $50.0 million aggregate principal amount of convertible subordinated notes issued in June 2003. The convertible subordinated notes are unsecured obligation of the Company and are subordinate to any secured debt we currently have or any future senior indebtness of the Company.

Under the Registration Rights Agreement in connection with the convertible notes offering, the Company is required to file a registration statement with the SEC 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). In the event that the Company fails to perform these obligations, the Company will pay to the noteholders an amount accruing at a rate per annum equal to 0.5% per annum of the aggregate principal amount of the convertible notes or to the stockholders an amount accruing at a rate per annum equal to 0.5% on the conversion price for each share if common stock has been issued upon conversion of a note as liquidated damages until such time as all such obligations with respect to such security have been satisfied in full. The Company filed the registration statement with the SEC on August 29, 2003 and expects to have the registration statement declared effective before December 15, 2003.

On August 15, 2003, we completed an acquisition of Absorbable Polymer Technologies, Inc. pursuant to an Agreement and Plan of Merger by and among the Company, Absorable 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.

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:

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;

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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 June 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.

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

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product. We anticipate that we will again restart clinical program to support regulatory approval of the product in the U.S. and other countries of the world by the end 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.

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

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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, 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.

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.

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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 June 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.

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

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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.

Under the ALZA agreement, we must pay ALZA royalties on sales of DUROS-based pharmaceutical systems we commercialize and a percentage of any up-front license fees, milestone or special fees, payments or other consideration we receive, excluding research and development funding. In addition, commencing upon the commercial sale of a product developed under the agreement, we are obligated to make minimum product payments to ALZA on a quarterly basis based on our good faith projections of our net product sales of the product. These minimum payments will be fully credited against the product royalty payments we must pay to ALZA.

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

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

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

We 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 and in April 2001, we completed the acquisition of SBS. 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.

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 and SBS, as well future acquisitions, may not generate any additional revenue or provide any benefit to our business.

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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.

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.

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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.

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 June 30, 2003, we held 16 issued U.S. patents and 6 issued foreign patents. In addition, we have 37 pending U.S. patent applications and have filed 34 patent applications under the Patent Cooperation Treaty, from which 68 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

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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.

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

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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.

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.

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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.

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

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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.

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 our acquisition of SBS, now merged into DURECT, due to our engagement in the business of manufacturing and selling biodegradable polymers through our subsidiary Birmingham Polymers, Inc. Although we believe that our safety procedures for storing, handling and disposing of

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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 our stock could decline in value

The average daily trading volume of our common stock for the three months ending June 30, 2003, was 256,925 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. Pursuant to a Common Stock Purchase Agreement with Endo Pharmaceuticals Inc., we are in the process of registering 1,533,742 shares of our common stock for resale which registration must be effective on or before November 8, 2003. Certain of our investors also have rights to have unregistered shares of common stock registered at the same time. Pursuant to a Purchase Agreement with Morgan Stanley & Co., Incorporated, we are in the process of registering an aggregate of $60.0 million in convertible subordinated notes which registration must be effective on or before December 15, 2003. The convertible subordinated notes are convertible into shares of our common stock at a conversion rate of 317.4603 shares per $1,000 principal amount of notes, subject to adjustment in certain circumstances and will bear interest at a rate of 6.25% per annum. Once these registration statements are declared effective by the SEC, shares become tradeable 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.

Our outstanding convertible subordinated 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 fundamental change redemption option associated with our outstanding convertible subordinated notes

If we engage in any transaction or event in connection with which all or substantially all of our common stock is exchanged for, converted into, acquired for or constitutes solely the right to receive consideration which is not all or substantially all common stock listed on a United States national securities exchange or approved for quotation on the NASDAQ National Market or any similar United States system of automated dissemination of quotations of securities prices, or, if for any reason, our common stock is no longer listed for trading on a United States national

securities exchange nor approved for trading on the NASDAQ National Market, we may be required to redeem all or 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.

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The fundamental change redemption rights in our outstanding convertible subordinated notes could discourage a potential acquirer

If we engage in any transaction or event in connection with which all or substantially all of our common stock is exchanged for, converted into, acquired for or constitutes solely the right to receive, consideration which is not all or substantially all common stock listed on a United States national securities exchange or approved for quotation on the NASDAQ National Market or any similar United States system of automated dissemination of quotations of securities prices, or, if for any reason, our common stock is no longer listed for trading on a United States national securities exchange nor approved for trading on the NASDAQ National Market (a fundamental change), we may be required to redeem all or part of the notes and this 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.

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

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

USE OF PROCEEDS

The proceeds from the sale of the common stock offered by this prospectus are solely for the account of the selling shareholders. We will not receive any proceeds from the sale of these shares.

ISSUANCE OF COMMON STOCK TO SELLING STOCKHOLDERS

On November 8, 2002 we issued 1,533,742 shares of our common stock to Endo Pharmaceuticals Inc. in connection with a development, commercialization and supply license agreement with Endo Pharmaceuticals Inc. On August 15, 2003, we issued 485,122 shares of our common stock to James P. English and Charlotte P. English in connection with an Agreement and Plan of Merger among us, Birmingham Polymers, Inc. (BPI) and Absorbable Polymer Technologies, Inc. (APT). This prospectus covers the resale of the shares of common stock sold in connection with those transactions.

PLAN OF DISTRIBUTION

We are registering shares on behalf of the selling stockholders. We are required to keep this Registration Statement on Form S-3 effective until August 15, 2004. 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 shares will be borne by the selling stockholders. Sales of shares may be effected by selling stockholders from time to time in one or more types of transactions (which may include block transactions) on the Nasdaq National Market, or otherwise in negotiated transactions at market prices prevailing at the time of sale, or at negotiated prices. Such transactions may or may not involve brokers or dealers.

The selling stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. The selling stockholders 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 stockholders 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 stockholders may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the selling stockholders in amounts to be negotiated immediately prior to the sale.

The selling stockholders 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 stockholders 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.

The selling stockholders 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

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common stock in connection with this offering.

Selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided they meet the criteria and conform to the requirements of such Rule. The 1,533,742 shares of common stock offered pursuant to this prospectus to Endo Pharmaceuticals Inc. were originally issued by us to Endo Pharmaceuticals Inc. on November 8, 2002 in connection with a development, commercialization and supply license agreement with Endo Pharmaceuticals Inc. 485,122 of the shares of common stock offered pursuant to this prospectus to James P. English and Charlotte P. English were originally issued by us on August 15, 2003 in connection with our acquisition of APT. As part of those transactions, we agreed to indemnify each selling stockholder against certain liabilities, including liabilities arising under the Securities Act that could arise in connection with the sale of the shares by the selling stockholders. The selling stockholders have also agreed to indemnify us against certain liabilities arising under the Securities Act.

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.

SELLING STOCKHOLDERS

The following table sets forth certain information as of September 24, 2003 with respect to the selling stockholders. The following table assumes that the selling stockholders sell all of the shares offered by this prospectus. We are unable to determine the exact number of shares that actually will be sold.

We have determined beneficial ownership in accordance with the rules of the Securities and Exchange Commission. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons and entities named in the tables below have sole voting and investment power with respects to all shares of common stock that they beneficially own, subject to applicable community property laws. We have based our calculation of the percentage of beneficial ownership on 50,547,385 shares of common stock outstanding on July 31, 2003.

Except as described in footnote (1), no selling stockholder has had any material relationship with us or any of our predecessors or affiliates within the last three years.

	Shares Beneficially Owned Prior to the Offering		Shares Offered by this	Shares Beneficially Owned After the Offering	
Selling Stockholder	Number	Percent	Prospectus	Number	Percent
Endo Pharmaceuticals Inc.	1,533,742	3.03%	1,533,742	0	*

100 Painters Drive Chadds Ford, PA 19317					
James P. English (1) C/O Birmingham Polymers, Inc. 2683 Pelham Parkway Pelham, AL 35124	218,305	*	218,305	0	*
Charlotte P. English C/O Birmingham Polymers, Inc. 2683 Pelham Parkway Pelham, AL 35124	266,817	*	266,817	0	*

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* Less than 1%

(1) James P. English serves as the Chief Operating Officer of Birmingham Polymers, Inc., a wholly-owned subsidiary of ours.

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LEGAL MATTERS

The validity of the issuance of the common stock offered by this prospectus will be passed upon by Venture Law Group, A Professional Corporation, Menlo Park, California, counsel to DURECT Corporation. Mark B. Weeks, a director of Venture Law Group, 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 stockholders have sold all the shares.

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 and September 23, 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.

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.

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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 1, 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 stockholders are payable individually by the selling stockholders. All amounts shown are estimates except the SEC registration fee.

	Amount to be Paid
SEC registration fee	$ 452.41
Legal fees and expenses	$ 65,000
Accounting fees and expenses	$ 10,000
Transfer Agent fees and expenses	$ 5,000
Miscellaneous expenses	$ 2,500
Total	$ 82,952.41

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.

Item 16. Exhibits.

Exhibit Number	Description of Document
2.2	Agreement and Plan of Merger dated August 15, 2003, among DURECT Corporation, Birmingham Polymers, Inc. and Absorbable Polymer Technologies, Inc. (1)
3.1	Amended and Restated Certificate of Incorporation of the Company (2).
3.2	Amended and Restated Bylaws of the Company (2).

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10.33 *	Development, Commercialization and Supply License Agreement dated as of November 8, 2002 among DURECT Corporation and Endo Pharmaceuticals Inc. (3).
5.1	Opinion of Venture Law Group, A Professional Corporation (1).
23.1	Consent of Ernst & Young LLP, Independent Auditors (see page II-5).
23.2	Consent of Counsel (included in Exhibit 5.1).

(1) Filed as an exhibit to our Registration Statement on Form S-3 (File No. 333-108396), originally filed with the SEC on August 29, 2003, and incorporated herein by reference.
(2) 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.
(3) Filed as an exhibit to our Registration Statement on Form 10-K (File No. 000-31615), filed with the SEC on March 14, 2003 and incorporated herein by reference.
* Confidential treatment granted with respect to certain portions of this Exhibit.

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 and 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.

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

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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 registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cupertino, State of California, on September 24, 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 registration statement has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ James E. Brown James E. Brown	President, Chief Executive Officer and Director (Principal Executive Officer)	September 24, 2003
* Felix Theeuwes	Chairman and Chief Scientific Officer	September 24, 2003
* Thomas A. Schreck	Chief Financial Officer and Director (Principal Financial and Accounting Officer)	September 24, 2003
* John L. Doyle	Director	September 24, 2003
* David R. Hoffman	Director	September 24, 2003
* Armand P. Neukermans	Director	September 24, 2003
* Albert L. Zesiger	Director	September 24, 2003

*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. 33-108396) and related Prospectus of DURECT Corporation for the registration of 2,018,864 shares of its common stock 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

September 24, 2003

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DURECT Corporation

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