DURECT CORP
Form 10-K
March 16, 2006
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2005

OR

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from_____ to_____

Commission file number: 000-31615

DURECT CORPORATION

(Exact name of registrant as specified in its charter)

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

2 Results Way

Cupertino, CA 95014

(Address of principal executive offices, including zip code)

Registrant s telephone number, including area code: (408) 777-1417

Securities registered pursuant to Section 12(b) of the Act:

None

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, $0.0001 par value

(Title of Class)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ¨ NO x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15 of the Act. YES ¨ NO x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period than the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES x NO ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer x	Non-accelerated filer ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). YES ¨ NO x

The aggregate market value of the voting stock held by non-affiliates of the registrant was approximately $207,087,561 as of June 30, 2005 based upon the closing sale price on the Nasdaq National Market reported for such date. Shares of Common Stock held by each officer and director and by each person who may be deemed to be an affiliate have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

There were 61,954,889 shares of the registrant s Common Stock issued and outstanding as of February 28, 2006.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference from the definitive Proxy Statement for the 2006 annual meeting of stockholders, which is expected to be filed not later than 120 days after the Registrant s fiscal year ended December 31, 2005.

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DURECT CORPORATION

ANNUAL REPORT ON FORM 10-K

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2005

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PART I

Item 1. Business.

Overview

We are an emerging specialty pharmaceutical company focused on the development of pharmaceutical products based on proprietary drug delivery technology platforms. We are developing and commercializing pharmaceutical systems that will deliver the right drug to the right place in the right amount at the right time to treat chronic or episodic diseases and conditions. By integrating chemistry and engineering advancements, we can achieve what drugs or devices alone cannot. Our pharmaceutical systems enable optimized therapy for a given disease or patient population by controlling the rate and duration of drug administration. Our proprietary drug delivery technology platforms include:

- SABER Delivery System a patented and versatile depot injectable useful for protein and small molecule delivery that can be formulated for systemic or local administration. The advantages of SABER may include reduced side effects, longer duration and smaller injection volume. Our first application is for controlled delivery of bupivacaine for post-operative pain relief (SABER-Bupivacaine), for which we own all worldwide rights. SABER-Bupivacaine is currently in Phase II clinical trials.

- ORADUR an oral sustained release gel-cap technology. We believe that ORADUR can transform short-acting oral capsule forms into oral sustained release technology products with the added benefit of being less prone to abuse. Our first application is Remoxy , a novel long-acting, abuse deterrent oral formulation of the opioid oxycodone, for which we have licensed worldwide rights to Pain Therapeutics, Inc. (Pain Therapeutics), which has in turn sublicensed the commercialization rights to King Pharmaceuticals, Inc. (King). Remoxy is currently in Phase III clinical trials. King and Pain Therapeutics have announced that they will commence a pivotal Phase III clinical trial in the first half of 2006.

- TRANSDUR Delivery System a proprietary transdermal patch technology. The advantages of TRANSDUR may include less potential for abuse, longer use per patch and smaller patch size. Our first application is for a transdermal sufentanil patch (TRANSDUR-Sufentanil) which we have licensed to Endo Pharmaceuticals for the U.S. and Canada. TRANSDUR-Sufentanil is currently in Phase II clinical trials.

- DURIN Biodegradable Implant a proprietary biodegradable drug-loaded implant that is absorbed into the body. DURIN enables parenteral (injectable) delivery over a period of weeks or months of both large and small molecules using our proprietary polymers. The advantages of DURIN may include small size, longer duration and constant rate of delivery. Our first application is Memryte, a novel long-acting potential therapy for the treatment of Alzheimer s disease using leuprolide, for which we have licensed worldwide rights to Voyager Pharmaceutical Corporation. Memryte is currently in Phase III clinical trials.

- DUROS® System an osmotic implant technology licensed to us for specified fields from ALZA Corporation, a Johnson & Johnson Company. DUROS is a miniature drug-dispensing subcutaneous pump which can be as small as a matchstick that can be used for therapies requiring systemic or site-specific administration of drug. The advantages of DUROS may include precise constant drug delivery of potent molecules. Our first application is CHRONOGESIC, designed to deliver sufentanil for a period of three months for treatment of chronic pain, which we have licensed to Endo Pharmaceuticals for the U.S. and Canada. CHRONOGESIC completed a pilot Phase III clinical trial. Clinical trials have been suspended pending system redesign.

- MICRODUR Biodegradable Microparticulates a microsphere injectable system.

NOTE: SABER , TRANSDUR , ORADUR , DURIN , CHRONOGESIC®, MICRODUR , ALZET® and LACTEL® are trademarks of DURECT Corporation. Other trademarks referred to belong to their respective owners.

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

Our pharmaceutical systems are suitable for providing long-term drug therapy because they store highly concentrated, stabilized drugs in a small volume and can protect the drug from degradation by the body. This, in combination with our ability to continuously deliver precise and accurate doses of a drug, allows us to extend the therapeutic value of a wide variety of drugs, including those which would otherwise be ineffective, too unstable, too potent or cause adverse side effects. In some cases, delivering the drug directly to the intended site of action can improve efficacy while minimizing unwanted side effects elsewhere in the body, which often limit the long-term use of many drugs. Our pharmaceutical systems can thus provide better therapy for chronic diseases or conditions by replacing multiple injection therapy or oral dosing, improving drug efficacy, reducing side effects and ensuring dosing compliance. Our pharmaceutical systems can improve patients quality of life by eliminating more repetitive treatments, reducing dependence on caregivers and allowing patients to lead more independent lives.

In addition to developing our own proprietary products, we also collaborate with pharmaceutical companies to develop and commercialize proprietary and enhanced pharmaceutical products based on our technologies.

Product Research and Development Programs

Our development efforts are focused on the application of our pharmaceutical systems technologies to potential products in a variety of chronic and episodic disease areas including pain, central nervous system, or CNS, disorders, cardiovascular disease and other chronic diseases. Our ongoing product research and development efforts in these areas are set forth in the following table:

Disease/Indication	Product	Collaborator	Technology Platform	Stage
Post Operative Pain	Controlled Release Injection of Local Anesthetic (SABER-Bupivacaine)	DURECT retains worldwide rights	SABER	Phase II
Chronic Pain	Transdermal sufentanil (TRANSDUR-Sufentanil)	Endo (U.S. & Canada)	TRANSDUR	Phase II
Chronic Pain	Oral controlled release oxycodone (Remoxy)	King/ Pain Therapeutics	ORADUR	Phase III
Alzheimer s Disease	Controlled Release Leuprolide Implant (Memryte)	Voyager	DURIN	Phase III
Chronic Pain	Systemic sufentanil (CHRONOGESIC)	Endo (U.S. & Canada)	DUROS	System redesign
Central Nervous System Disorders	Various	DURECT retains worldwide rights	SABER/DUROS/DURIN	Preclinical/Research Stages
Cardiovascular Disorders	Various	DURECT retains worldwide rights	SABER/DUROS/DURIN	Preclinical/Research Stage

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Local Post-Operative Pain

Market Opportunity. According to data published by the Center for Disease Control and Prevention, there are over 72 million ambulatory and inpatient procedures performed in the United States. We believe that more than 60% of patients who undergo surgery experience moderate to extreme post-operative pain. The current standard of care for post-surgical pain includes oral opiate and non-opiate analgesics, transdermal opiate patches and muscle relaxants. While oral analgesics can effectively control post-surgical pain, they commonly cause side effects such as drowsiness, constipation, cognitive impairment and other possible side effects. Effective pain management can be compromised if patients fail to adhere to recommended dosing regimens because they are sleeping or disoriented. We believe that the majority of post-surgical pain can be localized to the surgical site. Post-surgical pain can be treated effectively with local anesthetics; however, the usefulness of these current conventional medications is limited by their short duration of action.

Development Strategy. We are developing SABER-Bupivacaine, a sustained-release formulation of bupivacaine, a local anesthetic, using our SABER delivery system for the treatment of post-surgical pain. The physician would administer SABER-Bupivacaine at the time of surgery. Placed in the tissues immediately adjacent to the surgical site, this formulation is designed to provide sustained regional analgesia from a single dose. We believe that by delivering effective amounts of a potent analgesic to the location from which the pain originates, adequate pain control can be achieved with minimal exposure to the remainder of the body, and hence minimal side effects. SABER-Bupivacaine is intended to provide local analgesia of 3 days or more, which we believe coincides with the time period of greatest need for post-surgical pain control in most patients. We retain the full commercialization rights to SABER-Bupivacaine.

Clinical Program. We are currently conducting Phase II dose escalation trials in Australia and the United Kingdom designed for dose optimization of SABER-Bupivacaine. The Australian trial includes three cohorts, and the United Kingdom trial has two cohorts. Each trial will evaluate safety, pharmacokinetics and efficacy. We have completed dosing and analysis of all three cohorts in the Australian Phase II clinical trial, consisting of an aggregate of 81 patients, and we have announced positive preliminary results from this trial. Enrollment in the United Kingdom trial is ongoing.

The following summarizes the preliminary data from the Australian Phase II study as of December 2005:

Six patients were enrolled in cohort 1, fifteen patients were enrolled in cohort 2 and sixty patients in cohort 3.

Preliminary data indicate that all primary endpoints for the study were achieved, which include:

- Pharmacokinetic Evaluation of plasma bupivacaine concentrations showed that SABER-Bupivacaine achieved its target delivery profile of providing a delivery duration of over 72 hours with no burst upon injection.

- Safety No significant clinical adverse events or local or systemic toxicity were observed, and the injections were well tolerated by the patients.

- Established dose range for the product.

Other Preliminary Observations (Cohort 2 and Cohort 3, N=75)

- Using a standardized pain evaluation methodology that has been recognized by regulatory authorities to measure pain relief, patients treated with SABER-Bupivacaine reported a trend for better overall mean pain relief over the four days following treatment compared with patients treated with commercial bupivacaine (control).

- The SABER-Bupivacaine group had less pain intensity and required less supplemental opioid analgesics over the four days following treatment as compared to the control group.

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- The total numbers of doses of supplemental medication (opiate and non-opiate) were approximately the same in both the treatment and control groups; however, the SABER-Bupivacaine group utilized fifty percent (50%) less supplemental opioid medication for post-operative pain over the four days following treatment compared with the control group.

In the first quarter of 2006, the FDA accepted our Investigational New Drug (IND) application for SABER-Bupivacaine. In 2006, we intend to initiate additional Phase II studies in the U.S. for soft tissue and orthopedic surgical procedures, as well as continue our clinical studies outside of the U.S. We intend to initiate the Phase III clinical program in the second half of 2006.

Chronic Pain (Systemic)

Market Opportunity. Chronic pain, defined as lasting six months or longer, is usually the result of an ongoing condition or significant problem associated with chronic diseases, including cancer, various neurological and skeletal disorders and other ailments such as severe arthritis or a debilitating back injury. As the condition gets worse, the pain often gets worse. Also, long-lasting pain can affect the nervous system to the point where pain persists even if the condition that originally caused the pain is stabilized or improved. This is one reason patients often need stronger pain medication even if their underlying condition has been treated. Chronic pain affects as many as 34 million Americans annually. Worldwide opioid sales to treat chronic pain exceeded approximately $3.9 billion in 2004, of which OxyContin®, a brand name narcotic painkiller, and Duragesic®, a leading transdermal opioid product, accounted for approximately $1.8 billion and $2.1 billion in sales, respectively.

Development Strategy. We are developing several products for the chronic pain market:

- TRANSDUR-sufentanil, our proprietary transdermal patch licensed to Endo Pharmaceuticals (Endo) in the U.S. and Canada that is intended to provide sufentanil for a period of seven days from a single application;

- ORADUR-based oral sustained release, abuse deterrent opioid products, including Remoxy, licensed to Pain Therapeutics, which has in turn sublicensed the commercialization rights of these products to King; and

- CHRONOGESIC, a subcutaneous, implantable DUROS-based system licensed to Endo Pharmaceuticals in the U.S. and Canada that delivers sufentanil systemically at a constant rate for three months.

TRANSDUR-Sufentanil Patch

Our transdermal sufentanil patch (TRANSDUR-Sufentanil) under development is based on our proprietary TRANSDUR transdermal technology and is intended to provide continuous delivery of sufentanil for up to seven days from a single application, as compared to the three days of relief provided by currently available opioid patches. Sufentanil is an off-patent, highly potent opioid that is currently used in hospitals as an analgesic. We anticipate that the small size of our sufentanil patch (potentially as small as 1/5th the size of currently marketed transdermal fentanyl patches for a therapeutically equivalent dose) and longer duration of delivery may offer improved convenience and compliance for patients. Worldwide sales for Duragesic®, a leading transdermal fentanyl product, exceeded $2.1 billion in 2004.

In March 2005, we entered into an agreement with Endo granting Endo exclusive rights to develop, market and commercialize TRANSDUR-Sufentanil in the U.S. and Canada. We have received an initial payment of $10 million, and we will receive up to $35 million in

additional milestone payments if specified development and commercialization milestones are achieved. If commercialized, we will also receive royalties based on the sale of TRANSDUR-Sufentanil in the U.S. and Canada. We have also retained limited co-promotion rights to TRANSDUR-Sufentanil in the U.S. and Canada and full commercialization rights in the rest of the world. We continued to perform development activities for Endo with respect to TRANSDUR-Sufentanil throughout 2005.

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Clinical Program. In October 2004, we initiated a Phase I clinical trial for TRANSDUR-Sufentanil, consisting of a pharmacokinetic study in normal, healthy volunteers in Europe. The objectives of the clinical study were to determine the safety and tolerability of TRANSDUR-Sufentanil as well as to evaluate the pharmacokinetics of sufentanil following administration of TRANSDUR-Sufentanil. The study evaluated 24 subjects using TRANSDUR-Sufentanil. No clinically significant adverse events were reported. Some slight to moderate redness at patch site was observed by patients in the trial. Other results from the Phase I trial were as follows:

- the preliminary pharmacokinetics showed a rapid onset of the drug and the targeted plasma level over a 7-day period was achieved, and
- the clinical patches performed as designed.

We commenced the first clinical trial of the Phase II program for TRANSDUR-Sufentanil in February 2005. The clinical trial was an open-label study that was designed to evaluate the transition of chronic pain patients from Duragesic® (commercial fentanyl patch) to the TRANSDUR-Sufentanil patch. The clinical study also evaluated the pharmacokinetics and safety of repetitive applications of TRANSDUR-Sufentanil in patients for a period of up to four weeks. The clinical trial was conducted at two clinical sites (one in the United States and the other in Europe) and enrolled 13 adult patients in the primary study with malignant or non-malignant chronic pain. In December 2005, we announced positive preliminary results from this trial as follows:

Preliminary data indicate that all primary endpoints for the clinical trial were achieved, which include:

- Pharmacokinetic Evaluation of plasma level data indicate that TRANSDUR-Sufentanil performed as designed by achieving its target delivery profile of providing a rapid onset of drug and a delivery duration of over seven days. Targeted plasma levels over the consecutive four-week period (repetitive applications of TRANSDUR-Sufentanil) were achieved as intended.
- Safety The product was tolerated well with no apparent safety issues over the four-week treatment period.

Preliminary Efficacy Observations:

As this was an open label study, conclusions on efficacy cannot be drawn; on average, pain levels remained stable after the transition to TRANSDUR-Sufentanil.

Endo intends to conduct additional development activities, including clinical studies of TRANSDUR-Sufentanil in 2006.

ORADUR-Opioid Products In Development

Remoxy (ORADUR-Oxycodone)

Remoxy is an oral, long-acting oxycodone gelatin capsule under development with Pain Therapeutics, to which we have licensed exclusive, worldwide, development and commercialization rights under a development and license agreement entered into in December 2002. Pain Therapeutics has in turn sublicensed the commercialization rights of Remoxy to King. Remoxy is formulated with our ORADUR technology and incorporates several abuse-deterrent properties with the convenience of twice-a-day dosing. Oxycodone is also the active drug ingredient in OxyContin®, a brand name narcotic painkiller with annual sales exceeding $1.8 billion in 2004. We will receive payments if certain development and regulatory milestones are achieved. We also receive reimbursement for our research and development efforts on Remoxy and a manufacturing profit on our supply of key product excipients to Pain Therapeutics for use in Remoxy. In addition, if Remoxy is commercialized, we will receive royalties for Remoxy of between 6.0% to 11.5% of net sales depending the sales volumes.

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Clinical Program. Pain Therapeutics began the first Phase III clinical trial for Remoxy in December 2004 and in September 2005 announced positive results from this trial. Pain Therapeutics reported the following with respect to the trial:

- The study consisted of a randomized, double-blinded study designed to compare the safety and efficacy of Remoxy against placebo in osteoarthritic patients with moderate-to-severe chronic pain. Over 209 patients were enrolled in over 20 U.S. clinical sites. Patients were treated with Remoxy 20 mg or matching placebo twice daily over a four-week study period.

- The results demonstrated a statistically significant percent decrease in pain scores for patients using Remoxy as compared to placebo, as measured by a standard Likert Pain Scale. Patients also reported a statistically significant difference in quality of life using Remoxy as compared to placebo, as measured by as measured by a standard SF-12 Health Survey and in patients self-reported Quality of Analgesia. No drug-related safety issues were noted in the study. As expected, opioid-related adverse events (including nausea/vomiting, dizziness, pruritis (itching) and somnolence/sedation) and drop-out rates were higher in the Remoxy arm compared to placebo.

In February 2006, Pain Therapeutics and its commercialization sublicensee King reported that Remoxy had successfully completed a Special Protocol Assessment (SPA) with the FDA and that the parties were commencing a pivotal Phase III trial on Remoxy in 400 patients with severe chronic pain. According to Pain Therapeutics and King, under the terms of the SPA for Remoxy, one pivotal Phase III trial is required to file a New Drug Application. The randomized, double-blinded, placebo-controlled, multi-center pivotal trial will enroll 400 patients with moderate-to-severe osteoarthritic pain in multiple U.S. clinical sites. Following a titration period, patients will be randomized to either Remoxy (10-80 mg daily) or placebo for 12 weeks. The primary endpoint is reduction in pain scores over three months compared to baseline. King and Pain Therapeutics have announced that patient accrual is expected to begin shortly and continue through end of 2006.

Additional ORADUR- Opioid Products in Development

King and Pain Therapeutics have announced their intention to initiate Phase I clinical testing for the second ORADUR-based abuse deterrent sustained release oral formulation of an undisclosed opioid during the second half of 2006.

CHRONOGESIC

CHRONOGESIC, based on the DUROS technology, is intended for patients with chronic pain that is stable and opioid responsive and results from a variety of causes. CHRONOGESIC consists of a small titanium pump, about the size of a match stick, which is implanted under the skin of a patient in a simple out-patient procedure. Once implanted, CHRONOGESIC is designed to deliver sufentanil for period of up to three months from a single application. If approved for marketing and sale, CHRONOGESIC will provide an alternative to current therapies for the treatment of chronic pain such as pills and patches, as well as providing the potential advantages of physician controlled dosing, improved patient compliance and convenience and reduced potential for opioid abuse. We intend to develop a family of dosage strengths, tailored to meet market needs. CHRONOGESIC is being developed for the U.S. and Canadian markets in collaboration with Endo Pharmaceutics, to which we have granted exclusive commercialization rights pursuant to a development, commercialization and supply license agreement entered into effective November 2002. We will receive from Endo milestone payments if specified development milestones are achieved, and, if commercialized, we will receive royalties based on sale of CHRONOGESIC in the U.S. and Canada.

Clinical Program. We have completed an initial Phase I clinical trial, a Phase II clinical trial, a pilot Phase III clinical trial and a pharmacokinetic trial for CHRONOGESIC. In September 2001, DURECT presented data from a Phase II trial that enrolled 66 patients

experiencing chronic pain due to failed back surgery, cancer and other malignant and non-malignant causes. Patients were transitioned from their pre-study opioid medication to a six-week period of CHRONOGESIC therapy. In a post-study survey, 60% of patients indicated a preference

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for CHRONOGESIC over their pre-study medication and 35% of patients preferred their previous medication (5% of patients indicated no preference). CHRONOGESIC also demonstrated improvements in select side effects when compared to pre-study medication. In an 18 patient pilot Phase III study, the results of which were presented in March 2002, patients were successfully converted from the Duragesic® product, a 3-day transdermal fentanyl patch, to CHRONOGESIC without observing clinically-relevant side effects or adverse events.

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. Independently from the FDA s request for protocol changes, in October 2002, we started to implement manufacturing process enhancements to the CHRONOGESIC product to permit terminal sterilization of the product and system design enhancements to prevent a premature shutdown in the delivery of drug prior to the end of the intended three-month delivery period which was observed in a small fraction of units utilizing the previous system design. We are presently working to redesign the delivery system to address performance problems. We have stopped all clinical testing of CHRONOGESIC and will not resume clinical testing until the system design is completed.

Alzheimer s Disease

Market Opportunity. Alzheimer s disease is a progressive, degenerative and ultimately terminal brain disorder that gradually destroys a person s memory and ability to learn, reason, make judgments, communicate and carry out daily activities. There is currently no treatment that stops or materially slows the progression of Alzheimer s disease. As a result, it is one of the world s largest unmet medical needs. The global market for currently available Alzheimer s disease drugs is growing rapidly and was over $3 billion in 2004. The American Health Assistance Foundation estimates that approximately 18 million people worldwide, including approximately 4.5 million people in the United States, suffer from Alzheimer s disease.

Development Strategy. We are developing Memryte for the treatment of Alzheimer s disease in collaboration with Voyager, to which we have licensed exclusive, worldwide development and commercialization rights under a development and license agreement entered into in July 2002. Memryte uses our proprietary DURIN technology to provide sustained release of the peptide leuprolide acetate and is based on Voyager s patented method of treatment of Alzheimer s disease. We will receive from Voyager milestone payments if specified development milestones are achieved, and, if commercialized, royalties based on sale of the resulting product anywhere in the world.

Clinical Program. In December 2004, the FDA accepted an IND application and clinical protocol submitted by Voyager for Memryte. The trial consists of a pharmacokinetic study in normal, healthy volunteers, the objectives of which are to determine the safety and tolerability of the DURIN implant, as well as to evaluate the pharmacokinetic profile of the active agent (leuprolide acetate) following administration of the development product. Voyager completed enrollment of the clinical trial in January 2005. Voyager has completed dosing of one Phase I trial for Memryte, has performed one Phase II proof of concept trial using the active pharmaceutical agent for Memryte and has another such trial ongoing. Voyager has announced that the FDA has agreed to Voyager s clinical development plan and indicated that the results from Voyager s clinical trials to date were adequate to initiate Phase III trials. Voyager has initiated dosing for pivotal Phase III clinical studies using Memryte as an adjunctive therapy with acetyl cholinesterase inhibitors (ACIs) for the treatment of mild to moderate Alzheimer s disease. Voyager has stated its intention to complete patient enrollment for the first Phase III clinical study in the second half of 2006.

Central Nervous System Disorders

Market Opportunity. Millions of people suffer from chronic diseases and disorders of the central nervous system (CNS), including brain and spinal cord tumors, chronic pain, psychosis, epilepsy, spasticity, spinal meningitis, Parkinson s disease, and multiple sclerosis.

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We believe that there are over 39,000 new brain tumors diagnosed in the United States every year and approximately 350,000 patients living with primary brain tumors in the U.S., of which, about 170,000 are malignant. Current treatments for CNS tumors include radiation, resection and chemotherapy. Treatment success rates vary by tumor type, but are generally low, and the risk of side effects or disability is high. It is generally recognized that improvements in treating primary metastatic brain tumors are needed, particularly for those which are inoperable.

Schizophrenia, a disease of the brain that manifests itself through multiple signs and symptoms involving thought, perception and behavior, is another CNS disorder estimated to affect about 2.5 million patients in the U.S.; worldwide, the incidence is about 51 million. Patients typically begin exhibiting symptoms early in life and the illness is usually severe and long lasting, requiring lifelong treatment. Adherence to prescribed drug regimens is recognized as a significant treatment obstacle in the schizophrenic population. According to IMS, global sales of antipsychotics increased more than ten-fold following the introduction of the new drugs, from less than $500 million in 1991 to almost $5 billion in 2000. Opportunities exist to apply our pharmaceutical systems for treatment of these and other CNS disorders.

Development Strategy. We are developing our platform technologies for systemic and targeted delivery of drugs to treat select CNS disorders.

We are conducting preclinical research on a SABER-based injectable controlled release product to deliver a potent antipsychotic agent systemically in a controlled fashion, with a goal to deliver medication for 30 days from a single injection. We view our research activities as a proof-of-concept application of our drug delivery technologies to treat CNS disorders. Once we have demonstrated proof-of-concept, our long-term plan is to use our platform technologies with therapeutic agents to develop products for CNS disorders.

Cardiovascular Disease

Market Opportunity. Cardiovascular disease, principally heart disease and stroke, accounts for 41% of all deaths, or 960,000 fatalities, annually in the U.S. The aggregate annual cost of cardiovascular disease in the U.S., including treatment and lost productivity, is estimated at $287 billion.

Ischemic heart disease, one of the major forms of cardiovascular disease, is the leading cause of death worldwide. Existing treatments for ischemia, or insufficient blood flow to the heart muscle, include cardiovascular bypass, angioplasty and the use of cardiovascular stents and similar medical devices. While effective, these treatments are invasive, and ischemia returns in a significant number of patients. There is a need for less invasive and more long lasting treatments for ischemic heart disease.

Development Strategy. In collaboration with the University of Maastricht in The Netherlands, we are working to develop methods for treating ischemic heart disease and other chronic cardiovascular diseases through continuous delivery of drugs to the pericardial sac of the heart, a thin membrane that envelops the heart. To date, our research in animal models suggests that ischemic heart disease may be treated by the induction of new blood vessel growth as a way of regenerating normal blood flow to the heart and thereby restoring function to the diseased heart. Our research data showed that the delivery of a proprietary angiogenic factor directly to the pericardial sac of a test animal resulted in the growth of new blood vessels and increased bloodflow in the heart. Should we choose to develop and commercialize a pharmaceutical system using such proprietary angiogenic factor or other proprietary agent, we may be required to obtain a license to use such agent in our pharmaceutical system. Any required licenses may not be available to us on acceptable terms, if at all. See Risk Factors We may be required to obtain rights to certain drugs.

Other Development Programs

We intend to complete a Phase I clinical study for a new development project during the second half of 2006. DURECT retains full rights to this new development project.

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Industry Background

Chronic Diseases and Conditions

Although the pharmaceutical, biotechnology and medical device industries have played key roles in increasing life expectancy and improving health, many chronic, debilitating diseases continue to be inadequately addressed with current drugs or medical devices. Cardiovascular disease, cancer, neurodegenerative diseases, diabetes, arthritis, epilepsy and other chronic diseases claim the lives of millions of Americans each year. These illnesses are prolonged, are rarely cured completely, and pose a significant societal burden in mortality, morbidity and cost. The Centers for Disease Control estimates that the major chronic diseases are responsible for approximately 70% of all deaths in the U.S., and medical care costs for these conditions totaled more than $400 billion annually. Currently, more than 60% of total health care spending in the U.S. is devoted to the treatment of chronic diseases. Demographic trends suggest that, as the U.S. population ages, the cost of treating chronic diseases as a proportion of total health care spending will increase.

Current Approaches to Treatment

Drugs are available to treat many chronic diseases, but harmful side effects can limit prolonged treatment. In addition, patients with chronic diseases commonly take multiple medications, often several times a day, for the remainder of their lives. If patients fail to take drugs as prescribed, they often do not receive the intended benefits or may experience side effects, which are harmful or decrease quality of life. These problems become more common as the number of drugs being taken increases, the regimen of dosing becomes more complicated, or the patient ages or becomes cognitively impaired. It is estimated that only half of prescribed medicines are taken correctly.

The Pharmaceutical Industry. The pharmaceutical industry has traditionally focused on the chemical structure of small molecules to create drugs that can treat diseases and medical conditions. The ability to use these molecules as drugs is based on their potency, safety and efficacy. Therapeutic outcome and ultimately the suitability of a molecule as a drug depends to a large extent on how it gets into the body, distributes throughout the body, reacts with its intended site of action and is eliminated from the body. However, small molecules can act in diverse tissues throughout the body resulting in unwanted side effects.

Most drugs require a minimum level in blood and tissues to have significant therapeutic effects. Above a maximum level, however, the drug becomes toxic or has some unwanted side effects. These two levels define the therapeutic range of the drug. With conventional oral dosing and injections, typically a large quantity of drug is administered to the patient at one time, which results in high blood levels of drug immediately after dosing. Because of these high levels, the patient can be over-medicated during the period immediately following dosing, resulting in wasted drug and possible side effects. Due to distribution processes and drug clearance, the blood level of drug falls as time elapses from the last dose. For some duration, the patient is within the desired therapeutic range of blood levels. Eventually, the blood level of drug falls sufficiently such that the patient becomes under-medicated and experiences little or no drug effect until the next dose is administered.

The Biotechnology Industry. Over the past twenty-five years, the biotechnology revolution and the expanding field of genomics have led to the discovery of huge numbers of proteins and genes. Tremendous resources have been committed in the hope of developing drug therapies that would better mimic the body s own processes and allow for greater therapeutic specificity than is possible with small molecule drugs. Unfortunately, this huge effort has led to only a limited number of therapeutic products. The proteins and genes identified by the biotechnology industry are large, complex, intricate molecules, and many are unsuitable as drugs. If these molecules are given orally, they are often digested before they can have an effect; if given by injection, they may be destroyed by the body s natural processes before they can reach their intended sites of action. The body s natural elimination processes require frequent, high dose injections that may result in unwanted side effects. As a

result, the development of biotechnology molecules for the treatment of human diseases has been limited.

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The Drug Delivery Industry. In the last thirty-five years, a multibillion dollar drug delivery industry has developed on the basis that medicine can be improved by delivering drugs to patients in a precise, controlled fashion. Several commercially successful oral controlled release products, transdermal controlled release patches, and injectable controlled release formulations have been developed. These products demonstrate that the delivery system can be as important to the ultimate therapeutic value of a pharmaceutical product as the drug itself. However, drug delivery products on the market today can still be improved, for example, by providing reduced abuse potential, targeted delivery to minimize system effects and longer delivery durations where useful. Furthermore, traditional drug delivery products are generally not capable of administering biotechnology agents such as proteins, peptides and genes.

The Medical Device Industry. Advances in the field of medical device technology have dramatically improved device miniaturization and sophistication and allowed minimally invasive surgical access to remote locations within the body. For example, a coronary bypass patient can be treated with a stent in a procedure with a relatively short recovery, rather than with major surgery. Most devices, however, apply only mechanical solutions, rather than delivering chemical or biological agents.

The DURECT Solution: Pharmaceutical Systems

We are developing and commercializing pharmaceutical systems that will deliver the right drug to the right place in the right amount at the right time to treat chronic and episodic diseases and conditions. By integrating chemistry and engineering advancements, we can achieve what drugs or devices alone cannot. Our pharmaceutical systems enable optimized therapy for a given disease or patient population by controlling the rate and duration of drug administration. In addition, if advantageous for the therapy, our pharmaceutical systems can target the delivery of the drug to its intended site of action.

- The Right Drug: By precisely controlling the dosage or targeting delivery to a specific site, we can expand the therapeutic use of compounds that otherwise would be too potent to be administered systemically, do not remain in the body long enough to be effective, or have significant side effects when administered systemically. This flexibility allows us to work with a variety of drug candidates including small molecules, proteins, peptides or genes.

- The Right Place: In addition to enabling systemic delivery, if advantageous for the therapy, with precise placement of our proprietary catheters or biodegradable drug delivery formulations, we can design our pharmaceutical systems to deliver drugs directly to the intended site of action. This can ensure that the drug reaches the target tissue in effective concentrations, eliminate many side effects caused by delivery of drug to unintended sites in the body, and reduce the total amount of drug administered to the body.

- The Right Amount: Our pharmaceutical systems can automatically deliver drug dosages continuously within the desired therapeutic range for the duration of the treatment period, from days to up to one year, without the fluctuations in drug levels associated with conventional pills or injections. This can reduce side effects, eliminate gaps in drug therapy, conveniently ensure accurate dosing and patient compliance, and may reduce the total amount of drug administered to the body.

- The Right Time: Our pharmaceutical systems technologies are designed to minimize the need for intervention by the patient or care-giver and enhance dosing compliance. In addition to reducing the cost of care, continuous drug therapy frees the patient from repeated treatment or hospitalization, improving convenience and quality of life. Our systems are well-suited to deliver drug for the right period of time for the intended indication, whether for hours or days for acute indications or months or years for treating chronic, debilitating diseases such as chronic pain, cancer, heart disease, and neurodegenerative diseases. We believe that it is more effective to treat chronic diseases with continuous, long-term therapy than with alternatives such as multiple conventional injections or oral dosage forms that create short-term effects.

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DURECT Pharmaceutical Systems Technology

DURECT s pharmaceutical systems combine technology innovations from the drug delivery and medical device industries with proprietary pharmaceutical and biotechnology drug formulations. These capabilities can enable new drug therapies or optimize existing therapies based on a broad range of compounds, including small molecule pharmaceuticals as well as biotechnology molecules such as proteins, peptides and genes. We currently have six major technology platforms:

The SABER Delivery System

The SABER system is a patented controlled-release technology that can be formulated for systemic or local administration of active agents via the parenteral or oral route. We are researching and developing a variety of controlled-release products based on the SABER technology. These include injectable controlled release products for systemic and local delivery and oral products. We believe that our SABER system can provide the basis for the development of a state-of-the-art biodegradable, controlled-release injectable. The SABER system uses a high-viscosity base component, such as sucrose acetate isobutyrate (SAIB), to provide controlled release of the drug. When the high viscosity SAIB is formulated with drug, a biocompatible solvent and other additives, the resulting formulation is liquid enough to inject easily with standard syringes and needles. After injection of a SABER formulation, the solvent diffuses away, leaving a viscous depot. Depending on how it is formulated, the SABER system can successfully deliver therapeutic levels of a wide spectrum of drugs from one day to three months from a single injection. Based on research and development work to date, our SABER technology has shown the following advantages:

- *Peptide/Protein Delivery* The chemical nature of the SABER system tends to repel water and body enzymes from its interior and thereby stabilizes proteins and peptides. For this reason, we believe that the SABER system is well suited as a platform for biotechnology therapeutics based on proteins and peptides.

- *Less Burst* Typically, controlled release injections are associated with an initial higher release of drug immediately after injection (also called burst). Animal and human studies have shown that injectables based on the SABER technology can be associated with less post-injection burst than is typically associated with other commercially available injectable controlled release technologies.

- *High Drug Concentration* Drug concentration in a SABER formulation can be as high as 30%, considerably greater than is typical with other commercially available injectable controlled release technologies. As a result, smaller injection volumes are possible with this technology.

- *Ease of Administration* Prior to injection, SABER formulations are fairly liquid and therefore can be injected through small needles. Additionally, because of the higher drug concentration of SABER formulations, less volume is required to be injected. Small injection volumes and more liquid solutions are expected to result in easier, less painful administration.

- *Strong Patent Protection* The SABER system, SABER-like materials, and various applications of this technology to pharmaceuticals, medical devices and drug delivery are covered by United States and foreign patents. See Patents, Licenses and Proprietary Rights below.

- *Ease of Manufacture* Compared to microspheres and other polymer-based controlled release injectable systems, SABER is readily manufacturable at low cost.

The SABER Technology is the basis of SABER-Bupivacaine, which is currently in Phase II clinical testing. In our clinical studies thus far, SABER formulations have been observed to be safe and well-tolerated, and no significant side effects or adverse events were reported.

The TRANSDUR Transdermal Delivery System

Our TRANSDUR technology is a proprietary transdermal delivery system that enables delivery of drugs continuously for up to 7 days. The TRANSDUR technology is the basis for TRANSDUR-Sufentanil, which is currently in Phase II testing and which we have licensed to Endo in the U.S. and Canada.

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The ORADUR Sustained Release Gel Cap Technology

We are developing ORADUR sustained release oral technology based on our SABER technology. We believe that ORADUR can transform short-acting oral capsule dosage forms into sustained release oral products. Products based on our ORADUR technology (previously referred to as SABER oral gel cap technology) can take the form of an easy to swallow gelatin capsule that uses a high-viscosity base component such as sucrose acetate isobutyrate (SAIB) to provide controlled release of active ingredients for a period of 12 to 24 hours of drug delivery. Oral dosage forms based on the ORADUR gel-cap may also have the added benefit of being less prone to abuse (e.g., by crushing or alcohol or water extraction) than other controlled release dosage forms on the market today. ORADUR-based products can be manufactured by a simple process using conventional methods making them readily scalable. These properties have the potential to make ORADUR-based products an attractive option for pharmaceutical companies that seek to develop abuse resistant oral products. The ORADUR Technology is the basis of Remoxy, a novel long-acting oral formulation of the opioid oxycodone which is targeted to decrease the potential for oxycodone abuse currently under Phase III clinical testing by Pain Therapeutics and its commercialization sublicensee, King.

The DURIN Biodegradable Implant Technology

Our DURIN technology is a proprietary biodegradable implant that enables parenteral delivery of drugs from several weeks to six months or more using our Lactel® brand polymers and co-polymers of lactic and glycolic acid. The DURIN technology can deliver a wide variety of drugs including small and large molecule compounds. Our proprietary implant design allows for a variety of possible delivery profiles including constant rate delivery. Because DURIN implants are biodegradable, at the end of its delivery life, what remains of the DURIN implant is absorbed by the body. DURECT is researching and developing products based on the DURIN technology for a variety of chronic disease applications. The DURIN technology is the basis of Memryte for the treatment of Alzheimer s disease currently under Phase III clinical trials by Voyager.

The DUROS Technology

The DUROS system is a miniature drug-dispensing pump made out of titanium which can be as small as a wooden matchstick. We have licensed the DUROS system for specified fields of use from ALZA Corporation, a Johnson & Johnson Company, pursuant to a development and commercialization agreement entered into effective April 1998. The potential of the DUROS technology as a platform for providing drug therapy was demonstrated by the FDA s approval in March 2000 of ALZA s VIADUR® product (leuprolide acetate implant), a once-yearly implant for the palliative treatment of prostate cancer, the first approved product to incorporate the DUROS implant technology. The DUROS system can be used for therapies requiring systemic or site-specific administration of drug. To deliver drugs systemically as in our CHRONOGESIC product, the DUROS system is placed just under the skin, for example in the inner side of the upper arm, in an outpatient procedure that is completed in just a few minutes using local anesthetic. Removal or replacement of the product is also a simple and quick procedure completed in the doctor s office. To deliver drug to a specific site, we are developing proprietary miniaturized catheter technology that can be attached to the DUROS system to direct the flow of drug directly to a target organ, tissue or synthetic medical structure, such as a graft. The DUROS system is the basis of CHRONOGESIC under development in collaboration with Endo in the U.S. and Canada. Clinical trials have been suspended pending the redesign of the delivery system to address performance issues.

The MICRODUR Biodegradable Microparticulate Technology

Our MICRODUR technology is a patented biodegradable microparticulate depot injectable. We have experience in microencapsulation of a broad spectrum of drugs using our Lactel® brand polymers and co-polymers of lactic and glycolic acid. In our MICRODUR process, both

standard and proprietary polymers are used to entrap an active agent in solid matrices or capsules comprising particles generally between 10 and 125 microns in diameter. Through suitable choice of polymers and processing, sustained release from a few days to

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many months can be achieved. As with the DURIN technology, MICRODUR particles degrade fully in the body after the active agent is released. Our range of experience extends from manufacture of the polymer raw material to process and product development, scale up and cGMP manufacture.

DURECT Strategy

Our objective is to become a specialty pharmaceutical company by developing and commercializing pharmaceutical systems that address significant medical needs and improve patients quality of life. To achieve this objective, our strategy includes the following key elements:

Focus on Chronic Debilitating Medical Conditions. Many of the diseases that present the greatest challenges to medicine are chronic, debilitating diseases such as chronic pain, central nervous system disorders, cardiovascular disorders, cancer and degenerative neurological diseases. Our initial efforts will focus on using our versatile drug delivery platform technologies to develop products that address these diseases.

Minimize Product Development Risk and Speed Time-to-Market. Initially, we intend to minimize product development risk and speed time-to-market by using our drug delivery platform technologies to administer drugs for which medical data on efficacy and safety are available. This strategy reduces much of the development risk that is inherent in traditional pharmaceutical product discovery. We anticipate that we can expand the medical usefulness of existing well-characterized drugs in several ways:

- expand uses or create new uses for existing drugs by delivering drugs continuously for convenient long dosing intervals;
- create new uses for drugs which were previously considered to be too potent to be used safely by precisely controlling dosing or by delivering them directly to the site of action;
- enhance drug performance by minimizing side effects; and
- expand uses of drugs by delivering them to the target site.

We anticipate that our pharmaceutical systems can be more rapidly developed at lower cost than comparable products that are developed purely based on chemical solutions to the problems of efficacy, side effects, stability and delivery of the active agent. We believe that our ability to innovate more rapidly will allow us to respond more quickly to market feedback to optimize our existing pharmaceutical systems or develop line extensions that address new market needs.

Enable the Development of Pharmaceutical Systems Based on Biotechnology and Other New Compounds. We believe there is a significant opportunity for pharmaceutical systems to add value to therapeutic medicine by administering biotechnology products, such as proteins, peptides and genes. We believe our technologies will improve the specificity, potency, convenience and cost-effectiveness of proteins, peptides, genes and other newly discovered drugs. Our systems can enable these compounds to be effectively administered, thus allowing them to become viable medicines. We can address the stability and storage needs of these compounds through our advanced formulation technology and package them in a suitable pharmaceutical system for optimum delivery. Through continuous administration, the SABER, TRANSDUR, ORADUR, DURIN, DUROS and MICRODUR technology platforms may eliminate the need for multiple injections of these drugs. In addition, through the use of our proprietary miniature catheter technology or by precise placement of our proprietary biodegradable drug formulations, proteins and genes

can be delivered to specific tissues for extended periods of time, thus ensuring that large molecule agents are present at the desired site of action and minimizing the potential for adverse side effects elsewhere in the body.

Enable Product Development Through Strategic Collaborations. We believe that entering into selective collaborations with respect to our product development programs can enhance the success of our product development and commercialization, diversify our product portfolio and enable us to better manage our operating costs. Additionally, such collaborations enables us to leverage investment by our collaborators and reduce our net cash burn, while retaining significant economic rights.

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Build Our Own Sales and Marketing Organization. Our goal is to become a specialty pharmaceutical company where we commercialize products with significant market potential. To that end, we intend, over the course of a few years, to build up commercial, sales and marketing capability and other required infrastructure in focused specialty areas. We may still choose to enter into strategic alliances from time to time consistent with our strategy to leverage the established sales organizations of third-party collaborators to achieve greater market penetration for some of our products than we could on our own. If we choose to enter into third-party collaborations to commercialize our pharmaceutical systems, we believe we have the flexibility to enter into these alliances under circumstances that allow us to retain greater economic participation because our pharmaceutical systems combine drugs for which medical data on efficacy and safety are available with proven technology platforms.

Third-Party Collaborations

We have entered into the following collaboration agreements:

Pain Therapeutics, Inc. In December 2002, we entered into an exclusive agreement with Pain Therapeutics to develop and commercialize on a worldwide basis oral sustained release, abuse deterrent opioid products incorporating four specified opioid drugs using our ORADUR technology. The agreement also provides Pain Therapeutics with the exclusive right to commercialize products developed under the agreement on a worldwide basis. In connection with the execution of the agreement, Pain Therapeutics paid us an upfront fee. In November 2005, Pain Therapeutics sublicensed the commercialization rights to products developed under the agreement to King. In December 2005, we amended our agreement with Pain Therapeutics in order to specify our obligations with respect to the supply of key excipients for use in the licensed products. Under the agreement, as amended, we are responsible for formulation development, supply of selected key excipients used in the manufacture of licensed product and other specified tasks. We will receive additional payments if certain development and regulatory milestones are achieved. We receive reimbursement for our research and development efforts on the licensed products and a manufacturing profit on our supply of key product excipients to Pain Therapeutics for use in the licensed products. In addition, if commercialized, we will receive royalties for Remoxy and other licensed products which do not contain an opioid antagonist of between 6.0% to 11.5% of net sales of the product depending on the sales volumes. This agreement can be terminated by either party for material breach by the other party and by Pain Therapeutics without cause.

Voyager Pharmaceutical Corporation. In July 2002, we entered into a development and commercialization agreement with Voyager. Under the terms of the agreement, we will collaborate with Voyager to develop a product using our DURIN technology to provide sustained release of leuprolide based on Voyager s patented method of treatment of Alzheimer s disease. The agreement also provides Voyager with the right to commercialize the resulting product on a worldwide basis. We are responsible for preclinical development, product manufacture and other specified tasks. We will receive payments if certain development and regulatory milestones are achieved, and receive payments for our research and development efforts. If Memryte is commercialized, we will receive royalties based on product sales. This agreement can be terminated by either party for material breach by the other party and by Voyager without cause.

Endo Pharmaceuticals Inc. (CHRONOGESIC). In November 2002, we entered into a development, commercialization and supply license agreement with Endo under which the companies will collaborate on the development and commercialization of CHRONOGESIC for the U.S. and Canada. The agreement was amended in January 2004, in November 2004 and again in January 2006 to take into account the increase in the CHRONOGESIC development program timeline due to DURECT s implementation of necessary design and manufacturing enhancements. In connection with the execution of the agreement in November 2002, Endo purchased 1,533,742 shares of newly issued common stock of DURECT at an aggregate purchase price of approximately $5.0 million. Under the terms of the agreement, as amended, we will be responsible for the CHRONOGESIC product s design and development. Endo shall not be responsible for any development costs for CHRONOGESIC prior to May 1, 2007. Commencing on May 1, 2007, unless the agreement is earlier terminated by Endo, Endo will fund 50% of the ongoing development costs and will reimburse us for a portion of

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our prior development costs for CHRONOGESIC upon the achievement of certain milestones. Development- based milestone payments made by Endo under this agreement could total up to $52 million. Under the agreement, Endo has licensed exclusive promotional rights to CHRONOGESIC 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 product launch costs. We will be responsible for the manufacture of CHRONOGESIC. If commercialized, we will share profits from the commercialization of CHRONOGESIC in the U.S. and Canada with Endo based on the financial performance of CHRONOGESIC. Based on our projected financial performance of CHRONOGESIC in the U.S. and Canada, we anticipate that our share of such profits, if CHRONOGESIC is commercialized, will be approximately 50%. Our agreement with Endo provides each party with specified termination rights. In particular, our agreement can be terminated by Endo in the event that (i) we have not delivered to Endo on or before March 31, 2007 a written notice that a human pharmacokinetic trial had been completed with CHRONOGESIC, together with a full study report of the results of the trial or (ii) Endo, determines, in its sole discretion, to terminate the agreement during the sixty-day period after our delivery of our notice, provided, that, in each case Endo delivers to us its written notice of termination prior to April 30, 2007.

Endo Pharmaceuticals Inc. (TRANSDUR-Sufentanil). On March 10, 2005, we entered into a license agreement with Endo under which we granted to Endo the exclusive right to develop, market and commercialize TRANSDUR-Sufentanil in the U.S. and Canada. Under the terms of the agreement, Endo will assume all remaining development and regulatory filing responsibility in the U.S. and Canada, including the funding thereof. We will perform all formulation development for Endo unless we default on such obligations and we will be reimbursed for our fully allocated cost in performance of such work. Endo will also be responsible and pay for the manufacture, marketing, sales and distribution of TRANSDUR-Sufentanil in the U.S. and Canada. Endo has paid us an upfront fee of $10 million, and we will receive additional payments of up to approximately $35 million in the aggregate if predetermined regulatory and commercial milestones are achieved. If commercialized, Endo will also pay us product royalties based on the net sales of TRANSDUR-Sufentanil under the agreement. We have the right to co-promote TRANSDUR-Sufentanil under terms specified in the agreement. The agreement also contains terms and conditions customary for this type of arrangement, including representations, warranties and indemnities. The agreement shall continue in effect until terminated. The agreement provides each party with specified termination rights, including the right of each party to terminate the agreement upon material breach of the agreement by the other party. In addition, Endo shall have the right to terminate the agreement at any time without cause subject to a specified notice period and due to adverse product events, legal impediment or the issuance of a final, non-appealable court order enjoining Endo from selling TRANSDUR-Sufentanil in the U.S. and Canada as a result of an action for patent infringement by a third party, provided that in the latter instance, we will be required to pay Endo a termination fee ranging from $5 million to $10 million, depending on the date of termination. We have the right to terminate the agreement in the event that Endo pursues directly or indirectly any proceeding seeking to have any of our TRANSDUR-Sufentanil related patents revoked or declared invalid, unpatentable or unenforceable.

NeuroSystec Corporation. In May 2004, we entered into an exclusive license agreement with NeuroSystec Corporation (NeuroSystec), a privately held corporation founded by Al Mann, under which we granted to NeuroSystec exclusive worldwide rights to develop and commercialize products designed for the treatment of tinnitus and to improve post-operative recovery and tolerance of surgical implantation of cochlear devices using specified DURECT proprietary drug treatment methods and drug delivery technologies to deliver precise doses of appropriate medications directly to the middle or inner ear. The first development product is currently in pre-clinical development. We are responsible for formulation development of products utilizing our drug delivery platforms and manufacture and supply of product components consisting of our drug delivery platforms. We will receive certain milestone payments if certain development and commercialization milestones are achieved, as well as royalties based on product sales if products are commercialized under the agreement. This agreement can be terminated by either party for material breach by the other party and by NeuroSystec without cause. In connection with the agreement, we received equity constituting a minority ownership interest in NeuroSystec.

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Commercial Businesses

ALZET

We currently make and sell the ALZET® product on a worldwide basis. We market the ALZET product through a direct sales force in the U.S. and through a network of distributors outside the U.S.

The ALZET product is a miniature, implantable osmotic pump used for experimental research in mice, rats and other laboratory animals. These pumps are neither approved nor intended for human use. ALZET pumps continuously deliver drugs, hormones and other test agents at controlled rates from one day to four weeks without the need for external connections, frequent handling or repeated dosing. In laboratory research, these infusion pumps can be used for systemic administration when implanted under the skin or in the body. They can be attached to a catheter for intravenous, intracerebral, or intra-arterial infusion or for targeted delivery, where the effects of a drug or test agent are localized in a particular tissue or organ.

We acquired the ALZET product and assets used primarily in the manufacture, sale and distribution of this product from ALZA in April 2000. We believe that the ALZET business provides us with innovative design and application opportunities for potential new products.

Polymer Supply

We currently design, develop and manufacture a wide range of standard and custom biodegradable polymers based on lactide, glycolide and caprolactone under the LACTEL® brand for pharmaceutical and medical device clients for use as raw materials in their products. These materials are manufactured and sold by us directly from our facility in Pelham, Alabama and are used by us and our third-party customers for a variety of controlled-release and medical-device applications, including several FDA-approved commercial products. Until December 31, 2004, this business was conducted by our wholly owned subsidiary, Absorbable Polymers International Corporation (API), formerly known as Birmingham Polymers Inc., an Alabama corporation. API was merged with and into DURECT on December 31, 2004.

Marketing and Sales

Historically, we have established strategic distribution and marketing alliances for our pharmaceutical systems to take advantage of the established sales organizations that certain pharmaceutical companies have in markets we are targeting. However, our goal is to become a specialty pharmaceutical company that commercializes its own products with significant market potential. To that end, we intend, over the course of a few years, to build up commercial, sales and marketing capability and other required infrastructure in focused specialty areas although there can be no assurance that we will be able to do so. We may still choose to enter into strategic alliances from time to time consistent with our strategy to leverage the established sales organizations of third-party collaborators to achieve greater market penetration for some of our products than we could on our own. If we choose to enter into third-party collaborations to commercialize our pharmaceutical systems, we believe we have the flexibility to enter into these alliances under circumstances that allow us to retain greater economic participation because our pharmaceutical systems combine drugs for which medical data on efficacy and safety are available with a proven technology platform.

We market and sell our ALZET product in the U.S. through a direct sales force, and we have a network of distributors for this product outside of the U.S.

Suppliers

We purchase sucrose acetate isobutyrate, a raw material for our SABER-based pharmaceutical systems, including SABER-Bupivacaine and Remoxy, pursuant to a supply agreement with Eastman Chemical Company. We also purchase sufentanil for CHRONOGESIC pursuant to a supply agreement with Mallinckrodt, Inc. We believe that these agreements will provide a sufficient supply of these raw materials to meet our needs for the

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foreseeable future. We do not have in place long term supply agreements with respect to all of the components of any of our pharmaceutical systems, however, and are subject to the risk that we may not be able to procure all required components in adequate quantities, within acceptable time frames or at reasonable cost.

Customers

A substantial portion of our product revenues is derived from sale of the ALZET product line. Until such time that we are able to bring our pharmaceutical systems to market, if at all, we expect this trend to continue. We also receive revenue from collaborative research and development arrangements with our third-party collaborators. For the year ended December 31, 2005, revenues from our collaborative agreements with Pain Therapeutics (Remoxy), Endo (TRANSDUR-Sufentanil) and Voyager (DURIN-Leuprolide (Memryte)) represented 17%, 26% and 25% of our total revenues, respectively. At December 31, 2005, three customers accounted for 27%, 26% and 23% of our gross accounts receivables. At December 31, 2004, two customers accounted for 40% and 26% of our gross accounts receivables.

Manufacturing

The process for manufacturing our pharmaceutical systems is technically complex, requires special skills, and must be performed in a qualified facility. Our manufacturing facility in Cupertino, CA is a functional multi-discipline site that we have used to manufacture research and clinical supplies of several of our pharmaceutical systems under GMP, including SABER-Bupivacaine, Memryte, TRANSDUR-sufentanil, Remoxy and CHRONOGESIC. We have recently made significant site improvements and equipment installations to upgrade and expand our manufacturing capabilities. In the future, we intend to develop additional manufacturing capabilities for our pharmaceutical systems and components to meet our demands and those of our third party collaborators by contracting with third party manufacturers and by construction of additional manufacturing space at our current facilities in Cupertino, CA, Vacaville, CA and Pelham, AL. We manufacture our ALZET product at our Vacaville, CA facility.

Patents, Licenses and Proprietary Rights

Our success depends in part on our ability to obtain patents, to protect trade secrets, to operate without infringing upon the proprietary rights of others and to prevent others from infringing on our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. As of February 28, 2006, we held 26 issued U.S. patents and 69 issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have 36 pending U.S. patent applications and have filed 55 patent applications under the Patent Cooperation Treaty, from which 101 national phase applications are currently pending in Europe, Australia, Japan, Canada, Mexico, New Zealand, Brazil, Israel, India, Hong Kong and China. Our patents expire at various dates starting in the year 2012.

Proprietary rights relating to our planned and potential products will be protected from unauthorized use by third parties only to the extent that they are covered by valid and enforceable patents or are effectively maintained as trade secrets. Patents owned by or licensed to us may not afford protection against competitors, and our pending patent applications now or hereafter filed by or licensed to us may not result in patents being issued. In addition, the laws of certain foreign countries may not protect our intellectual property rights to the same extent as do the laws of the U.S.

The patent positions of biopharmaceutical companies involve complex legal and factual questions and, therefore, their enforceability cannot be predicted with certainty. Our patents or patent applications, or those licensed to us, if issued, may be challenged, invalidated or circumvented, and the rights granted thereunder may not provide proprietary protection or competitive advantages to us against competitors with similar technology.

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Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in existence for only a short period following commercialization, thus reducing any advantage of the patent, which could adversely affect our ability to protect future product development and, consequently, our operating results and financial position.

Because patent applications in the U.S. are maintained in secrecy for at least 18 months after filing and since publication of discoveries in the scientific or patent literature often lag behind actual discoveries, we cannot be certain that we were the first to make the inventions covered by each of our issued or pending patent applications or that we were the first to file for protection of inventions set forth in such patent applications.

Our planned or potential products may be covered by third-party patents or other intellectual property rights, in which case we would need to obtain a license to continue developing or marketing these products. Any required licenses may not be available to us on acceptable terms, if at all. If we do not obtain any required licenses, we could encounter delays in product introductions while we attempt to design around these patents, or could find that the development, manufacture or sale of products requiring such licenses is foreclosed. Litigation may be necessary to defend against or assert such claims of infringement, to enforce patents issued to us, to protect trade secrets or know-how owned by us, or to determine the scope and validity of the proprietary rights of others. In addition, interference proceedings declared by the U.S. Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications. Litigation or interference proceedings could result in substantial costs to and diversion of effort by us, and could have a material adverse effect on our business, financial condition and results of operations. These efforts by us may not be successful.

We may rely, in certain circumstances, on trade secrets to protect our technology. However, trade secrets are difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees and certain contractors. There can be no assurance that these agreements will not be breached, that we will have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may also arise as to the rights in related or resulting know-how and inventions.

Government Regulation

The Food and Drug Administration. The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, distribution, record keeping, approval, advertising and promotion of our products. We believe that our initial pharmaceutical systems will be regulated as drugs by the FDA rather than as biologics or devices, whereas later pharmaceutical systems may be regulated as combination products with a device designation for all or some of the final product components.

The process required by the FDA under the new drug provisions of the Federal Food, Drug and Cosmetics Act before our initial pharmaceutical systems may be marketed in the U.S. generally involves the following:

- preclinical laboratory and animal tests;

- submission of an IND application which must become effective before clinical trials may begin;

- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed pharmaceutical in our intended use; and

- FDA approval of a new drug application.

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The testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that any approval will be granted on a timely basis, if at all. Even though several of our pharmaceutical systems utilize active drug ingredients that are commercially marketed in the United States in other dosage forms, we need to establish safety and effectiveness of those active ingredients in the formulation and dosage forms that we are developing.

Preclinical tests include laboratory evaluation of the product, its chemistry, formulation and stability, as well as animal studies to assess the potential safety and efficacy of the pharmaceutical system. We then submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of an IND, which must become effective before we may begin human clinical trials. Each subsequent new clinical protocol must also be submitted to the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the trials as outlined in the IND and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. Our submission of an IND may not result in FDA authorization to commence clinical trials. Further, an independent Institutional Review Board at each medical center proposing to conduct the clinical trials must review and approve any clinical study as well as the related informed consent forms and authorization forms that permit us to use individually identifiable health information of study participants.

Human clinical trials are typically conducted in three sequential phases which may overlap:

- PHASE I: The drug is initially introduced into healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion.

- PHASE II: Involves studies in a limited patient population to identify possible adverse effects and safety risks, to determine the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- PHASE III: When Phase II evaluations demonstrate that a dosage range of the product is effective and has an acceptable safety profile, Phase III trials are undertaken to further evaluate dosage, clinical efficacy and to further test for safety in an expanded patient population, at multiple, geographically dispersed clinical study sites.

In the case of products for severe diseases, such as chronic pain, or life-threatening diseases such as cancer, the initial human testing is often conducted in patients with disease rather than in healthy volunteers. Since these patients already have the target disease or condition, these studies may provide initial evidence of efficacy traditionally obtained in Phase II trials, and thus these trials are frequently referred to as Phase I/II trials. We cannot be certain that we will successfully complete Phase I, Phase II or Phase III testing of our pharmaceutical systems within any specific time period, if at all. Furthermore, the FDA or the Institutional Review Board or the sponsor may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. During the clinical development of products, sponsors frequently meet and consult with the FDA in order to ensure that the design of their studies will likely provide data both sufficient and relevant for later regulatory approval; however, no assurance of approvability can be given by the FDA.

The results of product development, preclinical studies and clinical studies are submitted to the FDA as part of a new drug application, or NDA, for approval of the marketing and commercial shipment of the product. Submission of an NDA requires the payment of a substantial user fee to the FDA, and although the agency has defined user fee goals for the time in which to respond to sponsor applications, we cannot assure you that the FDA will act in any particular timeframe. The FDA may deny a new drug application if the applicable regulatory criteria are not satisfied or may require additional clinical data. Even if such data is submitted, the FDA may ultimately decide that the new drug application does not satisfy the criteria for approval. Once issued, the FDA may withdraw product approval if compliance with regulatory standards is not maintained or if safety problems

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occur after the product reaches the market. Requirements for additional Phase IV studies to confirm safety and effectiveness in a broader commercial use population may be imposed as a condition of marketing approval. In addition, the FDA requires surveillance programs to monitor approved products which have been commercialized, and the agency has the power to require changes in labeling or to prevent further marketing of a product based on the results of these post-marketing programs. Any comparative claims that we would like to make for our products vis-à-vis other dosage forms or products will need to be substantiated generally by two adequate and well-controlled head-to-head clinical trials.

In addition to the drug approval requirements applicable through the Center for Drug Evaluation and Research (CDER), the FDA, through its Office of Combination Products, may require an intercenter consultation review by the Center for Devices and Radiological Health (CDRH), in order to determine a product s Primary Method of Action (PMOA). This request for consultation may be based on the device-like nature of a number of aspects of the DUROS technology.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years and the actual time required may vary substantially, based upon the type, complexity and novelty of the pharmaceutical product. Government regulation may delay or prevent marketing of potential products for a considerable period of time and impose costly procedures upon our activities. We cannot be certain that the FDA or any other regulatory agency will grant approval for any of our pharmaceutical systems under development on a timely basis, if at all. Success in preclinical or early stage clinical trials does not assure success in later stage clinical trials. Data obtained from preclinical and clinical activities is not always conclusive and may be susceptible to varying interpretations which could delay, limit or prevent regulatory approval. Evolving safety concerns can result in the imposition of new requirements for expensive and time consuming tests, such as for QT interval cardiotoxicity testing. Even if a product receives regulatory approval, the approval may be significantly limited to specific indications. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Any pharmaceutical systems that we may develop and obtain approval for would also be subject to adverse findings of the active drug ingredients being marketed in different dosage forms and formulations. Delays in obtaining, or failures to obtain regulatory approvals would have a material adverse effect on our business. Marketing our pharmaceutical systems abroad will require similar regulatory approvals and is subject to similar risks. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

Any pharmaceutical systems manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and state agencies for compliance with good manufacturing practices, which impose procedural and documentation requirements upon us and our third party manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the GMP regulations and other FDA regulatory requirements.

The FDA regulates drug labeling and promotion activities. The FDA has actively enforced regulations prohibiting the marketing of products for unapproved uses, and federal and state authorities are also actively litigating against sponsors who promote their drugs for unapproved uses under various fraud and abuse and false claims act statutes. We and our pharmaceutical systems are also subject to a variety of state laws and regulations in those states or localities where our pharmaceutical systems are or will be marketed. Any applicable state or local regulations may hinder our ability to market our pharmaceutical systems in those states or localities. We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

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The FDA s policies may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our potential pharmaceutical systems. Moreover, increased attention to the containment of health care costs in the U.S. and in foreign markets could result in new government regulations that could have a material adverse effect on our business. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the U.S. or abroad.

The Drug Enforcement Administration. The Drug Enforcement Administration (DEA) regulates chemical compounds as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. Certain active ingredients in TRANSDUR-sufentanil, Remoxy and CHRONOGESIC are listed by the DEA as Schedule II under the Controlled Substances Act of 1970. Consequently, their manufacture, research, shipment, storage, sale and use are subject to a high degree of oversight and regulation. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription. Furthermore, the amount of Schedule II substances we can obtain for clinical trials and commercial distribution is limited by the DEA and our quota may not be sufficient to complete clinical trials or meet commercial demand. There is a risk that DEA regulations may interfere with the supply of the drugs used in our clinical trials, and, in the future, our ability to produce and distribute our products in the volume needed to meet commercial demand.

Competition

We may face competition from other companies in numerous industries including pharmaceuticals, medical devices and drug delivery. SABER-Bupivacaine, TRANSDUR-Sufentanil, Remoxy and CHRONOGESIC, if approved, will compete with currently marketed oral opioids, transdermal opioid patches, and implantable and external infusion pumps which can be used for infusion of opioids. Products of these types are marketed by Purdue Pharma, Knoll, Janssen, Medtronic, Endo Pharmaceuticals, AstraZeneca, Arrow International, Tricumed and others, including compounding pharmacies operating under state pharmacy licensure. Numerous companies are applying significant resources and expertise to the problems of drug delivery and several of these are focusing or may focus on delivery of drugs to the intended site of action, including Alkermes, Atrix, Inovio, The Liposome Company, Focal, I-Flow and others. Some of these competitors may be addressing the same therapeutic areas or indications as we are. Our current and potential competitors may succeed in obtaining patent protection or commercializing products before us.

If approved, Memryte will compete against the five drugs currently approved for the treatment of Alzheimer s disease. Four of the drugs are ACIs, including: Aricept, marketed by Pfizer, Inc. and Eisai Company, Ltd.; Exelon, marketed by Novartis AG; Reminyl, marketed by Shire Pharmaceuticals Group plc and Janssen Pharmaceutical Products, LP; and Cognex, marketed by First Horizon Pharmaceutical Corporation. The fifth drug, Namenda, marketed by Forest Pharmaceuticals, Inc., is an NMDA receptor antagonist. In addition, Memryte could face competition from other leuprolide acetate products that are already on the market or may later be approved for other indications, if they are used or prescribed off label for Alzheimer s disease.

Any products we develop using our pharmaceutical systems technologies will compete in highly competitive markets. Many of our potential competitors in these markets have greater development, financial, manufacturing, marketing, and sales resources than we do and we cannot be certain that they will not succeed in developing products or technologies which will render our technologies and products obsolete or noncompetitive. In addition, many of those potential competitors have significantly greater experience than we do in their respective fields.

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Corporate History, Headquarters and Website Information

DURECT Corporation was incorporated in Delaware in February 1998. We completed our initial public offering on September 28, 2000. Our principal executive offices are located at 2 Results Way, Cupertino, California, 95014. Our telephone number is (408) 777-1417, and our web site address is www.durect.com. We make our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports available free of charge on our web site as soon as reasonably practicable after we file these reports with the Securities and Exchange Commission. Durect Corporation s Code of Ethics can be found free of charge on our website.

Employees

As of December 31, 2005 we had 138 employees, including 86 in research and development, 20 in manufacturing and 32 in selling, general and administrative. From time to time, we also employ independent contractors to support our research, development and administrative organizations. None of our employees are represented by a collective bargaining unit, and we have never experienced a work stoppage. We consider our relations with our employees to be good.

Executive Officers of the Registrant.

The executive officers of DURECT Corporation and their ages as of February 28, 2006 are as follows:

Name	Age	Position
Felix Theeuwes, D.Sc.	68	Chairman, Chief Scientific Officer and Director
James E. Brown, D.V.M.	49	President, Chief Executive Officer and Director
Jean I Liu	37	Senior Vice President, General Counsel and Secretary
Paula Mendenhall, Ph.D.	62	Senior Vice President, Operations
Su Il Yum, Ph.D.	66	Senior Vice President, Engineering
Steven Halladay, Ph.D.	58	Vice President, Clinical and Regulatory
Jian Li	35	Vice President, Finance and Corporate Controller
Andrew R. Miksztal, Ph.D.	54	Vice President, Pharmaceutical Systems Research and Development

Felix Theeuwes, D.Sc. co-founded DURECT in February 1998 and has served as our Chairman, Chief Scientific Officer and a Director since July 1998. Prior to that, Dr. Theeuwes held various positions at ALZA Corporation, a pharmaceutical and drug delivery company which is an affiliate of us, including President of New Ventures from August 1997 to August 1998, President of ALZA Research and Development from 1995 to August 1997, President of ALZA Technology Institute from 1994 to April 1995 and Chief Scientist from 1982 to June 1997. Dr. Theeuwes is also a director of Inovio Biomedical Corporation, a medical device company. Dr. Theeuwes holds a D.Sc. degree in Physics from the University of Leuven (Louvain), Belgium. He also served as a post-doctoral fellow and visiting research assistant professor in the Department of Chemistry at the University of Kansas and has completed the Stanford Executive Program.

James E. Brown, D.V.M. co-founded DURECT in February 1998 and has served as our President, Chief Executive Officer and a Director since June 1998. He previously worked at ALZA Corporation as Vice President of Biopharmaceutical and Implant Research and Development from

June 1995 to June 1998. Prior to that, Dr. Brown held various positions at Syntex Corporation, a pharmaceutical company, including Director of Business Development from May 1994 to May 1995, Director of Joint Ventures for Discovery Research from April 1992 to May 1995, and held a number of positions including Program Director for Syntex Research and Development from October 1985 to March 1992. Dr. Brown holds a B.A. from San Jose State University and a D.V.M. (Doctor of Veterinary Medicine) from the University of California, Davis where he also conducted post-graduate work in pharmacology and toxicology.

Jean I Liu has served as our Senior Vice President and General Counsel since February 2003. She was appointed Secretary of the corporation in March 2004. She served as our Vice President of Legal and General

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Counsel from February 1999 to February 2003. Previously, from October 1998, Ms. Liu served as our Vice President of Legal. Prior to that, Ms. Liu worked as an attorney at Venture Law Group, a law firm, from May 1997 to October 1998. Ms. Liu worked as an attorney at Pillsbury Madison & Sutro LLP, a law firm, from September 1993 to May 1997. Ms. Liu holds a B.S. in Cellular & Molecular Biology from University of Michigan, an M.S. in Biology from Stanford University and a J.D. from Columbia University School of Law. Ms. Liu is a member of the State Bar of California and is admitted to practice before the United States Patent and Trademark Office.

Paula Mendenhall, Ph.D. has served as our Senior Vice President of Operations since January 2005. Prior to joining DURECT, Dr. Mendenhall was an independent consultant for various pharmaceutical companies for in-house and outsourcing of pharmaceutical manufacturing, including development of manufacturing strategies and plans and development and training of personnel. From 1997 to 2000, Dr. Mendenhall served as Vice President, Group Vice President and President of Oread Pharmaceutical Manufacturing at Oread Inc. From 1979 to 1997, Dr. Mendenhall served in a variety of roles for Hoffmann-La Roche Inc./Syntex, including in the areas of manufacturing, quality assurance, finance, planning and facilities, as well as provided technical assistance and support to Syntex Global Operations for marketed products and new product launches. Dr. Mendenhall received a Pharm D. degree from the University of California, San Francisco, and is a member of the American Association of Pharmaceutical Scientists (AAPS), the American Pharmaceutical Association and the Society of Cosmetic Chemists.

Dr. Su IL Yum, Ph.D. has served as our Senior Vice President, Engineering since December 2003. Previously, Dr. Yum served as our Vice President of Engineering from December 1999 to December 2003. Prior to joining DURECT, Dr. Yum served as Senior Technical Advisor at Amira Medical in Scotts Valley, California, where he participated in the development of a pain-free blood glucose detector called AtLast®. Prior to joining Amira, he held a number of senior positions in project management and engineering at Alza Corporation. Dr. Yum earned his Ph.D. degree in Chemical Engineering from the University of Minnesota, and completed a Post-doctoral research in Biomedical Engineering at the University of Utah. Dr. Yum is a Fellow of the AAPS.

Steven Halladay, Ph.D. has served as Vice President of Clinical and Regulatory since April 2003. Prior to that, Dr. Halladay served as our Medical Director from November 2002 and April 2003. Prior to joining DURECT, Dr. Halladay held various positions at Clingenix, Inc., Research Services, Inc., Hoffmann-La Roche, Syntex Laboratories, ALZA Corporation and Dynapol. Following 20 years with Syntex and Hoffmann-La Roche, Dr. Halladay founded Research Services, Inc., an innovative pharmaceutical research company. After 5 years as President and CEO, Research Services merged with Clingenix, Inc. As Senior Executive Vice President at Clingenix his corporate responsibilities included pharmacogenomic program development, new business development, strategic alliances/relationships, and all aspects associated with clinical research and pharmacogenomic medical application. Dr. Halladay holds a B.S. from Southern Utah University, M.S. in Toxicology from University of Arizona and a Ph.D. from the Arizona Medical Center, Tucson, Arizona in Clinical Pharmacology.

Jian Li has served as our Vice President of Finance and Corporate Controller since December 2003. Previously, Ms. Li served as our Corporate Controller from April 2001 to December 2003, Assistant Controller from December 2000 to April 2001 and our Accounting Manager from March 2000 to December 2000. Prior to joining DURECT, she held various positions at Elan Pharmaceuticals in California and GTE Hawaiian Telephone in Honolulu, Hawaii in the roles of Financial Analyst, Accountant and Marketing Analyst. Ms. Li holds an M.B.A. from the University of Hawaii at Manoa. She is also a Certified Public Accountant and a member of American Institute of Certified Public Accountants.

Andrew R. Miksztal, Ph.D. has served as our Vice President of Pharmaceutical Research and Development since January 2006. Dr. Miksztal joined DURECT in March 2000 as Senior Director of Pharmaceutical Development and was promoted to Executive Director of Pharmaceutical Development in October 2000. Prior to joining DURECT, Dr. Miksztal was the Associate Director of the Pharmaceutical Analysis Department at Oread

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Laboratories from 1996 to 2000, a Senior Scientist in Pharmaceutical Research at Roche Bioscience from 1995 to 1996, and a Scientist in the Preformulation and Pharmaceutical Analysis Departments at Syntex Research from 1987 to 1995. Dr. Miksztal earned his Ph.D. degree in Chemistry from Rutgers University, and completed an NIH postdoctoral research fellowship in the Chemistry Department at the University of California, San Diego. Dr. Miksztal is a member of the American Association of Pharmaceutical Scientists, the Parenteral Drug Association and the American Chemical Society.

Item 1A. Risk Factors.

In addition to the other information in this Form 10-K, a number of factors may affect our business and prospects. These factors include but are not limited to the following, which you should consider carefully in evaluating our business and prospects.

Risks Related To Our Business

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

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

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

The time frame necessary to achieve these developmental milestones for any individual product is long and uncertain, and we may not successfully complete these milestones for any of our products in development. Other than for Remoxy, we have not yet selected the drug dosages nor finalized the formulation or the system design of any of our pharmaceutical systems, including our SABER-Bupivacaine, TRANSDUR-Sufentanil, Memryte and CHRONOGESIC, and we have limited experience in developing such products. We may not be able to

finalize the design or formulation of any of these pharmaceutical systems. In addition, we may select components, solvents, excipients or other ingredients to include in our pharmaceutical systems that have not been previously approved for use in pharmaceutical products, which may require us to perform additional studies and may delay clinical testing and regulatory approval of our pharmaceutical systems. Even after we complete the design of a pharmaceutical system, the pharmaceutical system must still complete required clinical trials and additional safety testing in animals before approval for commercialization. See We must conduct and satisfactorily complete required laboratory performance and safety testing, animal studies and clinical trials for our pharmaceutical systems before we can sell them. We are continuing testing and development of our pharmaceutical systems and may explore possible design or formulation changes to address issues of safety, manufacturing efficiency and performance. We may not be able to complete development of any pharmaceutical

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systems that will be safe and effective and that will have a commercially reasonable treatment and storage period. If we or our third-party collaborators are unable to complete development of SABER-Bupivacaine, TRANSDUR-Sufentanil, Remoxy, Memryte, CHRONOGESIC or other pharmaceutical systems, we will not be able to earn revenue from them, which would materially harm our business.

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

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

- SABER-Bupivacaine Phase I trial completed and Phase II trials initiated in Australia and the United Kingdom. Dosing of all three cohorts consisting of an aggregate of 81 patients in the Phase II clinical trial in Australia completed as of September 2005. Positive preliminary results from Phase II trial in Australia announced in October 2005. Dosing for the United Kingdom trial is ongoing.

- TRANSDUR-Sufentanil Patch Dosing of Phase I trial completed and first trial of Phase II program initiated as of February 2005. Positive preliminary results from first Phase II trial announced in December 2005.

- Remoxy Phase I and Phase III trials completed by Pain Therapeutics. Pain Therapeutics announced positive results from the first Phase III study in September 2005. In February 2006, Pain Therapeutics and its commercialization sublicensee King announced that Remoxy had successfully completed a Special Protocol Assessment (SPA) with the FDA and that the parties were going to commence a pivotal Phase III trial on Remoxy in 400 patients with severe chronic pain.

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

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

We are currently in the preclinical or research stages with respect to all our other pharmaceutical systems 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 pharmaceutical systems. These studies include laboratory performance studies and safety testing, clinical trials and animal toxicological studies necessary to support regulatory approval of development products in the United States and other countries of the world. These studies are costly, complex and last for long durations, and may not yield the data required for regulatory approval. We may not be permitted to begin or continue our planned clinical trials for our potential pharmaceutical systems. If our trials are permitted, our potential pharmaceutical systems 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 pharmaceutical systems which we have not planned or anticipated that could delay commercialization of such pharmaceutical systems and harm our business and financial conditions.

The length of clinical trials will depend upon, among other factors, the rate of trial site and patient enrollment and the number of patients required to be enrolled in such studies. We or our third-party collaborators may fail to obtain adequate levels of patient enrollment in our clinical trials. Delays in planned patient enrollment may result in increased costs, delays or termination of clinical trials, which could have a material adverse effect

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on us. In addition, even if we or our third-party collaborators enroll the number of patients we expect in the time frame we expect, such clinical trials may not provide the data necessary to support regulatory approval for the pharmaceutical systems for which they were conducted. Additionally, we or our third-party collaborators may fail to effectively oversee and monitor these clinical trials, which would result in increased costs or delays of our clinical trials. Even if these clinical trials are completed, we or our third-party collaborators may fail to complete and submit a new drug application as scheduled. The Food and Drug Administration (FDA) may not clear any such application in a timely manner or may deny the application entirely.

Data already obtained from preclinical studies and clinical trials of our pharmaceutical systems do not necessarily predict the results that will be obtained from later preclinical studies and clinical trials. Moreover, preclinical and clinical data such as ours is susceptible to varying interpretations, which could delay, limit or 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 pharmaceutical system under development could delay or prevent regulatory clearance of the potential pharmaceutical system, resulting in delays to the commercialization of our pharmaceutical system, and could materially harm our business. Clinical trials may not demonstrate the sufficient levels of safety and efficacy necessary to obtain the requisite regulatory approvals for our pharmaceutical systems, and thus our pharmaceutical systems may not be approved for marketing.

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

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

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

If we and our third-party collaborators, where relevant, are unable to manufacture pharmaceutical systems or components in a timely manner or at an acceptable cost, quality or performance level, and attain and maintain

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compliance with applicable regulations, the clinical trials and the commercial sale of our pharmaceutical systems and those of our third-party collaboratorss could be delayed. Additionally, we may need to alter our facility design or manufacturing processes, install additional equipment or do additional construction or testing in order to meet regulatory requirements, optimize the production process, increase efficiencies or production capacity or for other reasons, which may result in additional cost to us or delay production of product needed for the clinical trials and commercial launch of our pharmaceutical systems and those of our third-party collaborators. We and our third-party collaborators, where relevant, may also need or choose to subcontract with third-party contractors to perform manufacturing steps of our pharmaceutical systems or supply required components for our pharmaceutical systems in which case we will be subject to the schedule, expertise and performance of third parties as well as incur significant additional costs. See We rely heavily on third parties to support development, clinical testing and manufacturing of our development products and Key Components of our pharmaceutical systems are provided by limited numbers of suppliers, and supply shortages or loss of these suppliers could result in interruptions in supply or increased costs. 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 systems to third parties which have not been approved by ALZA.

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

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

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

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

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

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approval for our development products, we or they will not be able to market and sell our pharmaceutical systems, which will limit our ability to generate revenue.

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

Marketing or promoting a drug is subject to very strict controls. Furthermore, clearance or approval may entail ongoing requirements for post-marketing studies. The manufacture and marketing of drugs are subject to continuing FDA and foreign regulatory review and requirements that we update our regulatory filings. Later discovery of previously unknown problems with a product, manufacturer or facility, or our failure to update regulatory files, may result in restrictions, including withdrawal of the product from the market. Any of the following events, if they were to occur, could delay or preclude us from further developing, marketing or realizing full commercial use of our pharmaceutical systems, 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 pharmaceutical systems under development; or
- identification of serious and unanticipated adverse side effects in our pharmaceutical systems 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 development 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, our third-party collaborators or our respective suppliers do not achieve compliance for our pharmaceutical systems we or they manufacture, the FDA may refuse or withdraw marketing clearance or require product recall, which may cause interruptions or delays in the manufacture and sale of our pharmaceutical systems.

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

Our near-term revenues are based to a significant extent on collaborative arrangements with third parties, pursuant to which we receive payments based on our performance of research and development activities and the attainment of milestones set forth in the agreements. We may not be able to fulfill our obligations or attain milestones set forth in any specific agreement, which could cause our revenues to fluctuate or be less than anticipated and may expose us to liability for contractual breach. In addition, these agreements may require us to devote significant time and resources to communicating with and managing our relationship with such collaborators and resolving possible issues of contractual interpretation which may detract from time our management would otherwise devote to our managing our operations. Such agreements are generally complex and contain provisions that could give rise to legal disputes, including potential disputes concerning ownership of intellectual property under collaborations. Such disputes can delay or prevent the development of potential new pharmaceutical systems, or can lead to lengthy, expensive litigation or arbitration. In general, our collaboration agreements, including our agreements with Endo with respect to

CHRONOGESIC and TRANSDUR-Sufentanil,

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Pain Therapeutics with respect to Remoxy and Voyager with respect to Memryte, may be terminated by the other party at will or upon specified conditions including, for example, if we fail to satisfy specified performance milestones or if we breach the terms of the agreement.

In addition to customary termination rights, our agreement with Endo for the development and commercialization of CHRONOGESIC in the United States and Canada can be terminated by Endo in the event that (i) we have not delivered to Endo on or before March 31, 2007 a written notice that a human pharmacokinetic trial had been completed with CHRONOGESIC, together with a full study report of the results of the trial or (ii) Endo, determines, in its sole discretion, to terminate the agreement during the sixty-day period after our delivery of the notice, provided, that, in each case Endo delivers to us its written notice of termination prior to April 30, 2007.

If any of our collaborative agreements are terminated, our revenues will be reduced or not materialize, and our development products related to those agreements may not be commercialized.

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

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

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

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

We and our third-party collaborators may not effectively sell our pharmaceutical systems

We and our third-party collaborators compete with many other companies that currently have extensive and well-funded marketing and sales operations. Our marketing and sales efforts and those of our third-party

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collaborations may be unable to compete successfully against these other companies. We and our third-party collaborators, if relevant, may be unable to establish a sufficient sales and marketing organization on a timely basis, if at all. We and our third-party collaborators, if relevant, may be unable to engage qualified distributors. Even if engaged, these distributors may:

- fail to satisfy financial or contractual obligations to us;
- fail to adequately market our pharmaceutical systems;
- cease operations with little or no notice to us;
- offer, design, manufacture or promote competing product lines;
- fail to maintain adequate inventory and thereby restrict use of our pharmaceutical systems; or
- build up inventory in excess of demand thereby limiting future purchases or our pharmaceutical systems resulting in significant quarter-to-quarter variability in our sales.

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

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

We rely on third-party contract research organizations, service providers and suppliers to provide critical services to support development, clinical testing, and manufacturing of our pharmaceutical systems. For example, we currently depend on third-party vendors to manage and monitor our clinical trials and to perform critical manufacturing steps for our pharmaceutical systems. We rely on third-parties to manufacture or perform manufacturing steps relating to our pharmaceutical systems or components. See We may not be able to manufacture sufficient quantities of our development 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 development products, increase our expenses and materially harm our business, financial condition and results of operations.

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

Certain components and drug substances used in our pharmaceutical systems (including SABER-Bupivacaine, TRANSDUR-Sufentanil, Remoxy, Memryte and CHRONOGESIC) 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 pharmaceutical systems due to a failure to obtain a single source component;

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

- reduced control over pricing, quality and time delivery.

We have supply agreements in place for certain components of our pharmaceuticals systems, but do not have in place long term supply agreements with respect to all of the components of any of our pharmaceutical system candidates. Therefore the supply of a particular component could be terminated at any time without penalty to the supplier. In addition, we may not be able to procure required components or drugs from third-party suppliers at a quantity, quality and cost acceptable to us. Any interruption in the supply of single source

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components could cause us to seek alternative sources of supply or manufacture these components internally. Furthermore, in some cases, we are relying on our third-party collaborators to procure supply of necessary components. If the supply of any components for our pharmaceutical systems is interrupted, components from alternative suppliers may not be available in sufficient volumes or at acceptable quality levels within required timeframes, if at all, to meet our needs or those of our third-party collaborators. This could delay our ability to complete clinical trials and obtain approval for commercialization and marketing of our pharmaceutical systems, causing us to lose sales, incur additional costs and delay new product introductions and could harm our reputation.

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

As of December 31, 2005, we had approximately $57.3 million in long-term convertible subordinated notes which mature in June 2008, $27,000 in non-current lease obligations and $675,000 in non-current bonds payable. Our substantial indebtedness, which totals $58.0 million, has impacted and will continue to impact us by:

- making it more difficult to obtain additional financing;
- requiring interest payments to service the debt; and
- constraining our ability to react quickly in an unfavorable economic climate.

Currently we are not generating positive cash flow. Adverse occurrences related to our product development efforts will adversely impact our ability to meet our obligations to repay the principal amounts on our convertible subordinated notes when due in June 2008. In addition, if the market price of our common stock on the due date of our notes is below $3.15 per share, the approximate equity conversion price of the notes, it will be highly unlikely that the holders of a large percentage of our outstanding convertible subordinated notes will convert such securities to equity in accordance with their existing terms. If we are unable to satisfy our debt service requirements, substantial liquidity problems could result. As of December 31, 2005, we had cash and investments valued at approximately $91.0 million. We expect to use substantially all of these assets to fund our on-going operations over the next few years. We may not generate sufficient cash from operations to repay our convertible subordinated notes or satisfy any other of these obligations when they become due and may have to raise additional financing from the sale of equity or debt securities or otherwise restructure our obligations in order to do so. There can be no assurance that any such financing or restructuring will be available to us on commercially acceptable terms, if at all. If we are unable to restructure our obligations, we may be forced to seek protection under applicable bankruptcy laws. Any restructure or bankruptcy could materially impair the value of our common stock.

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

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

- any transaction or event in connection with which all or substantially all of our common stock is exchanged for, converted into, acquired for or constitutes solely the right to receive consideration which is not all or substantially all common stock listed on a United

States national securities exchange or approved for quotation on the NASDAQ National Market or any similar United States system of automated dissemination of quotations of securities prices, or,

- if for any reason, our common stock is no longer listed for trading on a United States national securities exchange nor approved for trading on the NASDAQ National Market.

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

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

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

We have incurred significant operating losses since our inception in 1998 and, as of December 31, 2005, had an accumulated deficit of approximately $182.0 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 pharmaceutical systems, obtain the required regulatory clearances and manufacture and market our proposed pharmaceutical systems. 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 pharmaceutical systems and do not expect to receive significant revenue in the near future. Our current product revenues are from the sale of the ALZET product we acquired in April 2000 from ALZA and the sale of biodegradable polymers. We do not expect these product revenues to increase significantly in future periods. We do not anticipate commercialization and marketing of our pharmaceutical systems in development in the near future, and therefore do not expect to generate sufficient revenues to cover expenses or achieve profitability in the near future.

We may have difficulty raising needed capital in the future

Our business currently does not generate sufficient revenues to meet our capital requirements and we do not expect that it will do so in the near future. We have expended and will continue to expend substantial funds to complete the research, development and clinical testing of our pharmaceutical systems. 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 pharmaceutical systems. 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;

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- 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 pharmaceutical systems;
- costs involved in establishing manufacturing capabilities for clinical and commercial quantities of our pharmaceutical systems;
- competing technological and market developments;
- market acceptance of our pharmaceutical systems; 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 collaboratorss or other sources, which may be dilutive to existing stockholders and may cause the price of our common stock to decline. In addition, in the event that additional funds are obtained through arrangements with collaborators or other sources, we may have to relinquish rights to some of our technologies or pharmaceutical systems 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.

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 or our third-party collaborators may choose to terminate their agreements with us

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 February 28, 2006, we held 26 issued U.S. patents and 69 issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have 36 pending U.S. patent applications and have filed 55 patent applications under the Patent Cooperation Treaty, from which 101 national phase applications are currently pending in Europe, Australia, Japan, Canada, Mexico, New Zealand, Brazil, Israel, India, Hong Kong and China. Our patents expire at various dates starting in the year 2012.

Under our agreement with ALZA, we must assign to ALZA any intellectual property rights relating to the DUROS system and its manufacture and any combination of the DUROS system with other components, active agents, features or processes. In addition, ALZA retains the right to enforce and defend against infringement actions relating to the DUROS system, and if ALZA exercises these rights, it will be entitled to the proceeds of these infringement actions.

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

We are party to several collaborative agreements. See Our near-term revenues depend on collaboration agreements with other companies. These agreements subject us to obligations which must be fulfilled and require

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us to manage complex relationships with third parties. If we are unable to meet our obligations or manage our relationships with our collaborators under these agreements or enter into additional collaboration agreements or if our existing collaborations are terminated, our revenues may decrease. Our third-party collaborators have entered into these agreement based on the exclusivity that our intellectual property rights confer on the products being developed. The loss or diminishment of our intellectual property rights could result in a decision by our third-party collaborators to terminate their agreements with us. In addition, these agreements are generally complex and contain provisions that could give rise to legal disputes, including potential disputes concerning ownership of intellectual property under collaborations. Such disputes can lead to lengthy, expensive litigation or arbitration requiring us to devote management time and resources to such dispute which we would otherwise spend on our business. To the extent that our agreements call for future royalties to be paid conditional on our having patents covering the royalty-bearing subject matter, a decision by the Supreme Court adverse to the patent holder in the case of MedImmune, Inc. v. Genentech, Inc., U.S. Supreme Court No. 05-608 (Feb. 21, 2006) could encourage our licensees to challenge the validity of our patents and thereby seek to avoid future royalty obligations without losing the benefit of their license. Should they be successful in such a challenge, our ability to collect future royalties could be substantially diminished.

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. In addition, interference proceedings declared by the U.S. Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications. Enforcing or defending our proprietary rights is expensive, could cause diversion of our resources and may not prove successful. Any failure to enforce or protect our rights could cause us to lose the ability to exclude others from using our technology to develop or sell competing products.

We may be sued by third parties which claim that our development 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 pharmaceutical systems 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. We also may not have sufficient funds to litigate against parties with substantially greater resources. Intellectual property litigation or claims could force us to do one or more of the following, any of which could harm our business or financial results:

- cease selling, incorporating or using any of our pharmaceutical systems 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

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- redesign our pharmaceutical systems, which would be costly and time-consuming.

We may be required to obtain rights to certain drugs

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

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

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

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

- increased costs associated with the acquisition and operation of the new businesses or technologies and the management of geographically dispersed operations;
- the risks associated with the assimilation of new technologies, operations, sites and personnel;
- the diversion of resources from our existing business and technologies;
- the inability to generate revenues to offset associated acquisition costs;
- the requirement to maintain uniform standards, controls, and procedures; and
- the impairment of relationships with employees and customers or third party collaborators as a result of any integration of new management personnel.

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

Some of our pharmaceutical systems 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 pharmaceutical systems 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. TRANSDUR-Sufentanil patch, Remoxy and CHRONOGESIC and other pharmaceutical systems we have under development contain opioids which are classified as Schedule II controlled substances under the regulations of the U.S. Drug Enforcement Agency. For our pharmaceutical systems 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

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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 pharmaceutical systems containing controlled substances and subject us to enforcement action. In addition, because of their restrictive nature, these regulations could limit our commercialization of our pharmaceutical systems containing controlled substances.

Write-offs related to the impairment of long-lived assets and other non-cash charges, as well as future stock-based 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.

We will continue to incur non-cash charges related to amortization of other intangible assets. We are required to perform periodic impairment reviews of our goodwill at least annually. To the extent these reviews conclude that the expected future cash flows generated from our business activities are not sufficient to recover the cost of our long-lived assets, we will be required to measure and record an impairment charge to write down these assets to their realizable values. We completed our last review during the fourth quarter of 2005 and determined that goodwill was not impaired as of December 31, 2005. 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.

In December 2004, the FASB issued Statement No. 123 (revised 2004, or SFAS 123R), Share-Based Payment, which was originally effective for annual or interim periods beginning after June 15, 2005. SFAS 123R supersedes APB Opinion No. 25, Accounting for Stock Issued to Employees, and will require companies to recognize compensation expense, using a fair-value based method, for costs related to share-based payments including stock options and stock issued under our employee stock purchase plans. We adopted SFAS 123R using the modified prospective basis on January 1, 2006. We expect that our adoption of SFAS 123R will have a material adverse impact on our consolidated results of operations and will adversely impact or delay our profitability. Furthermore, we have issued to ALZA common stock and a warrant to purchase common stock with an aggregate value of approximately $13.5 million, which will be amortized over time based on sales of our DUROS-based products and which will also adversely impact or delay our profitability.

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

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

We may not successfully manage our growth

Our success will depend on the timely expansion of our operations and the effective management of growth, which will place a significant strain on our management and on our administrative, operational and financial

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resources. To manage such growth, we must expand our facilities, augment our operational, financial and management systems and hire, train and supervise additional qualified personnel. If we were unable to manage growth effectively our business would be harmed.

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

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

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

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

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

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

- sufentanil to treat chronic pain; and

- select cancer antigens.

We may not develop, manufacture or commercialize DUROS-based pharmaceutical systems outside of these specific fields without ALZA s prior approval. In addition, if we develop or commercialize any drug delivery technology for use in a manner similar to the DUROS technology in a field covered in our license agreement with ALZA, then we may lose our exclusive rights to use the DUROS technology in such field as well as the right to develop new pharmaceutical systems using DUROS technology in such field. In order to maintain commercialization rights for our products on a worldwide basis, we must diligently develop our pharmaceutical systems, procure required regulatory approvals and commercialize the pharmaceutical systems in selected major market countries. If we fail to meet commercialization diligence requirements, we may lose rights for products in

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some or all countries, including the United States. These rights would revert to ALZA, which could then develop DUROS-based pharmaceutical products in such countries itself or license others to do so. In addition, in the event that our rights terminate with respect to any product or country, or this agreement terminates or expires in its entirety (except for termination by us due to a breach by ALZA), ALZA will have the exclusive right to use all of our data, rights and information relating to the products developed under the agreement as necessary for ALZA to commercialize these products, subject to the payment of a royalty to us based on the net sales of the products by ALZA.

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

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

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

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

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

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

ALZA retains complete rights to the DUROS technology for fields outside the specific fields licensed to us. Accordingly, ALZA may develop and commercialize DUROS-based products or license others to do so, so long as there is no conflict with the rights granted to us. ALZA received FDA approval to market its first DUROS-based product, VIADUR (leuprolide acetate implants) for the palliative treatment of advanced prostate cancer in

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March 2000. If ALZA or its commercialization collaborators, Bayer, fails to commercialize this product successfully, or encounters problems associated with this product, negative publicity could be created about all DUROS-based products, which could result in harm to our reputation and cause reduced sales of our DUROS-based pharmaceutical systems. In addition, if any third party that may be licensed by ALZA fails to develop and commercialize DUROS-based products successfully, the success of all DUROS-based systems could be impeded, including ours, resulting in delay or loss of revenue or damage to our reputation, any one of which could harm our business.

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

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

Risks Related To Our Industry

The market for our pharmaceutical systems 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 pharmaceutical systems 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 engaged in the development of novel therapeutic technologies. Our resources are limited and we may experience technical challenges inherent in such novel technologies. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these products may have an entirely different approach or means of accomplishing similar therapeutic effects than our pharmaceutical systems. Our competitors may develop products that are safer, more effective or less costly than our pharmaceutical systems 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 pharmaceutical systems even if commercialized. Chronic and post-operative pain are currently being treated by oral medication, transdermal drug delivery systems, such as drug patches, and implantable drug delivery devices which will be competitive with our pharmaceutical systems. 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 pharmaceutical systems to receive widespread acceptance if commercialized.

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

The testing, manufacture, marketing and sale of our pharmaceutical systems involve an inherent risk that product liability claims will be asserted against us. Although we are insured against such risks up to an annual aggregate limit in connection with clinical trials and commercial sales of our pharmaceutical systems, our present

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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 pharmaceutical systems, 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 pharmaceutical systems.

Acceptance of our pharmaceutical systems 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 SABER-Bupivacaine, TRANSDUR-Sufentanil, Remoxy, DURIN-Leuprolide (Memryte) and CHRONOGESIC. Even if approved for marketing, our pharmaceutical systems 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, hospital formularies 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 third-party collaborators and the availability of capital. For example, in certain foreign markets, pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, recent federal and state government initiatives have been directed at lowering the total cost of health care, and the U.S. Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid systems. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of such proposals could materially harm our business, financial condition and results of operations.

The successful commercialization of our pharmaceutical systems will depend in part on the extent to which appropriate reimbursement levels for the cost of our pharmaceutical systems 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

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proposals to reform health care or reduce government insurance programs, may limit reimbursement or payment for our products. The cost containment measures that health care payors and providers are instituting and the effect of any health care reform could materially harm our ability to operate profitably.

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

Broad use of our pharmaceutical systems will require extensive training of numerous physicians on the proper and safe use of our pharmaceutical systems. 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 pharmaceutical systems 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 pharmaceutical systems and harm our business and financial results. In addition, we may expend significant funds towards such training before any orders are placed for our products, which would increase our expenses and harm our financial results.

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

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

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

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

In June 2005, the FASB ratified the consensus reached by the Emerging Issues Task Force No. 05-6 (EITF 05-6). The Task Force reached a consensus that leasehold improvements that are placed in service significantly after and not contemplated at or near the beginning of the lease term should be amortized over the shorter of the useful life of the assets or a term that includes required lease periods and renewals that are

deemed to be reasonably assured at the date the leasehold improvements are purchased. In addition, leasehold improvements acquired in a business combination should be amortized over the shorter of the useful lives of the assets or a term that includes required lease periods and renewals that are deemed to be reasonably assured at the date of

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acquisition. EITF 05-6 is effective for leasehold improvements (within the scope of this issue) that are purchased or acquired in the reporting period beginning after June 29, 2005. Adoption of EITF 05-6 did not have an impact on our consolidated financial condition or results of operations.

Risks Related To Our Common Stock

Our operating history makes evaluating our stock difficult

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

Investors may experience substantial dilution of their investment

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

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

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

The price of our common stock may be volatile

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

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

- failure of our third-party collaborators (such as Endo Pharmaceuticals, Pain Therapeutics or Voyager Pharmaceuticals) to develop and commercialize successfully the respective pharmaceutical systems they are developing;

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- adverse results or delays in our clinical trials of SABER-Bupivacaine, TRANSDUR-Sufentanil, Remoxy, Memryte, CHRONOGESIC or other pharmaceutical systems;

- announcements of FDA non-approval of our pharmaceutical systems, or delays in the FDA or other foreign regulatory agency review process;

- adverse actions taken by regulatory agencies with respect to our pharmaceutical systems or our or our third-party collaborator s clinical trials, manufacturing processes or sales and marketing activities;

- announcements of technological innovations, patents or new products by our competitors;

- regulatory developments in the United States and foreign countries;

- any lawsuit involving us or our pharmaceutical systems;

- announcements concerning our competitors, or the biotechnology or pharmaceutical industries in general;

- developments concerning our strategic alliances or acquisitions;

- actual or anticipated variations in our operating results;

- changes in recommendations by securities analysts or lack of analyst coverage;

- deviations in our operating results from the estimates of analysts;

- sales of our common stock by our executive officers, directors and five percent stockholders or sales of substantial amounts of common stock;

- changes in accounting principles; and

- loss of any of our key scientific or management personnel.

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

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

The average daily trading volume of our common stock for the year ended December 31, 2005, was 338,817 shares. The limited trading volume of our stock may contribute to its volatility, and an active trading market in our stock might not continue. Pursuant to a Purchase Agreement with Morgan Stanley & Co., Incorporated, we filed a registration statement on August 29, 2003 with the SEC on Form S-3 to register an aggregate of $60.0 million in convertible subordinated notes and the shares of common stock issuable upon conversion of the notes for resale. The registration statement was declared effective by the SEC on November 3, 2003. The convertible subordinated notes are convertible into shares of our common stock at a conversion rate of 317.4603 shares per $1,000 principal amount of notes, subject to adjustment and will bear interest at a rate of 6.25% per annum. So long as this registration is effective, shares covered thereunder are tradable without limitation. If substantial amounts of our common stock issued upon conversion of our promissory notes or otherwise were to be sold in the public market, the market price of our common stock could fall. In addition, the existence of our convertible subordinated notes may encourage short selling by market participants. The market price of our common stock may fluctuate significantly in response to factors which are beyond our control. The stock market in general has recently experienced extreme price and volume fluctuations. In addition, the market 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.

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

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

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

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

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

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

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

- authorizing the issuance of blank check preferred stock without any need for action by stockholders;
- providing for a dividend on our common stock, commonly referred to as a poison pill , which can be triggered after a person or group acquires 17.5% or more of common stock;
- providing for a classified board of directors with staggered terms;
- requiring supermajority stockholder voting to effect certain amendments to our certificate of incorporation and bylaws;

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

- prohibiting stockholder action by written consent; and

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

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We are headquartered in Cupertino, California, where we lease four buildings: a building consisting of approximately 30,000 square feet of office, laboratory and manufacturing space, under a lease expiring in February 2009 with an option to extend for up to an additional five years; a building consisting of approximately

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20,000 square feet of office and laboratory space, under a lease expiring in February 2009 with an option to extend for up to an additional five years; and a building consisting of approximately 40,560 square feet of office space, under a lease expiring in December 2012 with an option to extend for up to an additional six years.

We also lease approximately 7,800 square feet of manufacturing space in Vacaville, California under a lease expiring in August 2008 with an option to extend for three years. We lease approximately 2,500 square feet of office and laboratory space in Birmingham, Alabama, under a lease which expires in April 2006. In addition, we lease approximately 9,400 square feet of office and laboratory space in Pelham, Alabama, under a lease expiring in September 2009 with one option to extend for five years.

We believe that our existing facilities are adequate to meet our current and foreseeable requirements or that suitable additional or substitute space will be available as needed.

Item 3. Legal Proceedings.

We are not a party to any material legal proceedings.

Item 4. Submission of Matters to a Vote of Security Holders.

Not applicable**.**

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PART II

Item 5. Market for Registrant s Common Equity, Related Stockholder Matter and Issuer Purchases of Equity Securities.

Price Range of Common Stock

Our common stock has been listed for quotation on the Nasdaq National Market under the symbol DRRX since our initial public offering on September 28, 2000. The following table shows the high and low sales prices of our common stock as reported by the Nasdaq National Market for the period indicated.

	Common Stock Price	
Year ended December 31, 2004	**Low**	**High**
First Quarter	$ 2.51	$ 3.49
Second Quarter	3.25	4.23
Third Quarter	1.26	3.36
Fourth Quarter	1.41	3.45
Year ended December 31, 2005	**Low**	**High**
First Quarter	$ 2.64	$ 3.78
Second Quarter	2.73	5.09
Third Quarter	4.85	7.15
Fourth Quarter	4.85	7.18

The closing sale price of the common stock as reported on the Nasdaq National Market on February 28, 2006 was $5.69 per share. As of that date there were approximately 184 holders of record of the common stock. This does not include the number of persons whose stock is in nominee or street name accounts through brokers. The market price of our common stock has been and may continue to be subject to wide fluctuations in response to a number of events and factors, such as progress in our development programs, quarterly variations in our operating results, announcements of technological innovations or new products by us or our competitors, changes in financial estimates and recommendations by securities analysts, the operating and stock performance of other companies that investors may deem comparable to us, and news reports relating to trends in our markets. These fluctuations, as well as general economic and market conditions, may adversely affect the market price for our common stock.

Dividend Policy

We have never paid cash dividends on our common stock. We currently intend to retain any future earnings to fund the development and growth of our business. Therefore, we do not currently anticipate paying any cash dividends in the foreseeable future.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. Selected Financial Data.

The following selected consolidated financial data should be read in conjunction with and are qualified by reference to Management s Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and related notes, which are included in this Form 10-K. The statement of operations data for the years ended December 31, 2005, 2004 and 2003 and the balance sheet data at December 31, 2005 and 2004 are derived from, and are qualified by reference to, the audited financial statements

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included elsewhere in this Form 10-K. The statement of operations data for the years ended December 31, 2002 and 2001, and the balance sheet data at December 31, 2003, 2002 and 2001 are derived from our audited statements not included in this Form 10-K. Historical operating results are not necessarily indicative of results in the future. See Note 1 of notes to consolidated financial statements for an explanation of the determination of the shares used in computing net loss per share.

	Year Ended December 31,				
	2005	2004	2003	2002	2001
	(in thousands, except per share data)				
Statement of Operations Data:					
Collaborative research and development and other revenue	20,032	7,437	5,144	871	358
Product revenue, net	$ 6,939	$ 6,416	$ 6,691	$ 6,314	$ 6,166
Revenue from sale of intellectual property rights	1,600				
Total revenue	28,571	13,853	11,835	7,185	6,524
Operating expenses:					
Cost of revenue	2,815	2,730	2,445	3,158	3,398
Research and development	29,141	24,390	20,738	30,176	26,805
Selling, general and administrative	11,034	9,793	8,588	11,480	9,849
Amortization of intangible assets	1,209	1,249	1,343	1,340	1,844
Acquired in-process research and development					14,030
Total operating expenses	44,199	38,162	33,114	46,154	55,926
Loss from operations	(15,628)	(24,309)	(21,279)	(38,969)	(49,402)
Other income (expense):					
Interest income and other	2,270	1,236	1,041	2,076	4,796
Interest expense	(4,363)	(4,546)	(2,460)	(280)	(322)
Debt conversion expense	(403)				
Net other income (expense)	(2,496)	(3,310)	(1,419)	1,796	4,474
Loss before income taxes	(18,124)	(27,619)	(22,698)	(37,173)	(44,928)
Income tax provision	4	18			
Net loss	(18,128)	(27,637)	(22,698)	(37,173)	(44,928)
Net loss attributable to common stockholders	$ (18,128)	$ (27,637)	$ (22,698)	$ (37,173)	$ (44,928)
Basic and diluted net loss attributable to common stockholders per common share	$ (0.34)	$ (0.54)	$ (0.45)	$ (0.77)	$ (0.97)
Shares used in computing basic and diluted net loss per common share	53,719	51,507	50,510	48,318	46,414

	As of December 31,				
	2005	2004	2003	2002	2001
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and investments	$ 90,997	$ 61,813	$ 85,167	$ 48,268	$ 76,622

Working capital	84,202	42,082	61,050	41,856	54,463
Total assets	117,414	85,468	112,407	72,971	104,943
Long-term liabilities, net of current portion	64,185	61,589	62,278	1,604	2,147
Stockholders equity	43,352	18,390	45,115	66,182	97,048

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Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations.

This Management s Discussion and Analysis of Financial Condition and Results of Operations as of December 31, 2005, 2004, and 2003 should be read in conjunction with our Consolidated Financial Statements, including the Notes thereto, and Risk Factors section included elsewhere in this Form 10-K. This Form 10-K contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended. When used in this report or elsewhere by management from time to time, the words believe, anticipate, intend, plan, estimate, expect and similar expressions are forward-looking statements. Such forward-looking statements contained herein are based on current expectations. Any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties. Actual events or results may differ materially from those discussed in the forward-looking statements as a result of various factors. For a more detailed discussion of such forward looking statements and the potential risks and uncertainties that may impact upon their accuracy, see the Risk Factors section and Overview section of this Management s Discussion and Analysis of Financial Condition and Results of Operations. These forward-looking statements reflect our view only as of the date of this report. We undertake no obligations to update any forward-looking statements. You should also carefully consider the factors set forth in other reports or documents that we file from time to time with the Securities and Exchange Commission.

Overview

We are an emerging specialty pharmaceutical company focused on the development of pharmaceutical systems based on proprietary drug delivery technology platforms. We are developing and commercializing pharmaceutical systems that will deliver the right drug to the right place in the right amount at the right time to treat chronic or episodic diseases and conditions. By integrating chemistry and engineering advancements, we can achieve what drugs or devices alone cannot. Our pharmaceutical systems enable optimized therapy for a given disease or patient population by controlling the rate and duration of drug administration and providing sustained drug delivery.

In addition to developing our own proprietary products, we enter into strategic collaborations with pharmaceutical companies to develop and commercialize proprietary and enhanced pharmaceutical products based on our technologies. We have five disclosed on-going development programs of which four are in collaboration with third-party pharmaceutical companies. The following are our most advanced pharmaceutical systems in development:

SABER-Bupivacaine

Our post-operative pain relief depot (SABER-Bupivacaine) is a sustained release injectable using our SABER delivery system to deliver bupivacaine. SABER is a patented controlled drug delivery technology that can be formulated for systemic or local administration of drugs via the parenteral (i.e., injectable) route. SABER-Bupivacaine is designed to be administered around a surgical site after surgery for post-operative pain relief and is intended to provide local analgesia for 3 days or more, which we believe coincides with the time period of the greatest need for post surgical pain control in most patients. SABER-Bupivacaine is currently in Phase II clinical trials.

TRANSDUR-Sufentanil

Our transdermal sufentanil patch (TRANSDUR-Sufentanil) uses our proprietary TRANSDUR delivery system to deliver sufentanil, an opioid medication. TRANSDUR-Sufentanil is designed to provide extended chronic pain relief for up to seven days, as compared to the three days of

relief provided with currently available opiate patches. We anticipate that the small size of our sufentanil patch (potentially as small as 1/5th the size of currently marketed transdermal fentanyl patches for a therapeutically equivalent dose) may offer improved convenience and compliance for patients. In March 2005, we entered into an agreement with Endo Pharmaceuticals granting Endo exclusive rights to develop, market and commercialize TRANSDUR-Sufentanil in the U.S. and Canada. TRANSDUR-Sufentanil is currently in Phase II clinical trials.

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Remoxy

In December 2002, we entered into an agreement with Pain Therapeutics, Inc. (Pain Therapeutics), amended in December 2005, under which we granted Pain Therapeutics the exclusive, worldwide right to develop and commercialize selected long-acting oral opioid products using our ORADUR technology incorporating four specified opioid drugs. The first product being developed under the collaboration is Remoxy, a novel long-acting oral formulation of the opioid oxycodone targeted to decrease the potential for oxycodone abuse. Remoxy is intended for patients with chronic pain. Remoxy is currently in Phase III trials.

Memryte

In July 2002, we entered into a development and commercialization agreement with Voyager Pharmaceuticals Corporation under which we granted Voyager the exclusive, worldwide right to develop and commercialize a development product using the DURIN implant system to deliver the peptide leuprolide acetate to treat Alzheimer s disease based on Voyager s patented method of treatment. Memryte, which Voyager is developing under this agreement, is currently in Phase III clinical trials.

CHRONOGESIC (sufentanil) Pain Therapy System

The CHRONOGESIC (sufentanil) Pain Therapy System is an osmotic implant that is intended to continuously deliver sufentanil for an extended duration. CHRONOGESIC is intended to treat chronic pain, and is based on the DUROS System, a miniature osmotic pump capable of continuously delivering drugs for up to a year in duration. We have granted to Endo exclusive commercialization rights for CHRONOGESIC in the U.S. and Canada. CHRONOGESIC completed a pilot Phase III clinical trial. Clinical trials have been suspended pending system redesign.

DURECT Research Programs

We are also currently researching and developing additional pharmaceutical systems in a variety of therapeutic areas, including chronic pain, central nervous system disorders and cardiovascular diseases based on our proprietary drug delivery platform technologies.

Collaborative Research and Development Revenues

We generate substantially all collaborative research and development revenues from three collaborative agreements related to the development and commercialization of pharmaceutical systems based on our technologies: one with Endo Pharmaceuticals, Inc. related to TRANSDUR-Sufentanil, one with Pain Therapeutics, Inc. related to Remoxy, and one with Voyager Pharmaceutical Corporation related to Memryte.

Product Revenues

We currently generate product revenue from the sale of two product lines:

- ALZET osmotic pumps for animal research use; and

- LACTEL biodegradable polymers which are used by our customers as raw materials in their pharmaceutical and medical products. This product line was sold through our wholly-owned subsidiary API until it was merged with and into us as of December 31, 2004.

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. 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 collaborators to develop pharmaceutical systems based on our drug delivery technologies.

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Since our inception in 1998, we have had a history of operating losses. At December 31, 2005, we had an accumulated deficit of $182.0 million and our net losses were $18.1 million, $27.6 million and $22.7 million for the twelve months ended December 31, 2005, 2004 and 2003, respectively. These losses have resulted primarily from costs incurred to research and develop our development 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 increase in the near future as we expect to continue to expand our animal studies, clinical trials and other research and development activities. We expect our general and administrative expenses to increase modestly in the near future in light of the additional cost to support the infrastructure of our business operations. 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.

Critical Accounting Policies and Estimates

General

The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the dates of the financial statements and the reported amounts of revenues and expenses during the reporting periods. The most significant estimates and assumptions relate to revenue recognition, the recoverability of our long-lived assets, including goodwill and other intangible assets, accrued liabilities and contract research liabilities and stock-based compensation. Actual amounts could differ significantly from these estimates.

Revenue Recognition

Revenue from the sale of products is recognized at the time the product is shipped and title transfers to customers, provided no continuing obligation exists and the collectibility of the amounts owed is reasonably assured.

Revenue from the sale of intellectual property rights is recognized upon assignment of such rights by us to a third party, provided the collectibility is assured and we have no future performance obligations related to such rights, except for the on-going de minimus assistance we would provide to the third party with respect to the maintenance of such rights.

Upfront payments received upon execution of collaborative agreements are recorded as deferred revenue and recognized as collaborative research and development revenue based on a straight-line basis over the period our continuing involvement with the third party collaborator pursuant to the applicable agreement. Such period generally represents the research and development period set forth in the work plan defined in the respective agreements between us and our third-party collaborators.

Research and development revenue related to services performed under the collaborative arrangements with our corporate collaborators is recognized as the related research and development services are performed. These research payments received under each respective agreement are not refundable and are generally based on reimbursement of qualified expenses, as defined in the agreements. Research and development expenses under the collaborative research and development agreements generally approximate or exceed the revenue recognized under such agreements over the term of the respective agreements. Deferred revenue may result when we do not expend the required level of effort during a specific period in comparison to funds received under the respective agreement.

Milestone payments under collaborative arrangements are recognized as revenue upon achievement of the milestone events, which represent the culmination of the earnings process. Milestone payments are triggered

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either by the results of our research and development efforts or by events external to us, such as regulatory approval to market a product or the achievement of specified sales levels by a third-party collaborator. As such, the milestones are substantially at risk at the inception of the collaboration agreement, and the amounts of the payments assigned thereto are commensurate with the milestone achieved. In addition, upon the achievement of a milestone event, we have no future performance obligations related to that milestone payment.

Revenue on cost-plus-fee contracts, such as under contracts to perform research and development for others, is recognized only to the extent of reimbursable costs incurred plus estimated fees thereon. In all cases, revenue is recognized only after a signed agreement is in place. For contracts that have a ceiling price or contract value, losses on contracts are recognized in the period in which the losses become known and estimable.

Intangible Assets and Goodwill

We record intangible assets when we acquire other companies. The cost of an acquisition is allocated to the assets acquired and liabilities assumed, including intangible assets, with the remaining amount being classified as goodwill. Certain intangible assets such as completed or core technology are amortized over time, while acquired in-process research and development is recorded as a one-time charge on the acquisition date. Acquired in-process research and development represents the value of research projects in process at the time of acquisition which have not yet reached technological feasibility, and which have no alternative future use. The determination of the amount of acquired in-process research and development involves several estimates and judgments, including the percentage of completion of the in-process technology and assumptions about future cash flows to be derived from the technology and discount rates. Different assumptions employed in determining the value of in-process research and development could result in a greater or lesser amount being recorded.

Goodwill is not amortized to expense but rather periodically assessed for impairment. The allocation of the cost of an acquisition to intangible assets and goodwill therefore has a significant impact on our future operating results. The allocation process requires the extensive use of estimates and assumptions, including estimates of future cash flows expected to be generated by the acquired assets. We are also required to estimate the useful lives of those intangible assets subject to amortization, which determines the amount of amortization that will be recorded in a given future period and how quickly the total balance will be amortized. We periodically review the estimated remaining useful lives of our intangible assets. A reduction in our estimate of remaining useful lives, if any, could result in increased amortization expense in future periods.

We assess the impairment of identifiable intangible assets, long-lived assets and goodwill whenever events or changes in circumstances indicate that the carrying value may not be recoverable. Factors we consider important which could trigger an impairment review include the following:

- significant underperformance relative to expected historical or projected future operating results;
- significant changes in the manner of our use of the acquired assets or the strategy for our overall business;
- significant negative industry or economic trends;
- significant decline in our stock price for a sustained period; and

- our market capitalization relative to net book value.

When we determine that the carrying value of intangibles, long-lived assets and goodwill may not be recoverable based upon the existence of one or more of the above indicators of impairment, we measure any impairment based on a projected discounted cash flow method using a discount rate determined by our management to be commensurate with the risk inherent in our current business model. The amount of any impairment charge is significantly impacted by and highly dependent upon assumptions as to future cash flows and the appropriate discount rate. Management believes that the discount rate used in this analysis is reasonable in light of currently available information. The use of different assumptions or discount rates could result in a materially different impairment charge.

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We perform a review for impairment of goodwill at least annually in accordance with SFAS 142, *Goodwill and Other Intangible Assets*. No impairment of goodwill has been recorded through December 31, 2005. However, there can be no assurance that at the time other periodic reviews are completed, a material impairment charge will not be recorded.

Accrued Liabilities and Contract Research Liabilities

We incur significant costs associated with third party consultants and organizations for clinical trials, engineering, validation, testing, and other research and development-related services. We are required to estimate periodically the cost of services rendered but unbilled based on managements estimates of project status. If these good faith estimates are inaccurate, actual expenses incurred could materially differ from our estimates.

Stock-based compensation

The preparation of the financial statement footnotes requires us to estimate the fair value of stock options granted to employees. While fair value may be readily determinable for awards of stock, market quotes are not available for long-term, nontransferable stock options because these instruments are not traded. We currently use the Black-Scholes option-pricing model to estimate the fair value of employee stock options. However, the Black-Scholes option-pricing model was developed for use in estimating the fair value of traded options, which have no vesting restrictions and are fully transferable. Option valuation models require the input of highly subjective assumptions, including but not limited to stock price volatility and employee stock option behaviors. Because our stock options have characteristics significantly different from those of traded options, changes to the assumptions used in the Black-Scholes option-pricing model may materially affect the fair value estimate. After evaluating our option valuation policies and assumptions in light of current accounting standards related to employee stock options, we expect to continue to use the Black-Scholes option-pricing model for determining the fair value of our stock options.

The above listing is not intended to be a comprehensive list of all of our accounting policies. In many cases, the accounting treatment of a particular transaction is specifically dictated by accounting principles generally accepted in the United States, with no need for management s judgment in their application. There are also areas in which management s judgment in selecting any available alternative would not produce a materially different result. See our audited consolidated financial statements and notes thereto in Item 8 of our Form 10-K which contain accounting policies and other disclosures required by generally accepted accounting principles.

Results of Operations

Comparison of years ended December 31, 2005 and 2004

Revenues. Net revenues were $28.6 million in 2005 compared to $13.9 million in 2004. The increase in total revenues in 2005 was primarily attributable to higher collaborative research and development revenue recognized from our agreements with third-party collaborators, as well as $1.6 million in revenue from sale of intellectual property rights.

Collaborative research and development and other revenue

We recognize revenues from collaborative research and development activities and service contracts. We recorded $19.9 million of collaborative research and development revenue in 2005 compared to $6.9 million in 2004. Collaborative research and development revenue represents reimbursement of qualified expenses related to the collaborative agreements with various third parties to research, develop and commercialize potential products using our drug delivery technologies. The increase in collaborative research and development revenue in 2005 was primarily attributable to increased development activities for TRANSDUR-Sufentanil (collaboration with Endo), Memryte (collaboration with Voyager) and Remoxy (collaboration with Pain Therapeutics) compared with 2004.

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We received $10.0 million up-front fee in connection with the license agreement signed with Endo in March 2005 relating to TRANSDUR-Sufentanil. The $10.0 million up-front fee is recognized as revenue ratably over the term of the Company s continuing involvement with Endo with respect to TRANSDUR-Sufentanil. The term of the continuing involvement has been estimated based on the current Product Development Plan pursuant to the agreement.

We expect our collaborative research and development revenue to fluctuate in the future years pending our third party collaborators commitment and progress to the research and development programs, although we will continue to increase our efforts to develop products with in connection with various strategic collaborations. The collaborative research and development revenues associated with our major collaborators are as follows (in thousands):

	Year ended December 31,	
	2005	2004
Collaborator		
Endo Pharmaceuticals, Inc.(1)	$ 7,325	$
Pain Therapeutics, Inc.(2)	4,873	3,979
Voyager Pharmaceutical Corporation	7,046	2,533
Others	704	341
Total collaborative research and development revenue	$ 19,948	$ 6,853

Notes:

1. Amounts related to up-front fees were $1.8 million and none in 2005 and 2004, respectively.

2. Amounts related to up-front fees were none and $140,000 in 2005 and 2004, respectively.

We amortize up-front fees on a straight-line basis over the period in which we have continuing involvement with the third-party collaborator pursuant to the applicable agreement. Such period generally represents the research and development period set forth in the work plan under each collaboration agreement between us and our third-party collaborator.

Other revenue from service contracts was $79,000 in 2005 and $502,000 in 2004. Service contract revenues were related to certain polymer related service contracts we signed with various customers through API, our former subsidiary. The decrease was primarily due to completion of certain service contracts in 2005. We do not expect to increase our effort to generate significant revenue from our service contracts related to polymer business in the future.

Other license revenue was $5,000 in 2005 compared with $82,000 in 2004. The license revenue in 2005 was recognized in connection with our agreement with NeuroSystec Corporation signed in 2004.

Product revenue

A portion of our revenues is derived from our product sales, which include our ALZET mini pump product line, and to a lesser extent our biodegradable polymer products. Net product revenues were $6.9 million in 2005 compared to $6.4 million in 2004. The increase in product revenue in 2005 was primarily due to higher product revenue from our ALZET mini pump product line resulting from a greater number of units sold in 2005, partially offset by lower product revenue from our biodegradable polymer products related to the timing of orders from major customers of our polymer products. In the future, we do not intend to significantly increase our investments in or efforts to sell or market any of our existing product lines.

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Revenue from sale of intellectual property rights

We recorded $1.6 million of revenue from the sale of intellectual property rights in 2005 compared with none in 2004. The $1.6 million of revenue was recognized upon our assignment of certain intellectual property rights to Intervet, Inc. in the third quarter of 2005. Under the agreement, we assigned to Intervet our entire right, title and interest to a U.S. Patent, previously jointly owned by the parties. In connection with this agreement, Intervet paid us $1.6 million in the third quarter of 2005. We do not have any continuing obligations under the agreement, except for the on-going de minimus assistance we would provide to Intervet with respect to the maintenance of such patent. In the foreseeable future, we do not expect to generate this type of revenue.

Cost of revenues. Cost of revenues were $2.8 million in 2005 compared with $2.7 million in 2004. Cost of revenues includes cost of product revenue from our ALZET mini pump product line and our biodegradable polymer products and, to a lesser extent, cost of certain polymer related service contracts entered into by API, our former subsidiary, and assumed by us.

Cost of product revenues were $2.7 million in 2005 compared with $2.3 million in 2004. The increase in the cost of revenues in 2005 was primarily the result of greater number of units sold for our ALZET mini pump product line and higher manufacturing cost for our polymer product line compared with the same period in 2004.

Cost of service revenues were $72,000 in 2005 compared $407,000 in 2004 due to a decline in our service contract revenue related to our polymer business in 2005. As of December 31, 2005 and 2004, we had 20 and 21 manufacturing employees, respectively. We expect cost of revenues to remain comparable in the future, as we do not expect product revenues to increase significantly in the future.

Research and Development. Research and development expenses are primarily comprised of salaries and benefits associated with R&D personnel, overhead and facility costs, preclinical and non-clinical development costs, clinical trial and related clinical manufacturing costs, contract services, and other outside costs. Research and development expenses were $29.1 million in 2005 compared with $24.4 million in 2004. The increases in research and development expenses in 2005 were primarily attributable to the higher employee costs and higher development expenses for SABER-Bupivacaine, Remoxy, TRANSDUR-Sufentanil and Memryte, partially offset by lower development expenses for CHRONOGESIC, compared with 2004.

In 2005, we incurred higher research and development expenses for SABER-Bupivacaine associated with Phase II clinical trials in Australia and U.K. and ongoing animal toxicological studies compared with 2004. We incurred higher development expenses for TRANSDUR-Sufentanil in 2005 compared with 2004 as we conducted Phase II clinical trials and additional animal studies for this product in 2005. We also incurred higher research and development expenses for Remoxy and DURIN-Leuprolide in 2005 to support the development activities related the Phase III clinical trials for these products compared with 2004. We incurred lower development expenses for CHRONOGESIC in 2005 compared with 2004 as we continued to work on the system design of the product and focused our development efforts on other pharmaceutical systems in 2005. As of December 31, 2005, we had 86 research and development employees compared with 72 as of the corresponding date in 2004. We expect research and development expenses to increase in the near future as we continue product development efforts for our internal programs and those subject to third-party collaborations.

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The research and development expenses associated with our major development products approximate the following (in thousands):

	Year ended December 31,	
	2005	2004
SABER-Bupivacaine	$ 7,814	$ 2,852
TRANSDUR-Sufentanil	6,109	4,648
Remoxy	3,604	2,408
Memryte	5,633	2,260
CHRONOGESIC	1,851	8,549
Others	4,130	3,673
Total research and development expenses	$ 29,141	$ 24,390

We cannot reasonably estimate the timing and estimated costs of our research and development programs due to the risks and uncertainties associated with developing pharmaceutical systems as outlined in the Risk Factors section of this report. The duration of development of our research and development programs may span as many as ten years or more, and estimation of completion dates or costs to complete would be highly speculative and subjective due to the numerous risks and uncertainties associated with developing pharmaceutical products, including significant and changing government regulation, the uncertainties of future preclinical and clinical study results, the uncertainties with our collaborators commitment and progress to the programs and the uncertainties associated with process development and manufacturing as well as sales and marketing. In addition, with respect to our development programs subject to third-party collaborations, the timing and expenditures to complete the programs are subject to the control of our collaborators. Therefore, we cannot reasonably estimate the timing and estimated costs of the efforts necessary to complete the research and development programs. For additional information regarding these risks and uncertainties, see Risk Factors above.

Selling, General and Administrative. Selling, general and administrative expenses are primarily comprised of salaries and benefits associated with finance, legal, business development, sales and marketing and other administrative personnel, overhead and facility costs, and other general and administrative costs. Selling, general and administrative expenses were $11.0 million in 2005 compared with $9.8 million in 2004. The increases in selling, general and administrative expenses were primarily due to higher patent, market research and employee related expenses in 2005 compared with 2004.

As of December 31, 2005, we had 32 selling, general and administrative personnel compared with 34 as of the corresponding date in 2004. We expect selling, general and administrative expenses to increase slightly in the near future as we strive to conserve cash and leverage our existing infrastructure to support our current business activities and to comply with corporate governance requirements.

Amortization of intangible assets. Amortization of intangible assets was both $1.2 million in 2005 and 2004. We continue to amortize the existing intangible assets at a constant rate over their estimated useful lives. In 2005 and 2004, goodwill was evaluated for impairment in accordance with SFAS 142. Based on our evaluation, no indicators of impairment were noted. Should goodwill become impaired in the future, we may be required to record an impairment charge to write the goodwill down to its estimated fair value.

The net amount of other intangible assets at December 31, 2005 was $536,000, which will be amortized as follows: $424,000 for the year ending December 31, 2006, $31,000 in each of the years ending December 31, 2007, 2008 and 2009, and $19,000 for the year ending December 31, 2010. We periodically evaluate acquired intangible assets for impairment or obsolescence. Should the intangible assets become impaired or obsolete, we will write them down to their estimated fair value.

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Stock-Based Compensation. Since inception, we have recorded aggregate deferred compensation charges of $11.2 million in connection with stock options granted to employees and directors, including $918,000 that we recorded at the time of our acquisition of Southern BioSystems, Inc. (SBS) in April 2001 for the assumption of outstanding unvested stock options granted to employees and directors of that company. Of the total amount, we have amortized or reversed (due to employee terminations) approximately $11.2 million through December 31, 2005. Employee stock-based compensation expense, net of reversal, was $340,000 in 2005 and ($15,000) in 2004. Of these amounts, employee stock compensation related to the following: cost of revenue of none in 2005 and $1,000 in 2004; research and development expenses of $2,000 in 2005 and ($30,000) in 2004; and selling, general and administrative expenses of $338,000 in 2005 and $14,000 in 2004.

Total stock compensation expense related to modification of stock option terms was $336,000 in 2005 and $5,000 in 2004.

Total non-employee stock compensation was $251,000 in 2005 and $214,000 in 2004. Of these amounts, non-employee stock compensation related to the following: research and development expenses of $235,000 in 2005 and $182,000 in 2004 and selling, general and administrative expenses of $16,000 in 2005 and $30,000 in 2004. Expenses for non-employee stock options are recorded over the vesting period of the options, with the amount determined by the Black-Scholes option valuation method and remeasured over the vesting term.

The remaining deferred employee stock compensation at December 31, 2005 was none. Termination of employment of option holders could cause stock-based compensation in future years to be less than indicated.

Other Income (Expense). Interest income and other was $2.3 million in 2005 and $1.2 million in 2004. The increase in interest and other income was primarily the result of higher yields on our cash and investment balances. The increase in interest and other income in 2005 was also due to the receipt of approximately $300,000 settlement from our former third-party collaborators in 2005. We expect interest income to increase slightly in the future compared with 2005 as we completed a secondary follow-on offering with net proceeds of approximately $38.1 million in November 2005 and achieved higher yields on our current cash and investments.

Interest expense was $4.4 million in 2005 and $4.5 million and 2004. The interest expenses were primarily due to the interest accrued on the 6.25% convertible notes due 2008.

Debt conversion expense was $403,000 in 2005 compared with none in 2004. The debt conversion expense was recorded in connection with the induced conversion of approximately $2.2 million in aggregate principal amount of the 6.25% convertible notes in the third quarter of 2005. We expect interest expense to remain comparable in the near future as we continue to make interest payments on our convertible notes and to amortize the issuance costs to interest expenses.

Income taxes. Income tax provision was $4,000 in 2005 due to state income taxes paid for API in 2005 compared with $18,000 in 2004. Prior to 2004, we had no provision for income taxes, as we incurred losses for all periods presented. As of December 31, 2005, we had net operating loss carryforwards for federal income tax purposes of approximately $142.4 million, which expire in the years 2018 through 2025 and federal research and development tax credits of approximately $1.7 million, which expire at various dates beginning in 2018 through 2025, if not utilized.

As of December 31, 2005, we had net operating loss carryforwards for state income tax purpose of approximately $72.1 million, which expire in the years 2008 through 2015 and state research and development tax credits of approximately $1.6 million, which do not expire.

Utilization of the net operating losses may be subject to a substantial annual limitation due to federal and state ownership change limitations. The annual limitation may result in the expiration of net operating losses and credits before utilization.

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As of December 31, 2005 and 2004, we had net deferred tax assets of $64.8 million and $57.0 million. Deferred tax assets reflect the net tax effects of net operating loss and credit carryforwards and the temporary differences between the carrying amounts of assets and liabilities for financial reporting and the amounts used for income tax purposes. Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance.

Comparison of years ended December 31, 2004 and 2003

Revenue. Total revenues were $13.9 million in 2004 compared to $11.8 million in 2003. The increase in total revenue was primarily attributable to higher collaborative research and development and milestone revenue recognized from our agreements with Pain Therapeutics, Voyager Pharmaceutical Corporation and other strategic collaborators. A portion of our revenues is derived from our product sales, which include our ALZET mini pump product line, and to a lesser extent our polymer products and ear catheter products.

Collaborative research and development and other revenue

We recognize revenues from collaborative research and development activities, service contracts and to a lesser extent license activities. We recorded $6.9 million of collaborative research and development and milestone revenue in 2004 compared to $5.0 million in 2003. Collaborative research and development and milestone revenue represents reimbursement of qualified expenses related to the collaborative agreements with various third parties to research, develop and commercialize potential development products using our drug delivery technologies and milestone payments upon achieving certain regulatory milestones under the collaboration agreements. The increase in collaborative research and development revenue in 2004 was primarily attributable to our increased development activities for Remoxy (collaboration with Pain Therapeutics) and Memryte (collaboration with Voyager) compared with 2003. We recognized $1.0 million of milestone revenue in 2004 under the collaboration agreements with Pain Therapeutics and Voyager compared with none in 2003. We expect our collaborative research and development revenue to increase in the future years as we continue to increase our effort to develop products in connection with various strategic collaborations.

The collaborative research and development revenues associated with our major third-party collaborators are as follows (in thousands):

	Year ended December 31,	
	2004	2003
Collaborator		
Pain Therapeutics, Inc.(1)	$ 3,979	2,787
Voyager Pharmaceutical Corporation	2,533	1,175
Others	341	1,033
Total collaborative research and development revenue	$ 6,853	$ 4,995

Notes:

1. Amounts related to up-front fees were $140,000 and $860,000 in 2004 and 2003, respectively.

We amortize up-front fees on a straight-line basis over the period in which we have continuing involvement with the third-party collaborator pursuant to the applicable agreement. Such period generally represents the research and development period set forth in the work plan under each collaboration agreement between us and our third-party collaborator.

Other revenue from service contracts was $502,000 in 2004 compared to $149,000 in 2003. Service contract revenues were related to certain polymer related service contracts API signed with various customers. Other

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license revenue was $82,000 in 2004 compared with none in 2003. Our license revenue was recognized in connection with our agreement with NeuroSystec.

In 2004, revenues from our collaborative agreements with Pain Therapeutics and Voyager represented 29% and 18% of our total revenues. In 2003, revenues from our collaborative agreements with Pain Therapeutics and Voyager represented 24% and 10% of our total revenues. In the future, we do not intend to significantly increase our investments in or efforts to sell or market any of our existing product lines. However, 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 collaborators to develop products based on our drug delivery technologies.

Product revenue

Net product revenues were $6.4 million in 2004 compared to $6.7 million in 2003. The decrease was primarily due to a lower product revenue from our ALZET mini pump product line in 2004, partially offset by higher polymer revenue from our API biodegradable polymer product line. We ceased selling IntraEAR catheter products in September 2003 due to a change in business strategic focus. IntraEAR products comprised zero and $81,000 of net product revenue in 2004 and 2003, respectively.

Cost of revenue. Cost of revenue increased to $2.7 million in 2004 from $2.4 million in 2003. Cost of revenue includes cost of product revenue and cost of contract services provided by us. The increase in cost of revenue was primarily due to increased cost of service revenue related to API service contracts in 2004.

Cost of revenue associated with the product revenue was $2.3 million in both 2004 and in 2003. Cost of other revenue from service contracts increased to $407,000 in 2004 from $119,000 in 2003 due to higher manufacturing costs for additional service contracts we performed for API customers in 2004.

As of December 31, 2004, we had 21 manufacturing employees compared with 20 as of the corresponding date in 2003. We expect cost of revenue to remain comparable in the future, as we do not expect product revenues and service contract revenues to increase significantly in the future.

Research and development. Research and development expenses increased to $24.4 million in 2004 from $20.7 million in 2003. The increase was primarily attributable to higher development costs related to SABER-Bupivacaine, TRANDUR-Sufentanil, CHRONOGESIC and other pharmaceutical systems in development.

As of December 31, 2004, we had 72 research and development employees compared with 60 as of the corresponding date in 2003. We expect research and development expenses to increase in the near future as we continue to conduct clinical trials and toxicological studies for our SABER-Bupivacaine and TRANSDUR-Sufentanil and continue product development efforts for other pharmaceutical systems.

The approximate research and development expenses associated with our most advanced pharmaceutical systems in development are as follows (in thousands):

	Year ended December 31,	
	2004	2003
SABER-Bupivacaine	$ 2,852	$ 2,082
TRANSDUR-Sufentanil	4,648	69
Remoxy	2,408	1,421
Memryte	2,260	965
CHRONOGESIC	8,549	12,109
Others	3,673	4,092
Total research and development expenses	$ 24,390	$ 20,738

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Selling, general and administrative. Selling, general and administrative expenses increased to $9.8 million in 2004 from $8.6 million in 2003. The increase primarily resulted from higher internal and external expenses to comply with Section 404 of the Sarbanes-Oxley Act of approximately $700,000.

As of December 31, 2004, we had 34 selling, general and administrative personnel compared with 31 as of the corresponding date in 2003. We expect selling, general and administrative expenses to increase modestly in the near future in light of the additional cost of corporate governance requirements.

Amortization of intangible assets. Amortization of intangible assets was $1.2 million in 2004 compared with $1.3 million in 2003. The amortization of intangible assets decreased in 2004 as certain intangible assets were fully amortized in the quarter ended June 30, 2004. In 2004 and 2003, goodwill was evaluated for impairment in accordance with SFAS 142. Based on our evaluation, no indicators of impairment were noted. Should goodwill become impaired in the future, we may be required to record an impairment charge to write the goodwill down to its estimated fair value.

The net amount of intangible assets at December 31, 2004 was $1.7 million, which will be amortized as follows: $1.2 million in the year of 2005, $424,000 in the year 2006, $31,000 in each of the years 2007, 2008 and 2009, and $19,000 in the year 2010. Should other intangible assets become impaired, the Company will write them down to their estimated fair values.

Stock-based compensation. Since inception, we have recorded aggregate deferred compensation charges of $11.2 million in connection with stock options granted to employees and directors, including $918,000 that we recorded at the time of our acquisition of Southern BioSystems, Inc. (SBS) in April 2001 for the assumption of outstanding unvested stock options granted to employees and directors of that company. Of the total amount, we have amortized or reversed (due to employee terminations) approximately $11.2 million through December 31, 2004. Employee stock-based compensation expense, net of reversal, was ($15,000) in 2004 and ($276,000) in 2003. Of these amounts, employee stock compensation related to the following: cost of revenue of $1,000 in 2004 and $18,000 in 2003; research and development expenses of ($30,000) in 2004 and ($384,000) in 2003; and selling, general and administrative expenses of $14,000 in 2004 and $90,000 in 2003. Total stock compensation expense related to modification of stock option terms was $5,000 in 2004 and $78,000 in 2003.

Total non-employee stock compensation was $214,000 in 2004 and $96,000 in 2003. Of these amounts, non-employee stock compensation related to the following: research and development expenses of $182,000 in 2004 and $96,000 in 2003 and selling, general and administrative expenses of $30,000 in 2004 and none in 2003. Expenses for non-employee stock options are recorded over the vesting period of the options, with the amount determined by the Black-Scholes option valuation method and remeasured over the vesting term.

The remaining deferred employee stock compensation at December 31, 2004 was $4,000, which will be amortized as follows: $3,000 in 2005 and $1,000 in 2006. Termination of employment of option holders could cause stock-based compensation in future years to be less than indicated.

Other income (expense). Interest income increased to $1.2 million in 2004 from $1.0 million in 2003. The increase in interest income was primarily attributable to higher yields on cash and debt security investments. We expect interest income to decline as our average outstanding investment balances decline. The increase in interest expense to $4.5 million for 2004 from $2.5 million for 2003 was primarily due to interest expense incurred on the $60.0 million of convertible subordinated notes issued in June and July 2003. We expect interest expense to remain comparable in the near future as we continue to make interest payments on our convertible notes and to amortize the issuance costs to interest expenses.

Income taxes. Income tax provision was $18,000 in 2004 due to state income taxes paid for API in 2004 compared with zero in 2003. Prior to 2004, we had no provision for income taxes, as we incurred losses for all periods presented. As of December 31, 2004, we had net operating loss carryforwards for federal income tax

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purposes of approximately $132.3 million, which expire in the years 2018 through 2024 and federal research and development tax credits of approximately $1.6 million, which expire at various dates beginning in 2018 through 2024, if not utilized.

As of December 31, 2004, we had net operating loss carryforwards for state income tax purpose of approximately $71.1 million, which expire in the years 2008 through 2014 and state research and development tax credits of approximately $1.4 million, which do not expire.

Utilization of the net operating losses may be subject to a substantial annual limitation due to federal and state ownership change limitations. The annual limitation may result in the expiration of net operating losses and credits before utilization.

As of December 31, 2004 and 2003, we had net deferred tax assets of $57.0 million and $44.5 million. Deferred tax assets reflect the net tax effects of net operating loss and credit carryforwards and the temporary differences between the carrying amounts of assets and liabilities for financial reporting and the amounts used for income tax purposes. Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance.

Liquidity and Capital Resources

We had cash, cash equivalents, and investments totaling $91.0 million, $61.8 million and $85.2 million at December 31, 2005, 2004 and 2003, respectively. This includes $2.0 million, $2.8 million and $3.1 million of interest-bearing marketable securities classified as restricted investments on our balance sheet as of December 31, 2005, 2004 and 2003, respectively, which primarily serve as collateral for letters of credit securing our leased facilities and Alabama State Industrial Development Bonds payments which were assumed by us as part of our acquisition of SBS (SBS Bonds). The letters of credit related to security deposits of the leased facilities and the SBS bonds will expire in June 2006, December 2012 and November 2009, respectively.

From inception through the time of our initial public offering, we raised $53.2 million, net of issuance costs, through convertible preferred stock financings. We raised $84.0 million, net of issuance costs, through our sale of stock in our initial public offering in 2000. We received $56.7 million, net of issuance costs, through our issuance of $60.0 million aggregate principal amount of convertible subordinated notes due 2008 in June and July of 2003. We received $38.1 million, net of issuance costs, through our sale of stock in our follow-on public offering in November 2005. The increase in cash, cash equivalents and investments from 2004 to 2005 was primarily the result of receipt of net proceeds from issuance of the stock and payments received from customers and third-party collaborators, partially offset by ongoing operating expenses. The decrease in cash, cash equivalents and investments from 2003 to 2004 was primarily the result of increased operating and capital expenditures and interest payments for our convertible subordinated notes, offset by payments received from customers and third-party collaborators.

Working capital was $84.2 million, $42.1 million and $61.1 million at December 31, 2005, 2004 and 2003, respectively. The increase from 2004 to 2005 was primarily attributable to the net proceeds of $38.1 million from our follow-on offering in November and $10.0 million received from Endo in April 2005 in connection with our March 2005 license agreement for TRANSDUR-Sufentanil, offset by our operating expenditures primarily related to our research and development efforts. The decrease in working capital from 2003 to 2004 was primarily attributable to the expenditures related to our research and development efforts in general, and purchases of certain long-term investments in 2004.

We used $7.2 million, $22.2 million and $19.2 million of cash for operating activities in the years ended December 31, 2005, 2004 and 2003, respectively. The decrease in 2005 compared to 2004 was primarily due to $10.0 million of upfront fee received in connection with our agreement with Endo in 2005 and higher payments

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received from third parties for collaborative research and development revenue recognized in 2005. The increase in cash used in operating activities in 2004 compared to 2003 was primarily attributable to higher operating expenses related to our SABER-Bupivacaine, TRANSDUR-Sufentanil, CHRONOGESIC and other pharmaceutical systems in development.

We received $14.0 million and $20.8 million of cash from investing activities in the years ended December 31, 2005 and 2004, respectively, compared with $30.9 million of cash used in investing activities in the year ended December 31, 2003. The decrease in cash received from investing activities in 2005 was primarily due to higher purchases in property and equipment and lower net proceeds received from maturing of our investments compared with 2004. The $30.9 million of cash used in investing activities in 2003 was primarily due to higher purchases of available-for-sale securities in 2003, including our investment of the net proceeds from the $60 million convertible notes issued in June and July of 2003.

We received $38.7 million, $245,000 and $57.3 million of cash from financing activities in the years ended December 31, 2005, 2004 and 2003, respectively. In 2005, cash received from financing activities was primarily due to net proceeds from sales of our common stock in our follow-on public offering in November 2005. In 2004, cash received from financing activities was primarily due to proceeds from exercises of stock options and purchases of our common stock under our employee stock purchase plan, offset by payments on a term loan and long term debt. In 2003, cash received from financing activities was primarily due to the net proceeds from our $60.0 million aggregate principal amount of convertible notes issued in June and July of 2003.

In October 2005, we filed a shelf registration statement on Form S-3 with the SEC, which will allow us to offer up to $75 million of securities from time to time in one or more public offerings of our common stock. In November 2005, we closed a follow-on public offering of 8,183,274 shares of our common stock at $5.00 per share and received net proceeds of approximately $38.1 million, after deducting underwriting discounts and related expenses.

In June and July 2003, we completed a private placement of an aggregate of $60.0 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 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 $56.7 million after deducting underwriting fees of $3.0 million and related expenses of $300,000. The convertible subordinated notes are unsecured obligation of ours and are subordinate to any secured debt we currently have or any future senior debt we may have. The proceeds from the convertible notes will be used to fund the research, development, manufacture and commercialization of existing and future products and for general corporate purpose, including working capital and capital expenditures.

On July 21, 2005, we entered into a privately negotiated agreement with a holder of our 6.25% Convertible Subordinated Notes, due June 2008, to exchange up to $5.0 million in principal amount of convertible notes for 317.4603 shares of common stock per $1,000 principal amount as originally defined in the indenture, plus additional shares to compensate the note holder for early exchange. We exchanged approximately $2.2 million in principal amount of our 6.25% convertible notes for approximately 753,000 shares of our common stock pursuant to this agreement in the third quarter of 2005. We may enter into similar transactions from time to time with holders of its convertible notes if we are able to do so on acceptable terms and depending on capital market conditions. In September 2005, a holder of the Company s 6.25% Convertible Subordinated Notes voluntarily converted $500,000 in principal amount of convertible notes for 158,730 shares of common stock. These notes were cancelled as of September 30, 2005. As of December 31, 2005, the remaining principal balance of the Company s Convertible Subordinated Notes was $57.3 million.

In conjunction with the acquisition of SBS in April 2001, we assumed the SBS Bonds with remaining principal payments of $1.7 million and a current interest rate of 6.35% increasing each year up to 7.20% at

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maturity on November 1, 2009. As part of the acquisition agreement, we were required to guarantee and collateralize these bonds with a letter of credit of approximately $2.4 million that we secured with investments deposited with a financial institution in July 2001. Interest payments are due semi-annually and principal payments are due annually. Principal payments increase in annual increments from $150,000 to $240,000 over the term of the bonds until the principal is fully amortized in 2009. We have an option to call the SBS Bonds at any time. On December 31, 2002, SBS was merged into DURECT, and the SBS bonds were assigned to DURECT with the terms unchanged. At December 31, 2005, the remaining principal payments of the bonds were $875,000.

We anticipate that cash used in operating activities will increase in the near future as we continue to research, develop, and manufacture our pharmaceutical systems. In aggregate, we are required to make future payments pursuant to our existing contractual obligations as follows (in thousands):

Contractual Obligations	2006	2007	2008	2009	2010	2011 and thereafter	Total
Convertible subordinated notes(1)	$ 3,584	$ 3,584	$ 58,979	$	$		$ 66,147
Long-term debt(1)	263	258	258	257			1,036
Term loan and capital lease(1)	35	11	11	6			63
APT acquisition consideration payable(2)	500						500
Purchase commitments	210		100	350	500	4,000	5,160
Operating lease obligations	2,343	2,029	2,027	988	740	1,525	9,652
Total contractual cash obligations	$ 6,935	$ 5,882	$ 61,375	$ 1,601	$ 1,240	$ 5,525	$ 82,558

Notes

1 Includes principal and interest payments

2 To be paid in our common stock or cash at our election

We also anticipate incurring capital expenditures of at least $3 million over the next 12 months to purchase research and development and manufacturing equipment. The amount and timing of these capital expenditures will depend, among other things, on the success of clinical trials for our product candidates and our collaborative research and development activities.

We believe that our existing cash, cash equivalents and investments will be sufficient to fund our planned operations, existing debt and contractual commitments, and planned capital expenditures through at least 12 months. We may consume available resources more rapidly than currently anticipated, resulting in the need for additional funding. Additionally, we do not expect to generate revenues from our pharmaceutical systems currently under development for at least the next several years, if at all. Accordingly, we may be required to raise additional capital through a variety of sources, including:

- the public equity market;

- private equity financing;
- collaborative arrangements; and
- public or private debt.

There can be no assurance that additional capital will be available on favorable terms, if at all. If adequate funds are not available, we may be required to significantly reduce or refocus our operations or to obtain funds through arrangements that may require us to relinquish rights to certain of our products, technologies or potential markets, either of which could have a material adverse effect on our business, financial condition and results of operations. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of such securities would result in ownership dilution to our existing stockholders.

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We have not utilized and do not intend to utilize off-balance sheet arrangements, special purpose entities, hedging and derivative strategies, or other complex financial techniques to fund our operations or otherwise manage our financial position.

Our cash and investments policy emphasizes liquidity and preservation of principal over other portfolio considerations. We select investments that maximize interest income to the extent possible given these two constraints. We satisfy liquidity requirements by investing excess cash in securities with different maturities to match projected cash needs and limit concentration of credit risk by diversifying our investments among a variety of high credit-quality issuers.

Recent Accounting Pronouncements

In December 2004, the FASB issued Statement No. 123 (revised 2004, or FAS 123R), Share-Based Payment, effective for annual or interim periods beginning after June 15, 2005. FAS 123R supersedes APB Opinion No. 25, Accounting for Stock Issued to Employees, and will require companies to recognize compensation expense, using a fair-value based method, for costs related to share-based payments including stock options and stock issued under our employee stock purchase plans. We adopted FAS 123R using the modified prospective basis on January 1, 2006. Our adoption of FAS 123R is expected to result in compensation expense that will increase the net loss in 2006. Our estimate of future stock-based compensation expense is affected by our stock price, the number of stock-based awards our board of directors may grant in 2006, as well as a number of complex and subjective valuation assumptions. These valuation assumptions include, but are not limited to, the volatility of our stock price and employee stock option exercise behaviors. We expect that our adoption of FAS 123R will have a material adverse impact on our consolidated results of operations.

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

In June 2005, the FASB ratified the consensus reached by the Emerging Issues Task Force No. 05-6 (EITF 05-6). The Task Force reached a consensus that leasehold improvements that are placed in service significantly after and not contemplated at or near the beginning of the lease term should be amortized over the shorter of the useful life of the assets or a term that includes required lease periods and renewals that are deemed to be reasonably assured at the date the leasehold improvements are purchased. In addition, leasehold improvements acquired in a business combination should be amortized over the shorter of the useful lives of the assets or a term that includes required lease periods and renewals that are deemed to be reasonably assured at the date of acquisition. EITF 05-6 is effective for leasehold improvements (within the scope of this issue) that are purchased or acquired in the reporting period beginning after June 29, 2005. Adoption of EITF 05-6 did not have an impact on our consolidated financial condition or results of operations.

Management s Report on Controls and Procedures

Evaluation of Disclosure Controls and Procedures: The Company s principal executive and financial officers reviewed and evaluated the Company s disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e)) as of the end of the period covered by this Form 10-K. Based on that evaluation, the Company s principal executive and financial officers concluded that the Company s disclosure controls and procedures are effective in timely providing them with material information relating to the Company, as required to be disclosed in the reports the Company files under the Exchange Act.

Management s Annual Report on Internal Control Over Financial Reporting: The Company s management is responsible for establishing and maintaining adequate internal control over the Company s financial reporting (as defined in Exchange Act Rule 13a-15(f)). Management assessed the effectiveness of the

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Company s internal control over financial reporting as of December 31, 2005. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control-Integrated Framework*. Based on the assessment using those criteria, management concluded that, as of December 31, 2005, our internal control over financial reporting was effective.

The Company s independent registered public accountants, Ernst & Young LLP, audited the consolidated financial statements included in this Annual Report on Form 10-K and have issued an audit report on management s assessment of our internal control over financial reporting as well as on the effectiveness of the Company s internal control over financial reporting. The report on the audit of the consolidated financial statements appears on or about page 66 of this Annual Report on Form 10-K and the report on the audit of internal control over financial reporting appears on or about page 67 of this Annual Report on Form 10-K.

Changes in Internal Control Over Financial Reporting: There were no significant changes in the Company s internal control over financial reporting during the Company s most recently completed fiscal quarter that has materially affected, or is reasonably likely to materially affect, the Company s internal control over financial reporting.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Sensitivity

Our exposure to market risk for changes in interest rates relates primarily to our investment portfolio and long-term debt obligations. Fixed rate securities and borrowings may have their fair market value adversely impacted due to fluctuations in interest rates, while floating rate securities may produce less income than expected if interest rates fall and floating rate borrowings may lead to additional interest expense if interest rates increase. Due in part to these factors, our future investment income may fall short of expectations due to changes in interest rates or we may suffer losses in principal if forced to sell securities which have declined in market value due to changes in interest rates.

Our primary investment objective is to preserve principal while at the same time maximizing yields without significantly increasing risk. Our portfolio includes money markets funds, commercial paper, medium-term notes, corporate notes, government securities, corporate bonds and market auction preferreds. The diversity of our portfolio helps us to achieve our investment objective. As of December 31, 2005, approximately 94% of our investment portfolio is composed of investments with original maturities of one year or less and approximately 73% of our investment portfolio matures less than 90 days from the date of purchase.

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The following table presents the amounts of our cash equivalents and investments that may be subject to interest rate risk and the average interest rates as of December 31, 2005 by year of maturity (dollars in thousands):

	2006	2007	2008	Total
Cash equivalents:				
Fixed rate	$ 64,518	$	$	$ 64,518
Average fixed rate	4.36%			4.36%
Variable rate	$ 27			$ 27
Average variable rate	4.01%			4.01%
Short-term investments:				
Fixed rate	$ 18,022	$		$ 18,022
Average fixed rate	2.58%			2.58%
Long-term investments:				
Fixed rate	$	$ 3,474	$ 1,985	$ 5,459
Average fixed rate		3.65%	4.57%	4.01%
Restricted investments:				
Fixed rate	$ 1,974	$	$	$ 1,974
Average fixed rate	1.25%			1.25%
Total investment securities	$ 84,541	$ 3,474	$ 1,985	$ 90,000
Average rate	3.24%	3.65%	4.57%	3.33%

The following table presents the amounts of our cash equivalents and investments that may be subject to interest rate risk and the average interest rates as of December 31, 2004 by year of maturity (dollars in thousands):

	2005	2006	2007	Total
Cash equivalents:				
Fixed rate	$ 19,036	$	$	$ 19,036
Average fixed rate	2.31%			2.31%
Variable rate	$ 19			$ 19
Average variable rate	1.08%			1.08%
Short-term investments:				
Fixed rate	$ 19,515	$		$ 19,515
Average fixed rate	1.72%			1.72%
Variable rate	$ 2,250			$ 2,250
Average variable rate	2.43%			2.43%
Long-term investments:				
Fixed rate	$	$ 15,176	$ 2,042	$ 17,218
Average fixed rate		2.35%	3.35%	2.48%
Restricted investments:				
Fixed rate	$ 2,798	$	$	$ 2,798
Average fixed rate	0.88%			0.88%
Total investment securities	$ 43,618	$ 15,176	$ 2,042	$ 60,836
Average rate	1.79%	2.35%	3.35%	2.02%

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Item 8. Financial Statements and Supplementary Data.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders

DURECT Corporation

We have audited the accompanying consolidated balance sheets of DURECT Corporation as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders equity and cash flows for each of the three years in the period ended December 31, 2005. Our audits also included the financial statement schedule listed in the Index at Item 15(a)(2) of the Annual Report on Form 10-K for the year ended December 31, 2005. These financial statements and schedule are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements and schedule based on our audits.

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

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the consolidated financial position of DURECT Corporation at December 31, 2005 and 2004, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles. Also, in our opinion, the related financial statement schedule, when considered in relation to the basic financial statements taken as a whole, presents fairly in all material respects the information set forth therein.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of DURECT Corporation s internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 9, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Palo Alto, California

March 9, 2006

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders

DURECT Corporation

We have audited management s assessment, included in the accompanying Management s Annual Report on Internal Control Over Financial Reporting, that DURECT Corporation maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). DURECT Corporation s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management s assessment and an opinion on the effectiveness of the company s internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management s assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management s assessment that DURECT Corporation maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, DURECT Corporation maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, based on the COSO criteria**.**

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of DURECT Corporation as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders equity and cash flows for each of the three years in the period ended December 31, 2005 and our report dated March 9, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Palo Alto, California

March 9, 2006

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DURECT CORPORATION

CONSOLIDATED BALANCE SHEETS

(in thousands, except per share amounts)

	December 31,	
	2005	**2004**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 65,542	$ 20,032
Short-term investments	18,022	21,765
Restricted investments	321	
Accounts receivable, net of allowances of $128 and $208, respectively	4,488	2,481
Inventories	2,047	1,929
Prepaid expenses and other current assets	3,659	1,364
Total current assets	94,079	47,571
Property and equipment, net	7,304	7,112
Goodwill	6,399	6,399
Intangible assets, net	536	1,745
Long-term investments	5,459	17,218
Restricted investments	1,653	2,798
Other long-term assets	1,984	2,625
Total assets	$ 117,414	$ 85,468
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 1,835	$ 1,658
Accrued liabilities	3,874	2,549
Contract research liability	1,418	554
Interest payable on convertible notes	149	167
Deferred revenue	2,367	78
Equipment financing obligations and term loan, current portion	34	293
Bonds payable, current portion	200	190
Total current liabilities	9,877	5,489
Equipment financing obligations and term loan, noncurrent portion	27	60
Bonds payable, noncurrent portion	675	875
Convertible subordinated notes	57,337	60,000
Deferred revenue	6,016	
Other long-term liabilities	130	654
Commitments (Note 10)		
Stockholders equity:		
Common stock, $0.0001 par value: 110,000 shares authorized at December 31, 2005 and 2004 respectively; 61,609 and 51,870 shares issued and outstanding at December 31, 2005 and 2004, respectively	6	5

Additional paid-in capital	239,057	196,065
Notes receivable from stockholder		(37)
Deferred compensation		(4)
Deferred royalties and commercial rights	(13,480)	(13,480)
Accumulated other comprehensive loss	(212)	(268)
Accumulated deficit	(182,019)	(163,891)
Stockholders equity	43,352	18,390
Total liabilities and stockholders equity	$ 117,414	$ 85,468

The accompanying notes are an integral part of these consolidated financial statements.

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DURECT CORPORATION

CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except per share amounts)

	Year ended December 31,		
	2005	**2004**	**2003**
Collaborative research and development and other revenue	20,032	7,437	5,144
Product revenue, net	$ 6,939	$ 6,416	$ 6,691
Revenue from sale of intellectual property rights	1,600		
Total revenue	28,571	13,853	11,835
Operating expenses:			
Cost of revenue (1)	2,815	2,730	2,445
Research and development (1)	29,141	24,390	20,738
Selling, general and administrative (1)	11,034	9,793	8,588
Amortization of intangible assets	1,209	1,249	1,343
Total operating expenses	44,199	38,162	33,114
Loss from operations	(15,628)	(24,309)	(21,279)
Other income (expense):			
Interest income and other	2,270	1,236	1,041
Interest expense	(4,363)	(4,546)	(2,460)
Debt conversion expense	(403)		
Net other expense	(2,496)	(3,310)	(1,419)
Loss before income taxes	(18,124)	(27,619)	(22,698)
Income tax provision	4	18	
Net loss	$ (18,128)	$ (27,637)	$ (22,698)
Net loss per common share, basic and diluted	$ (0.34)	$ (0.54)	$ (0.45)
Shares used in computing basic and diluted net loss per share	53,719	51,507	50,510

(1) Stock-based compensation related to the following:

Cost of revenue	$	$ 1	$ 18
Research and development	237	157	(210)
Selling, general and administrative	354	46	90
	$ 591	$ 204	$ (102)

The accompanying notes are an integral part of these consolidated financial statements.

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DURECT CORPORATION

CONSOLIDATED STATEMENT OF STOCKHOLDERS EQUITY

(in thousands)

	Common Stock								
	Shares	Amount	Additional Paid-In Capital	Notes Receivable From Stockholders	Deferred Compensation	Deferred Royalties And Commercial Rights	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders Equity
Balance at December 31, 2002	50,443	$ 5	$ 194,312	$ (469)	$ (732)	$ (13,480)	$ 102	$ (113,556)	$ 66,182
Issuance of common stock upon exercise of stock options, warrants and purchases of ESPP shares	311		486						486
Repurchase of unvested stock for cash and cancellation of certain notes receivable from stockholders	(76)		(66)	66					
Repayment of notes receivable				353					353
Issuance of common stock in connection with acquisition of Absorbable Polymer Technologies, Inc.	485		1,053						1,053
Issuance costs in connection with issuance of common stock to corporate collaborator for cash			(42)						(42)
Amortization of deferred stock compensation					(276)				(276)
Stock compensation related to modifications of stock option terms			78						78
Reversal of deferred compensation related to cancelled employee stock options			(949)		949				
Noncash charges related to equity securities issued to non-employees			96						96
Net change in unrealized loss on available-for-sale securities							(117)		(117)
Net loss								(22,698)	(22,698)
Total comprehensive net loss									(22,815)
Balance at December 31, 2003 (carried forward)	51,163	$ 5	$ 194,968	$ (50)	$ (59)	$ (13,480)	$ (15)	$ (136,254)	$ 45,115

The accompanying notes are an integral part of these consolidated financial statements.

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DURECT CORPORATION

CONSOLIDATED STATEMENT OF STOCKHOLDERS EQUITY (Continued)

(in thousands)

	Common Stock								
	Shares	Amount	Additional Paid-In Capital	Notes Receivable From Stockholders	Deferred Compensation	Deferred Royalties And Commercial Rights	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders Equity
Balance at December 31, 2003 (carried forward)	51,163	$ 5	$ 194,968	$ (50)	$ (59)	$ (13,480)	$ (15)	$ (136,254)	$ 45,115
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	510		662						662
Repurchase of unvested stock for cash and cancellation of certain notes receivable from stockholders	(1)		(1)	1					
Repayment of notes receivable				49					49
Issuance of common stock in connection with acquisition of Absorbable Polymer Technologies, Inc.	185		250						250
Issuance of common stock to an employee for notes receivable	13		37	(37)					
Amortization of deferred stock compensation					(15)				(15)
Stock compensation related to modifications of stock option terms			5						5
Reversal of deferred compensation related to cancelled employee stock options			(70)		70				
Noncash charges related to equity securities issued to non-employees			214						214
Net change in unrealized loss on available-for-sale securities							(253)		(253)
Net loss								(27,637)	(27,637)
Total comprehensive net loss									(27,890)
Balance at December 31, 2004	51,870	5	196,065	(37)	(4)	(13,480)	(268)	(163,891)	18,390
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	602		1,115						1,115
Repayment of notes receivable				37					37
Issuance of common stock in connection with acquisition of Absorbable Polymer Technologies, Inc.	42		250						250
Amortization of deferred stock compensation					4				4
Stock compensation related to modifications of employee stock option terms			336						336
Noncash charges related to equity securities issued to non-employees			251						251

Early conversion of convertible notes	912		2,975						2,975
Secondary equity offering	8,183	1	38,065						38,066
Net change in unrealized gain on available-for-sale securities							56		56
Net loss								(18,128)	(18,128)
Total comprehensive net loss									(18,072)
Balance at December 31, 2005	61,609	$ 6	$ 239,057	$	$	$ (13,480)	$ (212)	$ (182,019)	$ 43,352

The accompanying notes are an integral part of these consolidated financial statements.

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DURECT CORPORATION

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

	Year ended December 31,		
	2005	**2004**	**2003**
Cash flows from operating activities			
Net loss	$ (18,128)	$ (27,637)	$ (22,698)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	1,960	3,391	3,402
Amortization	1,209	1,249	1,343
Noncash charges related to stock-based compensation	591	204	(102)
Loss on impairment and disposal of fixed assets	245		
Inventory write-off	86		
Debt conversion expense	403		
Changes in assets and liabilities:			
Accounts receivable	(2,007)	(513)	(956)
Inventories	(204)	(27)	(47)
Prepaid expenses and other assets	(1,745)	672	233
Accounts payable	177	1,042	264
Accrued liabilities	1,051	(71)	91
Accrued liabilities to related party		(17)	
Contract research liability	864	(433)	(141)
Interest payable on convertible notes	(18)		167
Deferred revenue	8,305	(68)	(802)
Total adjustments	10,917	5,429	3,452
Net cash and cash equivalents used in operating activities	(7,211)	(22,208)	(19,246)
Cash flows from investing activities			
Purchase of property and equipment	(2,397)	(1,138)	(961)
Purchase of available-for-sale securities	(13,852)	(47,729)	(113,971)
Proceeds from maturities of available-for-sale securities	30,234	69,659	84,069
Payment for acquisition, net of cash acquired			(81)
Net cash and cash equivalents provided by (used in) investing activities	13,985	20,792	(30,944)
Cash flows from financing activities			
Net proceeds from convertible subordinated notes			56,700
Proceeds from term loan			850
Payments on term loan and equipment financing obligations	(292)	(287)	(873)
Payment on long term debt	(190)	(180)	(170)
Net proceeds from issuances of common stock through secondary offering	38,066		
Net proceeds from issuances of common stock and stockholders notes	1,152	712	797
Net cash and cash equivalents provided by financing activities	38,736	245	57,304

Net increase (decrease) in cash and cash equivalents	45,510	(1,171)	7,114
Cash and cash equivalents at beginning of year	20,032	21,203	14,089
Cash and cash equivalents at end of year	$ 65,542	$ 20,032	$ 21,203
Supplemental disclosure of cash flow information			
Cash paid during the year for income taxes	$ 4	$ 18	$
Cash paid during the year for interest	$ 3,753	$ 3,874	$ 2,073
Supplemental disclosure of noncash investing and financing activities			
Notes receivable issued in connection with exercise of stock options	$	$ 37	$
Issuance of common stock for acquisition of APT	$ 250	$ 250	$ 1,053

The accompanying notes are an integral part of these consolidated financial statements.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Summary of Significant Accounting Policies

Nature of Operations and Basis of Presentation

DURECT Corporation (the Company) was incorporated in the state of Delaware on February 6, 1998. The Company is a pharmaceutical company developing therapies for the treatment of chronic diseases and conditions with its proprietary drug formulations and delivery platform technologies. The Company has several products under development by itself and with third party collaborators in the areas of pain and other chronic diseases and disorders. The Company also manufactures and sells osmotic pumps used in laboratory research. In addition, the Company conducts research and development of pharmaceutical products in collaboration with third party pharmaceutical and biotechnology companies.

The Company also designs, develops and manufactures a wide range of standard and custom biodegradable polymers for pharmaceutical and medical device clients for use as raw materials in their products. Until December 31, 2004, this business was conducted by the Company s wholly owned subsidiary, Absorbable Polymers International Corporation (API), formerly known as Birmingham Polymers Inc., an Alabama corporation. API was merged with and into DURECT on December 31, 2004.

Basis of Consolidation

The consolidated financial statements include the accounts of the Company and its subsidiary existing as of the reported period. All significant intercompany accounts and transactions have been eliminated.

Reclassifications

Certain prior period amounts related to stock-based compensation expenses in the statements of operations have been reclassified to conform to current period presentation. Such reclassification did not impact the Company s net loss or financial position.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and disclosure of contingent assets and liabilities at the date of the

financial statements and the reported amounts of revenue and expenses during the reported period. Actual results could differ materially from those estimates.

Cash, Cash Equivalents and Investments

The Company considers all highly liquid investments with maturities of 90 days or less from the date of purchase to be cash equivalents. Investments with original maturities of greater than 90 days from the date of purchase but less than one year from the balance sheet date are classified as short-term investments, while investments with maturities beyond one year from the balance sheet date are classified as long-term investments. Management determines the appropriate classification of its cash equivalents and investment securities at the time of purchase and re-evaluates such determination as of each balance sheet date. Management has classified the Company s cash equivalents and investments as available-for-sale securities in the accompanying consolidated financial statements. Available-for-sale securities are carried at fair value, with unrealized gains and losses reported as a component of accumulated other comprehensive income (loss). Realized gains and losses are included in interest income. There were no material realized gains or losses in the periods presented. The cost of securities sold is based on the specific identification method.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The Company invests its excess cash in debt instruments of financial institutions and corporations, and money market funds with high credit ratings. The Company has established guidelines regarding diversification of its investments and their maturities with the objectives of maintaining safety and liquidity, while maximizing yield.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to credit risk consist principally of interest-bearing investments and trade receivables. The Company maintains cash, cash equivalents and investments with various major financial institutions. The Company performs periodic evaluations of the relative credit standing of these financial institutions and limits the amount of credit exposure with any one institution. In addition, the Company performs periodic evaluations of the relative credit quality of its investments.

Universities, pharmaceutical companies and hospitals account for a substantial portion of the Company s trade receivables. The Company provides credit in the normal course of business to its customers and collateral for these receivables is generally not required. The risk associated with this concentration is limited due to the large number of accounts and their geographic dispersion. The Company monitors the creditworthiness of its customers to which it grants credit terms in the normal course of business. The Company maintains reserves for estimated credit losses and, to date, such losses have been within management s expectations. At December 31, 2005, three customers accounted for 27%, 26% and 23% of the Company s net accounts receivables. At December 31, 2004, two customers accounted for 43% and 28% of the Company s net accounts receivables.

Customer and Product Line Concentrations

A substantial portion of the Company s revenue is derived from its ALZET product line, which accounted for 20%, 36% and 44% of total revenues in fiscal years 2005, 2004 and 2003, respectively. Total revenue by geographic region for the years 2005, 2004 and 2003 is as follows (in thousands):

	Year ended December 31,		
	2005	2004	2003
United States	$ 25,869	$ 11,928	$ 8,566
Japan	916	705	940
Europe	953	754	1,899
Other	833	466	430

Total	$ 28,571	$ 13,853	$ 11,835

Revenues by geography is determined by the location of the customer.

In fiscal year 2005, Pain Therapeutics, Endo and Voyager accounted for 17%, 26% and 25% of the Company s total revenues, respectively. In fiscal year 2004, Pain Therapeutics and Voyager accounted for 29% and 18% of the Company s total revenues, respectively.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Inventories

Inventories are stated at the lower of cost or market, with cost determined on a first-in, first-out basis. The Company s inventories consisted of the following (in thousands):

	December 31,	
	2005	2004
Raw materials	$ 203	$ 175
Work in-process	493	452
Finished goods	1,351	1,302
Total inventories	$ 2,047	$ 1,929

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation, which is computed using the straight-line method over the estimated useful lives of the assets, which range from three to five years. Leasehold improvements are amortized using the straight-line method over the estimated useful lives of the assets, or the terms of the related leases, whichever are shorter.

Acquired Intangible Assets and Goodwill

Acquired intangible assets consist of patents, developed technology, trademarks, assembled workforce and customer lists related to the Company s acquisitions accounted for using the purchase method. Amortization of these purchased intangibles is calculated on a straight-line basis over the respective estimated useful lives of the assets ranging from four to seven years. Acquired in-process research and development without alternative future use is charged to operations when acquired. In July 2001, the FASB issued Statement of Financial Accounting Standards No. 142, *Goodwill and Other Intangible Assets* (SFAS 142), which requires the elimination of the amortization of goodwill and assembled workforce to be replaced with the periodic evaluation of intangibles for impairment. The Company assesses goodwill for impairment on at least annually in accordance with SFAS 142.

Impairment of Long-Lived Assets

In accordance with the provisions of Statement of Financial Accounting Standards No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets* (SFAS 144), the Company reviews long-lived assets, including property and equipment, intangible assets, and other long-term assets, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors we consider important which could trigger an impairment review include, but are not limited to, the following:

- significant underperformance relative to expected historical or projected future operating results;
- significant changes in the manner of our use of the acquired assets or the strategy for our overall business;
- significant negative industry or economic trends;
- significant decline in our stock price for a sustained period; and
- our market capitalization relative to net book value.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Under SFAS 144, an impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition is less than its carrying amount. Impairment, if any, is calculated as the amount by which an asset s carrying value exceeds its fair value, typically using discounted cash flows to determine fair value. Through December 31, 2005, there have been no material impairment losses.

Stock-Based Compensation

The Company accounts for stock-based employee compensation arrangements in accordance with the provisions and related interpretations of Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25), and has elected to follow the disclosure only alternative prescribed by Financial Accounting Standards Board s Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation* (SFAS 123). Under APB 25, stock-based compensation is based on the difference, if any, on the date of grant, between the fair value of the Company s stock and the exercise price. Unearned compensation is amortized using the graded vesting method and expensed over the vesting period of the respective options.

At December 31, 2005, the company has five stock-based employee compensation plans, which are described more fully in Note 11. The Company accounts for those plans under the recognition and measurement principles of APB Opinion No. 25, *Accounting for Stock Issued to Employees,* and related Interpretations. No stock-based employee compensation is reflected in the statement of operations when options granted under those plans have an exercise price equal to or greater than the market value of the underlying common stock on the date of grant. The following table illustrates the effect on net loss and net loss per share if the company had applied the fair value recognition provisions of FASB Statement No. 123, *Accounting for Stock-Based Compensation,* to stock-based employee compensation (in thousands, except per share amounts).

	Year Ended December 31,		
	2005	2004	2003
Net loss	$ (18,128)	$ (27,637)	$ (22,698)
Add: Stock-based employee compensation expense included in reported net loss	340	(10)	(198)
Deduct: Total stock-based employee compensation expense determined under fair value based method for all awards	(3,470)	(3,017)	(2,211)
Pro forma net loss	$ (21,258)	$ (30,664)	$ (25,107)
Net loss per share:			
Basic and diluted as reported	$ (0.34)	$ (0.54)	$ (0.45)
Basic and diluted pro forma	$ (0.40)	$ (0.60)	$ (0.50)

The Company accounts for equity instruments issued to non-employees in accordance with the provisions of SFAS 123 and Emerging Issues Task Force 96-18, *Accounting for Equity Instruments that are Issued to other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services.* The fair value of equity instruments granted to non-employees is periodically remeasured as the underlying options vest.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Revenue Recognition

Revenue from the sale of products is recognized at the time the product is shipped and title transfers to customers, provided no continuing obligation exists and the collectibility of the amounts owed is reasonably assured.

Revenue from the sale of intellectual property rights is recognized upon assignment of such rights by the Company to a third party, provided the collectibility is assured and the Company has no future performance obligations related to such rights, except for the on-going de minimus assistance the Company would provide to the third party with respect to the maintenance of such rights.

Upfront payments received upon execution of collaborative agreements are recorded as deferred revenue and recognized as collaborative research and development revenue based on a straight-line basis over the period of the Company s continuing involvement with the third-party collaborator pursuant to the applicable agreement. Such period generally represents the research and development period set forth in the work plan defined in the respective agreements between the Company and its third-party collaborators.

Research and development revenue related to services performed under the collaborative arrangements with the Company s third-party collaborators is recognized as the related research and development services are performed. These research payments received under each respective agreement are not refundable and are generally based on reimbursement of qualified expenses, as defined in the agreements. Research and development expenses under the collaborative research and development agreements generally approximate or exceed the revenue recognized under such agreements over the term of the respective agreements. Deferred revenue may result when the Company does not expend the required level of effort during a specific period in comparison to funds received under the respective agreement.

The collaborative research and development revenues associated with the Company s major third-party collaborators are as follows (in thousands):

	Year ended December 31,		
	2005	2004	2003
Collaborator			
Endo Pharmaceuticals, Inc.(1)	$ 7,325	$	$
Pain Therapeutics, Inc.(2)	4,873	3,979	2,787
Voyager Pharmaceutical Corporation	7,046	2,533	1,175
Others	704	341	1,033

Total collaborative research and development revenue	$ 19,948	$ 6,853	$ 4,995

Notes:

1. Amounts related to up-front fees were $1.8 million, $0 and $0 in 2005, 2004 and 2003, respectively.

2. Amounts related to up-front fees were $0, $140,000 and $860,000 in 2005, 2004 and 2003, respectively.

The Company amortizes up-front fees on a straight-line basis over the period in which the Company has continuing involvement with the third-party collaborator pursuant to the applicable agreement. Such period generally represents the research and development period set forth in the work plan under each collaboration agreement between the Company and its third-party collaborator.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Milestone payments under collaborative arrangements are recognized as revenue upon achievement of the milestone events, which represent the culmination of the earnings process. Milestone payments are triggered either by the results of the Company s research and development efforts or by events external to the Company, such as regulatory approval to market a product or the achievement of specified sales levels by a third-party collaborator. As such, the milestones are substantially at risk at the inception of the collaboration agreement, and the amounts of the payments assigned thereto are commensurate with the milestone achieved. In addition, upon the achievement of a milestone event, the Company has no future performance obligations related to that milestone payment.

Revenue on cost-plus-fee contracts, such as under contracts to perform research and development for others, is recognized only to the extent of reimbursable costs incurred plus estimated fees thereon. In all cases, revenue is recognized only after a signed agreement is in place. For contracts that have a ceiling price or contract value, losses on contracts are recognized in the period in which the losses become known and estimable.

Research and Development Expenses

Research and development expenses are primarily comprised of salaries and benefits associated with research and development personnel, overhead and facility costs, preclinical and non-clinical development costs, clinical trial and related clinical manufacturing costs, contract services, and other outside costs. Research and development costs are expensed as incurred. Research and development costs paid to third parties under sponsored research agreements are recognized as the related services are performed, generally ratably over the period of service. Purchased research and development is recognized in purchase business combinations for the portion of the purchase price allocated to the appraised value of in-process technologies. The portion assigned to in-process technologies excludes the value of core and developed technologies, which are recorded as intangible assets.

The research and development expenses associated with our major development products approximate the following (in thousands):

	Year Ended December 31,		
	2005	2004	2003
SABER-Bupivacaine	$ 7,814	$ 2,852	$ 2,082
TRANSDUR-Sufentanil	6,109	4,648	69
Remoxy	3,604	2,408	1,421
Memryte	5,633	2,260	965
CHRONOGESIC	1,851	8,549	12,109
Others	4,130	3,673	4,092
Total research and development expenses	$ 29,141	$ 24,390	$ 20,738

Comprehensive Loss

Components of other comprehensive income (loss), including unrealized gains and losses on the Company s available-for-sale securities, are included in total comprehensive loss. The difference between net loss and comprehensive loss in all periods presented resulted from unrealized gains and losses on available-for-sale investments.

	Year Ended December 31,		
	2005	**2004**	**2003**
Net loss	$ (18,128)	$ (27,637)	$ (22,698)
Net change in unrealized gain (loss) on available for sale investments	56	(253)	(117)
Comprehensive loss	$ (18,072)	$ (27,890)	$ (22,815)

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Segment Reporting

The Company follows Statement of Financial Accounting Standard No. 131, *Disclosures about Segments of an Enterprise and Related Information* (SFAS 131). SFAS 131 establishes standards for reporting financial information about operating segments in financial statements, as well as additional disclosures about products and services, geographic areas, and major customers. The Company operates in one operating segment, research and development of pharmaceutical systems.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of common shares outstanding, less the weighted average number of common shares during the year subject to repurchase or held in escrow pursuant to an acquisition agreement. Diluted net loss per share is computed using the weighted-average number of common shares outstanding and common stock equivalents (i.e., options and warrants to purchase common stock, convertible subordinated notes) outstanding during the year, if dilutive, using the treasury stock method for options and warrants and the if-converted method for convertible subordinated notes.

The following table presents the calculations of basic and diluted net loss per share (in thousands, except per share amounts):

	Year ended December 31,		
	2005	2004	2003
Net loss	$ (18,128)	$ (27,637)	$ (22,698)
Basic and diluted weighted average shares:			
Weighted-average shares of common stock outstanding	53,719	51,522	50,719
Less: weighted-average shares subject to repurchase		(15)	(209)
Weighted-average shares used in computing basic and diluted net loss per share	53,719	51,507	50,510
Basic and diluted net loss per share	$ (0.34)	$ (0.54)	$ (0.45)

The computation of diluted net loss per share for the fiscal year ended December 31, 2005 excludes the impact of options to purchase 8.0 million shares of common stock and 18.7 million shares of common stock issuable upon conversion of the subordinated notes at December 31, 2005, as

such impact would be antidilutive.

The computation of diluted net loss per share for the fiscal year ended December 31, 2004 excludes the impact of options to purchase 7.2 million shares of common stock, warrants to purchase 1.0 million shares of common stock and 19.0 million shares of common stock issuable upon conversion of the subordinated notes at December 31, 2004, as such impact would be antidilutive.

The computation of diluted net loss per share for the fiscal year ended December 31, 2003 excludes the impact of options to purchase 5.9 million shares of common stock, warrants to purchase 1.0 million shares of common stock and 10.3 million shares of common stock issuable upon conversion of the subordinated notes at December 31, 2003, as such impact would be antidilutive.

Shipping and Handling

Costs related to shipping and handling are included in cost of good sold for all periods presented.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Operating Leases

The Company leases administrative, manufacturing and laboratory facilities under operating leases. Lease agreements may include rent holidays, rent escalation clauses and tenant improvement allowances. The Company recognizes scheduled rent increases on a straight-line basis over the lease term beginning with the date the Company takes possession of the leased space. The Company records tenant improvement allowances as deferred rent liabilities on the consolidated balance sheets and amortizes the deferred rent over the terms of the lease to rent expense on the consolidated statements of operations.

Recent Accounting Pronouncements

In December 2004, the FASB issued Statement No. 123 (revised 2004, or FAS 123R), Share-Based Payment, effective for annual or interim periods beginning after June 15, 2005. FAS 123R supersedes APB Opinion No. 25, Accounting for Stock Issued to Employees, and will require companies to recognize compensation expense, using a fair-value based method, for costs related to share-based payments including stock options and stock issued under the employee stock purchase plans. The Company adopted FAS 123R using the modified prospective basis on January 1, 2006. The Company s adoption of FAS 123R is expected to result in stock-based compensation expense that will increase the net loss in 2006. The Company s estimate of future stock-based compensation expense is affected by the Company s stock price, the number of stock-based awards the Company s board of directors may grant in 2006, as well as a number of complex and subjective valuation assumptions. These valuation assumptions include, but are not limited to, the volatility of the Company s stock price and employee stock option exercise behaviors. The Company s adoption of FAS 123R will have a material adverse impact on its consolidated results of operations.

In March 2005, the SEC issued SAB No. 107 regarding the interaction between SFAS 123R which was revised in December 2004, and certain SEC rules and regulations and provides the SEC s staff views regarding the valuation of share-based payment arrangements for public companies. The Company expects that this guidance will have a material adverse impact on its consolidated results of operations.

In June 2005, the FASB ratified the consensus reached by the Emerging Issues Task Force No. 05-6 (EITF 05-6). The Task Force reached a consensus that leasehold improvements that are placed in service significantly after and not contemplated at or near the beginning of the lease term should be amortized over the shorter of the useful life of the assets or a term that includes required lease periods and renewals that are deemed to be reasonably assured at the date the leasehold improvements are purchased. In addition, leasehold improvements acquired in a business combination should be amortized over the shorter of the useful lives of the assets or a term that includes required lease periods and renewals that are deemed to be reasonably assured at the date of acquisition. EITF 05-6 is effective for leasehold improvements (within the scope of this issue) that are purchased or acquired in the reporting period beginning after June 29, 2005. Adoption of EITF 05-6 did not have an impact on the Company s consolidated financial condition or results of operations.

2. Strategic Agreements

Agreements with Endo Pharmaceuticals

CHRONOGESIC

In November 2002, the Company entered into a development, commercialization and supply license agreement with Endo under which the companies will collaborate on the development and commercialization of CHRONOGESIC for the U.S. and Canada. The agreement was amended in January 2004, in November 2004 and again in January 2006 to take into account the increase in the CHRONOGESIC development program timeline

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

due to DURECT s implementation of necessary design and manufacturing enhancements. In connection with the execution of the agreement in November 2002, Endo purchased 1,533,742 shares of newly issued common stock of DURECT at an aggregate purchase price of approximately $5.0 million. Under the terms of the agreement, as amended, DURECT will be responsible for CHRONOGESIC s design and development. Endo shall not be responsible for any development costs for the CHRONOGESIC development product prior to May 1, 2007. Commencing on May 1, 2007, unless the agreement is earlier terminated by Endo, Endo will fund 50% of the ongoing development costs and will reimburse the Company for a portion of our prior development costs for the product upon the achievement of certain milestones. Development-based milestone payments made by Endo under this agreement could total up to $52 million. 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 product launch costs. The Company will be responsible for the manufacture of the CHRONOGESIC product. If commercialized, the Company will share profits from the commercialization of CHRONOGESIC in the U.S. and Canada with Endo based on the financial performance of the CHRONOGESIC product. Based on the Company s projected financial performance of the product in the U.S. and Canada, the Company anticipates that our share of such profits, if CHRONOGESIC is commercialized, will be approximately 50%. The agreement provides each party with specified termination rights. In particular, the agreement can be terminated by Endo in the event that (i) DURECT has not delivered to Endo on or before March 31, 2007 a written notice (Notice) that a human pharmacokinetic trial had been completed with CHRONOGESIC, together with a full study report of the results of the trial or (ii) Endo, determines, in its sole discretion, to terminate the Agreement during the sixty-day period after DURECT s delivery of the notice, provided, that, in each case Endo delivers to DURECT its written notice of termination prior to April 30, 2007.

TRANSDUR-Sufentanil

On March 10, 2005, the Company entered into a license agreement with Endo Pharmaceuticals Inc. (Endo) under which the Company granted to Endo the exclusive right to develop and commercialize the Company s proprietary sufentanil transdermal patch development product (TRANSDUR-Sufentanil) in the U.S. and Canada. Under the terms of the agreement, Endo will assume all remaining development and regulatory filing responsibility in the U.S. and Canada, including the funding thereof. The Company will perform all formulation development for Endo unless the Company defaults on such obligations and the Company will be reimbursed for its fully allocated cost in performance of such work. Endo will also be responsible and pay for the manufacture, marketing, sales and distribution of TRANSDUR-Sufentanil in the U.S. and Canada.

Pursuant to the agreement, Endo was obligated to pay an upfront, nonrefundable fee of $10 million. In April 2005, Endo paid the Company the $10 million upfront fee. Endo is also obligated to pay to the Company additional payments of up to approximately $35 million in the aggregate if predetermined regulatory and commercial milestones are achieved. In addition, Endo reimburses the Company for all qualified research and development expenses incurred for TRANSDUR-Sufentanil. If commercialized, Endo will also pay the Company product royalties based on the net sales of TRANSDUR-Sufentanil under the agreement. The Company has the right to co-promote TRANSDUR-Sufentanil under terms specified in the agreement. The agreement also contains terms and conditions customary for this type of arrangement, including representations, warranties and indemnities. The agreement shall continue in effect until terminated. The agreement provides each party with specified termination rights, including the right of each party to terminate the agreement upon material breach of the agreement by the other party. In addition, Endo shall have the right to terminate the agreement at any time without cause subject to a specified notice period and due to adverse product events, legal impediment or the issuance of a final, non-appealable court order enjoining Endo from selling TRANSDUR-Sufentanil in the U.S. and Canada as a result of an action for patent infringement by a third party, provided that in the latter instance,

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

the Company will be required to pay Endo a termination fee ranging from $5 million to $10 million, depending on the date of termination.

The $10 million up-front fee is recognized as revenue ratably over the term of the Company s continuing involvement with Endo with respect to TRANSDUR-Sufentanil. The term of the continuing involvement has been estimated based on the current Product Development Plan pursuant to the agreement. For the year ended December 31, 2005, the Company recognized $1.8 million in collaborative research and development revenue related to this upfront fee. Research and development expenses associated with TRANSDUR-Sufentanil from March 10, 2005 to December 31, 2005 reimbursable by Endo under the license agreement were recognized as collaborative research and development revenue in the twelve months ended December 31, 2005.

Agreement with Pain Therapeutics, Inc.

In December 2002, the Company entered into an exclusive agreement with Pain Therapeutics to develop and commercialize on a worldwide basis Remoxy and other oral sustained release, abuse deterrent opioid products incorporating four specified opioid drugs, using the ORADUR technology. The agreement also provides Pain Therapeutics with the exclusive right to commercialize products developed under the agreement on a worldwide basis. In connection with the execution of the agreement, Pain Therapeutics paid the Company upfront fees of $900,000 in December 2002 and $100,000 in October 2003. In December 2005, the Company amended its agreement with Pain Therapeutics in order to specify its obligations with respect to the supply of key excipients for use in the licensed products. Under the agreement, as amended, the Company is responsible for formulation development, supply of selected key excipients used in the manufacture of licensed products and other specified tasks. The Company will receive additional payments if certain development and regulatory milestones are achieved. In addition, if commercialized, the Company will receive royalties for Remoxy and other licensed products which do not contain an opioid antagonist of between 6.0% to 11.5% of net sales of the product depending on sales volume. This agreement can be terminated by either party for material breach by the other party and by Pain Therapeutics without cause. Under the agreement, Pain Therapeutics reimburses the Company qualified expenses incurred by the Company in connection with the development program. The Company recognizes collaborative research and development revenue related to research and development activities for Remoxy and other development programs based on reimbursement of qualified expenses as defined in the collaborative agreement and related amendment with Pain Therapeutics. Total collaborative research and development revenue recognized under the agreements with Pain Therapeutics was $4.9 million, $4.0 million and $2.8 million in 2005, 2004 and 2003, respectively.

Agreement with Voyager Pharmaceutical Corporation

In July 2002, the Company entered into a development and commercialization agreement with Voyager. Under the terms of the agreement, the Company will collaborate with Voyager to develop a product using the DURIN technology to provide sustained release of leuprolide based on Voyager s patented method of treatment of Alzheimer s disease. The agreement also provides Voyager with the right to commercialize the product on a worldwide basis. The Company is responsible for preclinical development, product manufacture and other specified tasks. The Company will receive payments if certain development and regulatory milestones are achieved. If commercialized, the Company will receive royalties based on product sales. This agreement can be terminated by either party for material breach by the other party and by Voyager without cause. Under the agreement, Voyager reimburses to the Company qualified expenses incurred by the Company in connection with the development program for Memryte. The Company recognizes collaborative research and development revenue related to research and

development activities for Memryte based on reimbursement of qualified expenses as defined in the collaborative agreement with Voyager. Total collaborative research and development revenue recognized under the agreement with Voyager was $7.0 million, $2.5 million and $1.2 million in 2005, 2004 and 2003, respectively.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Patent Assignment

On August 8, 2005, the Company entered into a Purchase Agreement and an Option Agreement with Intervet Inc. (collectively the Agreements). Under the Agreements, in addition to other covenants, rights and obligations specified to each party, the Company assigned to Intervet its entire right, title and interest to a U.S. patent, previously jointly owned by the parties, and Intervet agreed to pay the Company $1.6 million. The Company received the payment of $1.6 million from Intervet in August 2005 and recognized the $1.6 million as revenue in the year ended December 31, 2005 as the Company does not have continuing obligations under the purchase agreement except for the on-going de minimus assistance the Company would provide to Intervet with respect to the maintenance of such patent.

Agreements with ALZA

In April 1998, the Company entered into a development and commercialization agreement with ALZA Corporation (ALZA) for certain product development rights, patent rights, and other know-how relating to the DUROS system. The Company issued 5,600,000 shares of Series A-1 preferred stock, which were subsequently converted into 5,600,000 shares of common stock concurrent with our initial public offering in 2000, to ALZA in connection with this agreement and is required to pay ALZA a royalty on the net sales of products and a percentage of up-front license fees, milestone payments, or any other payments or consideration received by the Company, excluding research and development funding.

In April 2000, ALZA and the Company amended and restated their development and commercialization agreement. This amendment includes a reduction in product royalties and up-front payments to ALZA by the Company under the agreement. As consideration for these amendments, ALZA received 1,000,000 shares of the Company s common stock and, subject to conditions on exercise, a warrant to purchase 1,000,000 shares of common stock at an exercise price of $12.00 per share. The deemed fair value of the stock and the warrant was $13.5 million (See Note 10). This value was recorded as additional paid-in capital and deferred royalties and commercial rights, included as a contra-equity account in the statement of stockholders equity, and will be amortized as royalty expense and sales and marketing expense, respectively, as associated product sales commence. This warrant expired in September 2004, which was the fourth anniversary after the warrant first became exercisable. The Company will periodically evaluate the recoverability of these amounts and assess whether any indicators of impairment have occurred. Indicators of impairment for products under the agreement may include: failure to complete product development, unfavorable outcomes from clinical trials, suspension of clinical trial activities, failure to receive approval from the FDA, and/or lack of market acceptance.

Effective October 1, 2002, the Company entered into a Third Amended and Restated Development and Commercialization Agreement with ALZA Corporation, which replaced and superseded the Second Amended and Restated Development and Commercialization Agreement entered into between ALZA and the Company effective April 28, 1999 and April 14, 2000. The agreement provides the Company with exclusive rights to develop, commercialize and manufacture products using ALZA s patented DUROS® technology in selected fields of use. Under the amended agreement, the Company s maintenance of exclusivity in these licensed fields is no longer subject to minimum annual requirements for development spending or the number of products under development by the Company.

In the years ended December 31, 2005, 2004 and 2003, the Company incurred development expenses of $0, $2,000, and $13,000, respectively, for work performed by ALZA, of which $0, $6,000 and $13,000 was paid during the years ended December 31, 2005, 2004, 2003, respectively.

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DURECT CORPORATION

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3. Acquisition of Absorbable Polymer Technologies, Inc.

On August 15, 2003, the Company acquired Absorbable Polymer Technologies, Inc. (APT), a privately held Alabama Corporation pursuant to an Agreement and Plan of Merger among Durect Corporation, Birmingham Polymers, Inc. and APT (the (Merger Agreement) for a total cost of approximately $2.2 million including the transaction cost of approximately $100,000. In connection with the acquisition, the Company issued an aggregate of 485,122 shares of its common stock, valued at $1.1 million and agreed to pay the remaining purchase consideration of $250,000, $250,000 and $500,000, respectively, through the issuance of additional shares of its common stock or cash in connection with the first, second and third anniversaries of the closing of the merger.

APT manufactured and sold polymer and provided analytical and product development services for third party pharmaceutical and biotechnology companies. This acquisition is intended to help the Company to gain market share in the polymers supply market and to expand custom polymer development capabilities. The purchase price was allocated to the tangible assets and identifiable intangible assets acquired based on their estimated fair value, as follows (in thousands):

Net tangible assets acquired	$ 254
Intangible assets acquired:	
Patents	56
Developed technology	160
Goodwill	1,683
Total purchase price allocation	$ 2,153

Tangible net assets acquired include cash, accounts receivable, inventories and fixed assets. Liabilities assumed principally include accrued expenses and notes payable. Intangible assets represent the excess of the total acquisition cost over the fair value of identifiable net assets of business acquired. Intangible assets except goodwill are each being amortized on a straight-line basis over their estimated useful lives, which are both 7 years.

The acquisition of APT has been accounted for as a purchase, with the results of APT s operations included in the Company s results of operations from the date of acquisition. Pro forma financial information reflecting the acquisition of APT is not provided as the operating results of APT were not significant in relation to the Company s operating results.

In August 2004 and 2005, the Company issued an aggregate of 184,910 and 41,545 shares of its common stock, valued at $250,000 each, at the first and second anniversary of the closing of the merger to former shareholders of APT pursuant to the Merger Agreement. The remaining purchase price consideration was $500,000 as of December 31, 2005 and this amount will be paid by the Company in August 2006.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

4. Goodwill and Intangible Assets

Intangible assets recorded in connection with our acquisitions consist of the following (in thousands):

	December 31, 2005		
	Gross Intangibles	Accumulated Amortization	Net Intangibles
Developed technology	$ 3,600	$ (3,302)	$ 298
Patents	466	(384)	82
Other intangible assets	3,260	(3,104)	156
Total	$ 7,326	$ (6,790)	$ 536

	December 31, 2004		
	Gross Intangibles	Accumulated Amortization	Net Intangibles
Developed technology	$ 3,600	$ (2,647)	$ 953
Patents	466	(319)	147
Other intangible assets	3,260	(2,615)	645
Total	$ 7,326	$ (5,581)	$ 1,745

The intangible assets are being amortized on a straight-line basis over estimated useful lives ranging from four to seven years.

The net amount of intangible assets at December 31, 2005 was $536,000, which will be amortized as follows: $424,000 in the year 2006, $31,000 in each of the years 2007, 2008 and 2009, and $19,000 in the year 2010. Should any intangible assets become impaired, the Company will write them down to their estimated fair value.

Goodwill totaled $6.4 million at December 31, 2005. The Company evaluates goodwill for impairment at least annually. In 2005, 2004 and 2003 goodwill was evaluated and no indicators of impairment were noted. Should goodwill become impaired, we may be required to record an

impairment charge to write the goodwill down to its estimated fair value.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

5. Financial Instruments

The carrying amount of cash and cash equivalents reported on the balance sheet approximates its fair value. Short-term and long-term investments consist of marketable debt securities. The fair values of investments are based upon quoted market prices. The carrying amounts of the Company s borrowings under its secured debt agreements approximate their fair values. The fair values are estimated using a discounted cash flow analysis based on the Company s current incremental borrowing rates for similar types of borrowing arrangements. As of December 31, 2005 and 2004, the fair market value of the Company s convertible notes was $94.7 million and $57.6 million, respectively, compared with the carrying value of $57.3 million and $60.0 million, respectively. The fair market value was obtained through quoted market prices.

The following is a summary of available-for-sale securities as of December 31, 2005 and 2004 (in thousands):

	December 31, 2005			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value
Money market funds	$ 27	$	$	$ 27
Certificates of deposit	650			650
Commercial paper	65,831	13	(2)	65,842
Corporate bonds and notes	6,108		(54)	6,054
Federal agency debt securities	17,596		(169)	17,427
	$ 90,212	$ 13	$ (225)	$ 90,000
Reported as:				
Cash and cash equivalents	$ 64,534	$ 13	$ (2)	$ 64,545
Short-term investments	18,176		(154)	18,022
Long-term investments	5,528		(69)	5,459
Short-term restricted investments	321			321
Long-term restricted investments	1,653			1,653
	$ 90,212	$ 13	$ (225)	$ 90,000

	December 31, 2004			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value

Money market funds	$ 19	$	$	$ 19
Certificates of deposit	1,414			1,414
Commercial paper	20,422		(1)	20,421
Market auction preferreds	3,250			3,250
Corporate bonds and notes	10,015		(91)	9,924
Federal agency debt securities	24,981	3	(178)	24,806
Others	1,003		(1)	1,002
	$ 61,104	$ 3	$ (271)	$ 60,836
Reported as:				
Cash and cash equivalents	$ 19,056	$	$ (1)	$ 19,055
Short-term investments	21,856		(91)	21,765
Long-term investments	17,393	3	(178)	17,218
Restricted investments	2,799		(1)	2,798
	$ 61,104	$ 3	$ (271)	$ 60,836

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The following is a summary of the cost and estimated fair value of available-for-sale securities at December 31, 2005, by contractual maturity (in thousands):

	2005	
	Amortized Cost	Estimated Fair Value
Mature in one year or less	$ 83,030	$ 82,887
Mature after one year through three years	7,182	7,113
Total	$ 90,212	$ 90,000

The follow is a summary of unrealized losses for available-for-sale securities at December 31, 2005 (in thousands):

	Unrealized Loss for Less than 12 Months	
	Fair Value	Unrealized Loss
Commercial paper	$ 9,185	$ (2)
Federal agency debt securities	5,459	(40)
	$ 14,644	$ (42)

	Unrealized Loss for More than 12 Months	
	Fair Value	Unrealized Loss
Corporate bonds and notes	$ 6,054	$ (54)
Federal agency debt securities	10,967	$ (129)

	$ 17,021	$ (183)

The follow is a summary of unrealized losses for available-for-sale securities at December 31, 2004 (in thousands):

	Unrealized Loss for Less than 12 Months	
	Fair Value	Unrealized Loss
Commercial paper	$ 20,421	$ (1)
Corporate bonds and notes	9,924	(91)
Federal agency debt securities	21,834	(150)
Others	1,002	(1)
	$ 53,181	$ (243)

	Unrealized Loss for More than 12 Months	
	Fair Value	Unrealized Loss
Federal agency debt securities	$ 1,972	$ (28)

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

To date the Company has not recorded any impairment charges on marketable securities related to other-than-temporary declines in market value. The Company recognizes an impairment charge when the decline in the estimated fair value of a marketable security below the amortized cost is determined to be other-than-temporary. The Company considers various factors in determining whether to recognize an impairment charge, including the duration of time and the severity to which the fair value has been less than our amortized cost, any adverse changes in the investees financial condition and our intent and ability to hold the marketable security for a period of time sufficient to allow for any anticipated recovery in market value.

6. Notes Receivable

In November 2003, the Company purchased a promissory note in the amount of $150,000 from a private company, Sinexus, Inc. and recorded the $150,000 as part of prepaid expenses and other current assets on the Company s balance sheet as of December 31, 2003. Sinexus is a start-up venture developing site specific treatments for chronic sinusitis, an inflammatory disease affecting the paranasal sinuses. In order to provide bridge funding for Sinexus, the Company and a venture capital firm agreed to loan Sinexus $150,000 each in convertible notes as a pre-Series A seed financing of Sinexus, Inc. The Company s investment in Sinexus represents an interest in a variable interest entity . However, the Company is not a primary beneficiary of Sinexus and the Company s maximum exposure to loss as a result of the Company s involvement with Sinexus is $150,000.

In 2003 and 2004, the Company performed certain research and development activities on behalf of Sinexus. Any amounts received from Sinexus in connection with the Company s performance of research and development activities were accounted for as a direct reduction of the Company s investment.

During 2004, the Company re-evaluated the recoverability of the note receivable. As a result of the impairment indicators noted in that analysis, the Company recorded a provision to reduce the carrying value of the note to zero.

In February 2006, the Company entered into a Note and Warrant Repurchase Agreement with Sinexus. Per the agreement, Sinexus repurchased from DURECT the note and warrant originally issued to DURECT in November 2003 at a purchase price of $150,000. Upon the closing of this agreement, both parties agreed that Sinexus has no outstanding obligations to DURECT and the note and warrant were cancelled in their entirety. The Company recognized $150,000 as other income in its statement of operations in 2005 and re-evaluated the carrying value of the notes receivable to $150,000 at December 31, 2005.

7. Property and Equipment

Property and equipment consist of the following (in thousands):

	December 31,	
	2005	2004
Equipment	$ 11,391	$ 9,914
Leasehold improvement	7,950	7,525
Construction-in-progress	241	178
	19,582	17,617
Less accumulated depreciation	(12,278)	(10,505)
Property and equipment, net	$ 7,304	$ 7,112

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Depreciation expense was $2.0 million, $3.4 million and $3.4 million in 2005, 2004 and 2003, respectively. At December 31, 2005 and 2004, no equipment was collateralized as security for equipment financing facilities.

8. Restricted Investments

In April 2001, the Company deposited $1.0 million in the form of a certificate of deposit with a financial institution as a letter of credit to secure a lease for the Company s office facility in Cupertino, California. The restriction on these funds will be released upon termination of the lease in June 2006, but may be reduced by $200,000 annually provided timely rental payments are made. $200,000 was released by the bank from restriction as of December 31, 2003. In 2004 and 2005, $200,000 and $400,000 were released from restriction, respectively.

In July 2001, the Company also deposited $2.4 million in investment grade securities with the same institution to guarantee bonds assumed in the acquisition of SBS (see Note 10). This guarantee will be released upon the sooner of the Company s exercise of its option to call the bonds at any time, or the bond s maturity date in November 2009. From 2002 to 2005, as allowed under the guarantee agreement, a total of approximately $1.1 million of this collateral was released from restriction following the exchange of the investment grade securities for corporate debt securities with a higher investment grade to conform with the Company s investment policy.

In January 2003, the Company refinanced the previous equipment loan and lease obligations with a three-year term loan with a local bank. The principal of the new term loan was $850,000 with a fixed interest rate of 4.95%. The term loan is secured by a certificate of deposit the Company placed with the same bank. From 2003 to 2005, approximately $730,000 of collateral was released from restriction.

In September 2005, the Company deposited $329,000 in the form of a certificate of deposit with a financial institution as a letter of credit to secure a lease signed in August 2005 for the Company s office facility in Cupertino, California. The restriction on these funds will be released upon termination of the lease in December 2012.

As of December 31, 2005 and 2004, the Company has $2.0 million and $2.8 million, respectively, recorded as restricted investments in connection with the above items.

9. Term Loan

In January 2003, the Company obtained a three-year term loan with a local bank. The principal of the new term loan was $850,000 with a fixed interest rate of 4.95%. The term loan is secured by a certificate of deposit the Company placed with the same bank. The Company does not have

any lines of credit or available balances under the term loan. At December 31, 2005, the remaining balance of the term loan was $24,000.

10. Long-term Debt and Commitments

Convertible Subordinated Notes due 2008

On June 18, 2003, the Company completed a private placement of an aggregate of $50.0 million in convertible subordinated notes (the notes). The notes bear interest at a fixed rate of 6.25% per annum and are due on June 15, 2008. On July 14, 2003, the initial purchaser of $50.0 million of the notes elected to exercise its option to purchase an additional $10.0 million in principal amount of such notes. 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-

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

annually in arrears in June and December. The Company received net proceeds of approximately $56.7 million after deducting underwriting fees of $3.0 million and related expenses of $300,000. The total issuance cost of approximately $3.3 million has been included in other long-term assets on the balance sheet and is amortized to interest expense using the effective interest rate method over the duration of the notes, which is 5 years. The notes are unsecured obligations of the Company and are subordinate to any secured debt the Company currently has or any future senior indebtedness of the Company.

In July 2005, the Company entered into an agreement with a holder of its 6.25% Convertible Subordinated Notes, due June 2008, to exchange up to $5.0 million in principal amount of convertible notes for 317.4603 shares of common stock per $1,000 principal amount as originally defined in the indenture, plus additional shares to compensate the note holder for the early exchange. In July and August 2005, the Company exchanged and converted approximately $2.2 million in principal amount of its 6.25% convertible notes for an aggregate of approximately 687,000 shares of the Company s common stock issuable pursuant to the original terms of the notes as defined in the indenture, plus approximately 67,000 additional shares to compensate the note holder for the early exchange pursuant to this agreement. In accordance with SFAS No. 84, *Induced Conversions of Convertible Debt* , the Company recorded debt conversion expense of approximately $403,000 associated with the induced conversion of this debt. The Company issued the shares of common stock under an exemption from the registration requirements of the 1933 Act provided by Section 3(a)(9) of the 1933 Act.

In September 2005, a holder of the Company s 6.25% Convertible Subordinated Notes due 2008 voluntarily converted $500,000 in aggregate principal amount of convertible notes for 158,730 shares of common stock pursuant to the original terms of the notes as defined in the indenture.

As of December 31, 2005, the remaining principal balance of the Company s 6.25% Convertible Subordinated Notes due 2008 was $57.3 million.

Alabama State Industrial Development Bonds

In conjunction with the acquisition of SBS in April 2001, the Company assumed Alabama State Industrial Development Bonds (SBS Bonds) with remaining principal payments of $1.7 million and a current interest rate of 6.35% increasing each year up to 7.20% at maturity on November 1, 2009. As part of the acquisition agreement, the Company was required to guarantee and collateralize these bonds with a letter of credit of approximately $2.4 million that the Company supported with investments deposited with a financial institution in July 2001. From 2002 to 2005, as allowed under the guarantee agreement, a total of approximately $1.1 million of this collateral was released from restriction following the exchange of the investment grade securities for corporate debt securities with a higher investment grade to conform with the Company s investment policy.

Interest payments are due semi-annually and principal payments are due annually. Principal payments increase in annual increments from $150,000 to $240,000 over the term of the bonds until the principal is fully amortized in 2009. The Company has an option to call the SBS Bonds at any time. As of December 31, 2005, the remaining principal payments totals $875,000.

Operating Leases

The Company leases its Cupertino, California office and research facility under a noncancelable operating lease which expires in February 2009, with an option to extend the lease for 5 years. In September 2005, the Company entered into a lease agreement to lease approximately 40,560 square feet of office and laboratory space in Cupertino, California. The lease term commences in December 2005 and expires in December 2012 with an option to extend for up to an additional six years.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The company also renewed the lease in its Vacaville, California manufacturing facility in July 2005 under a noncancelable operating lease which will expire in August 2008, with an option to extend the lease for a period of three years.

In March 2001, the Company leased additional office space in Cupertino, California, under a noncancelable operating lease which commenced in June 2001, expires in May 2006 and has two options to extend the lease term for three years and five years each.

In connection with the Company s acquisition of APT in August 2003, the Company assumed a lease for approximately 6,650 square feet of office and laboratory space in Pelham, Alabama, which expires in February 2006. Pursuant to the Merger Agreement, the Company amended the lease in September 2004 to lease additional office and laboratory space of approximately 2,750 square feet. The amended lease expires in September 2009 with one option to extend for five years.

In December 2003, the Company leased approximately 20,000 square feet of additional corporate office and laboratory space in Cupertino, California, under a lease expiring in February 2009 with options to extend for up to an additional five years.

In May 2004, the Company leased approximately 2,500 square feet of office and laboratory space in Birmingham, Alabama, under a lease which was subsequently amended in August 2004 and April 2005. This lease expires in April 2006.

Under these leases, the Company is required to pay certain maintenance expenses in addition to monthly rent. Rent expense is recognized on a straight-line basis over the lease term for leases that have scheduled rental payment increases. Rent expense under all operating leases was $2.7 million, $2.9 million and $2.7 million, for the years ended December 31, 2005, 2004 and 2003, respectively.

Future minimum payments under these noncancelable leases and long-term obligations are as follows (in thousands):

Year ending December 31,	Bond Maturities	Operating Leases
2006	$ 200	$ 2,343
2007	210	2,029
2008	225	2,027
2009	240	988
Thereafter		2,265
	$ 875	$ 9,652

11. Stockholders Equity

Common Stock

In October 2005, the Company filed a shelf registration statement on Form S-3 with the SEC, which will allow the Company to offer up to $75 million of securities from time to time in one or more public offerings of our common stock. In November 2005, the Company closed a follow on public offering of 8,183,274 shares of our common stock at $5.00 per share and received net proceeds of approximately $38.1 million, after deducting underwriting discounts and related expenses.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Warrants

As described in Note 2, in April 2000 the Company amended and restated its development and commercialization agreement with ALZA. As consideration for these amendments, ALZA received 1,000,000 shares of the Company s common stock and, subject to conditions on exercise, a warrant to purchase 1,000,000 shares of common stock at an exercise price of $12.00 per share. The common stock issued to ALZA was valued at $7.00 per share. The fair value of the stock and the warrant was $13.5 million. The fair value of the warrant was determined to be $6,480,000, calculated using the Black-Scholes option pricing model, using the following assumptions: stock price of $12.00 per share; no dividends; contractual term of four years; risk-free interest rate of 6%; and expected volatility of 64%. This warrant expired unexercised in September 2004, which was the fourth anniversary after the warrant first became exercisable.

In connection with the acquisition of SBS, the Company assumed outstanding warrants to purchase 124,839 shares of common stock at the weighted-average exercise price of $2.40 per share. These warrants were exercisable immediately at the time of acquisition. The deemed fair value of the warrants was $773,000, calculated using the Black-Scholes option pricing model, using the following assumptions: stock price of $8.384 per share; no dividends; contractual term of 1 1/2 years; risk-free interest rate of 4.1%; and expected volatility of 64%. The fair value of the assumed outstanding warrants were included as part of the purchase price for SBS. As of December 31, 2005, warrants to purchase 91,033 shares of the Company s common stock had been exercised and the remaining unexercised warrants expired on April 30, 2003 pursuant to the terms of the warrants. As of December 31, 2005, no warrants assumed from the SBS acquisition to purchase the Company s common stock were outstanding.

As of December 31, 2005, shares of common stock reserved for future issuance consisted of the following:

	December 31, 2005
Stock options outstanding	7,571,146
Stock options available for grant	5,224,301
Employee Stock Purchase Plan	316,706
Convertible subordinated notes	18,202,221
	31,314,374

1998 Stock Option Plan (Incentive Stock Plan)

In March 1998, the Company adopted the DURECT Corporation 1998 Stock Option Plan under which incentive stock options and non-statutory stock options may be granted to employees, directors of, or consultants to, the Company and its affiliates.

Options granted under the 1998 Stock Option Plan expire no later than ten years from the date of grant. Options may be granted with different vesting terms from time to time not to exceed five years from the date of grant.

The option price of an incentive stock option granted to an employee or of a nonstatutory stock option granted to any person who owns stock representing more than 10% of the total combined voting power of all classes of stock of the Company (or any parent or subsidiary) shall be no less than 110% of the fair market value per share on the date of grant. The option price of an incentive stock option granted to any other employee shall be no less than 100% of the fair market value per share on the date of grant. The option price of a nonstatutory

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

stock option that is granted to any other person shall be no less than 85% of the fair market value per share on the date of grant.

In January 2000, the Company ceased granting options from 1998 Stock Option Plan.

2000 Stock Plan (Incentive Stock Plan)

In January 2000, the Company s Board of Directors and stockholders adopted the DURECT Corporation 2000 Stock Plan, under which incentive stock options and non-statutory stock options and stock purchase rights may be granted to employees, consultants and non-employee directors. The 2000 Stock Plan was amended by written consent of the Board of Directors in March 2000 and written consent of the stockholders in August 2000.

In April 2005, the Board of Directors approved certain amendments to the 2000 Stock Plan. At the Company s annual shareholders meeting in June 2005, the shareholders approved the amendments of the 2000 Stock Plan to: (i) expand the types of awards that the Company may grant to eligible service providers under the Stock Plan to include restricted stock units, stock appreciation rights and other similar types of awards (including other awards under which recipients are not required to pay any purchase or exercise price) as well as cash awards; and (ii) include certain performance criteria that may be applied to awards granted under the Stock Plan. A total of 13,046,500 shares of common stock have been reserved for issuance and 1,239,998 shares of common stock have been exercised under this plan as of December 31, 2005.

Options granted under the 2000 Stock Plan expire no later than ten years from the date of grant. Options may be granted with different vesting terms from time to time not to exceed five years from the date of grant.

The option price of an incentive stock option granted to an employee or of a nonstatutory stock option granted to any person who owns stock representing more than 10% of the total combined voting power of all classes of stock of the Company (or any parent or subsidiary) shall be no less than 110% of the fair market value per share on the date of grant. The option price of an incentive stock option granted to any other employee shall be no less than 100% of the fair market value per share on the date of grant.

2000 Directors Stock Option Plan

In March 2000, the Board of Directors adopted the 2000 Directors Stock Option Plan. A total of 300,000 shares of common stock had been reserved initially for issuance under this plan. The directors plan provides that each person who becomes a non-employee director of the Company after the effective date of this offering will be granted a non-statutory stock option to purchase 20,000 shares of common stock on the

date on which the optionee first becomes a non-employee director of the Company. This plan also provides that each option granted to a new director shall vest at the rate of 33 1/3% per year and each annual option of 5,000 shares shall vest in full at the end of one year.

At the Company s annual shareholders meeting in June 2002, the shareholders approved an amendment of the 2000 Directors Stock Option Plan to: (i) increase the number of stock options granted to a non-employee director on the date which such person first becomes a director from 20,000 to 30,000 shares of common stock; (ii) increase the number of stock options granted to each non-employee director on the date of each annual meeting of the stockholders after which the director remains on the Board from 5,000 to 12,000 shares of common stock; and (iii) reserve 200,000 additional shares of common stock for issuance under the Directors Stock Option Plan so that the total number of shares reserved for issuance is 500,000.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

In April 2005, the Board of Directors approved certain amendments to the 2000 Directors Stock Option Plan. At the Company s annual shareholders meeting in June 2005, the shareholders approved the amendments of the 2000 Directors Stock Option Plan to: (i) increase the number of shares of common stock issuable under the Director s Plan by an additional 425,000 shares, to an aggregate of 925,000 shares; (ii) increase the number of option shares issued to nonemployee directors annually in connection with their continued service on the Board (from 12,000 shares) to 20,000 shares; and (iii) modify the vesting of such annual option grants so that such shares vest completely on the day before the first anniversary of the date of grant.

As of December 31, 2005, 925,000 shares have been reserved and 283,000 shares have been granted under the 2000 Director s Stock Option Plan.

1993 Stock Option Plan of Southern BioSystems, Inc.

In April 2001, the Company assumed the 1993 Stock Option Plan of Southern BioSystems, Inc. (1993 SBS Plan) in connection with its acquisition of SBS. Pursuant to the 1993 SBS Plan, incentive stock options may be granted to employees, and nonstatutory stock options may be granted to employees, directors, and consultants, of the Company and its affiliates. A total of 662,191 shares of common stock have been reserved for issuance under this plan. Options granted under the 1993 SBS Plan expire no later than ten years from the date of grant. Options may be granted with different vesting terms from time to time not to exceed five years from the date of grant. As of December 31, 2005, 242,171 shares of common stock have been exercised under the 1993 SBS Plan.

1995 Nonqualified Stock Option Plan of Southern Research Technologies, Inc.

In April 2001, the Company also assumed the 1995 Nonqualified Stock Option Plan of Southern Research Technologies, Inc. (1995 SRT Plan) in connection with its acquisition of SBS. Under this plan, non-statutory stock options may be granted to employees, directors, and consultants, of the Company and its affiliates. A total of 243,609 shares of common stock have been reserved for issuance under this plan. Options granted under the 1995 SRT Plan expire no later than ten years from the date of grant. Options may be granted with different vesting terms from time to time but not to exceed five years from the date of grant. As of December 31, 2005, 221,870 shares of common stock have been exercised under the 1995 SRT Plan.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Activity under all stock plans through December 31, 2005 is as follows:

	Shares Available for Grant	Number of Shares Granted	Weighted Average Exercise Price
Balance at December 31, 2002	2,870,805	4,209,014	$ 6.89
Shares authorized	2,250,000		
Options granted	(3,078,743)	3,078,743	$ 1.71
Options exercised		(159,388)	$ 0.95
Options cancelled and forfeited	1,166,460	(1,512,573)(1)	$ 4.62
Balance at December 31, 2003	3,208,522	5,615,796	$ 4.62
Shares authorized	2,250,000		
Options granted	(4,395,937)	4,395,937	$ 2.89
Options exercised		(431,181)	$ 1.26
Options cancelled and forfeited	915,505	(968,557)(1)	$ 4.34
Balance at December 31, 2004	1,978,090	8,611,995	$ 3.93
Shares authorized	2,675,000		
Options granted	(491,102)	491,102	$ 4.03
Options exercised		(446,867)	$ 1.95
Options cancelled and forfeited	1,062,313	(1,085,084)(1)	$ 4.90
Balance at December 31, 2005	5,224,301	7,571,146	$ 3.92

(1) Options to purchase 35,550 shares of common stock granted under the 1998 Stock Option Plan were forfeited in 2003 and are not available for future grant. In addition, options to purchase 1,032, 53,052 and 139,198 shares of common stock under the 1993 SBS Plan in 2005, 2004 and 2003, respectively, and options to purchase 21,739 shares of common stock under the 1995 SRT Plan in 2003 were forfeited and are not available for future grant.

Since inception, the Company has recorded aggregate deferred compensation charges of $11.2 million in connection with stock options granted to employees and directors, including $918,000 recorded at the time of the Company s acquisition of SBS in April 2001 for the assumption of outstanding stock options granted to employees and directors of that company. In 2005, 2004 and 2003, the Company reversed $0, $70,000 and $949,000 of deferred compensation, respectively, as a result of terminated employees.

The Company has amortized or reversed (due to employee terminations) approximately $11.2 million of deferred compensation charges through December 31, 2005. Employee stock-based compensation expense, net of reversal, was $4,000, ($15,000) and ($276,000) in 2005, 2004 and 2003.

Total stock compensation expense related to modification of employee stock option terms was $336,000 in 2005, $5,000 in 2004 and $78,000 in 2003.

The weighted-average grant-date fair value of options granted with exercise price equal to fair market value was $2.69 in 2005, $1.80 in 2004 and $1.01 in 2003. There were no options granted with exercise prices lower than fair market value in 2005, 2004 and 2003.

In 2005, the Company issued options to purchase 38,800 shares of common stock to several third party consultants in exchange for services. In connection with these options to purchase common stock, the Company

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

recorded a non-cash charge of $205,000 in its statement of operations for the year ended December 31, 2005. The Company also recorded non-cash charge of $46,000 related to modification of non-employee stock options in its statement of operations for the year ended December 31,2005.

In 2004, the Company issued options to purchase 121,600 shares of common stock to several third party consultants in exchange for services. In connection with these options to purchase common stock, the Company recorded a non-cash charge of $214,000 in its statement of operations for the year ended December 31, 2004.

In 2003, the Company issued options to purchase 67,500 shares of common stock to several third party consultants in exchange for services. In connection with these options to purchase common stock, the Company recorded a non-cash charge of $96,000 in its statement of operations for the year ended December 31, 2003.

Expenses for non-employee stock options are recorded over the vesting period of the options, with the amount determined by the Black-Scholes option valuation method and remeasured over the vesting term.

The following table summarizes information about stock options outstanding at December 31, 2005:

Range of Exercise Price		Number of Options Outstanding	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number of Options Exercisable	Weighted Average Exercise Price
			(In years)			
$ 0.35	1.55	327,566	6.25	$ 1.31	184,566	$ 1.24
$ 1.58	1.58	1,401,586	7.11	$ 1.58	649,894	$ 1.58
$ 1.75	2.48	172,600	7.72	$ 2.21	114,725	$ 2.19
$ 2.49	2.51	1,109,300	8.16	$ 2.51	258,013	$ 2.51
$ 2.57	3.15	644,126	7.44	$ 2.99	288,951	$ 2.96
$ 3.20	3.20	1,332,235	8.96	$ 3.20	333,699	$ 3.20
$ 3.22	3.45	776,750	8.19	$ 3.30	237,500	$ 3.29
$ 3.46	7.70	815,833	6.95	$ 5.85	582,476	$ 6.21
$ 7.79	11.63	903,150	5.56	$ 10.17	806,864	$ 10.29
$11.63	13.56	98,000	4.99	$ 12.23	98,000	$ 12.23
$ 0.35	13.56	7,571,146	7.47	$ 3.92	3,554,688	$ 5.06

2000 Employee Stock Purchase Plan

In August 2000, the Company adopted the 2000 Employee Stock Purchase Plan. A total of 150,000 shares of common stock have been reserved for issuance under the purchase plan. This purchase plan will be implemented by a series of overlapping offering periods of approximately 24 months duration, with new offering periods, other than the first offering period, beginning on May 1 and November 1 of each year and ending April 30 and October 31, respectively, two years later. The purchase plan allows eligible employees to purchase common stock through payroll deductions at a price equal to the lower of 85% of the fair market value of the Company s common stock at the beginning of each offering period or at the end of each purchase period. The initial offering period commenced on the effectiveness of the Company s initial public offering.

Pro Forma Information

The Company has elected to follow APB 25 and related interpretations in accounting for its employee stock-based compensation plans. Because the exercise price of the employee stock options equals the market price of

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

the underlying stock on the date of grant, no compensation expense is generally recognized. Pro forma information regarding net loss has been determined as if the Company accounted for its employee stock options (including shares issued under the Employee Stock Purchase Plan, collectively called stock based awards) under the fair value method prescribed by SFAS 123. The resulting effect on pro forma net loss disclosed is not likely to be representative of the effects on net loss on a pro forma basis in future years, due to additional grants and years of vesting in subsequent years. The fair value of the Company s stock based awards granted to employees from inception (February 6, 1998) to the time of the initial public offering in September 2000, were estimated on the date of grant using the minimum value method. Stock based awards granted subsequent to the Company s initial public offering have been valued using the Black Scholes option valuation model.

The fair value of the Company s stock based awards to employees was estimated using the following assumptions:

	Stock Options			Employee Stock Purchase Plan		
	Year ended December 31,			Year ended December 31,		
	2005	2004	2003	2005	2004	2003
Risk-free interest rate	3.7-4.4%	2.2-3.6%	1.9-2.6%	3.4-4.4%	1.8-2.4%	1.3-1.5%
Expected dividend yield						
Expected life of option (in years)	3.5-4.97	3.5	3.5	1.25	1.25	1.25
Volatility	90-102%	90-107%	79-90%	53-100%	90-100%	79-90%

The Black Scholes option-pricing model was developed for use in estimating the fair value of traded options that have no vesting restrictions and are fully transferable. The Black Scholes model requires the input of highly subjective assumptions including the expected stock price volatility. The Company s stock based awards to employees have characteristics significantly different from those of traded options. Changes in the subjective input assumptions can materially affect the fair value estimate.

Under the Black-Scholes option-pricing model, the Company historically estimated the expected life of option using its best estimate of employee exercise behavior at the time. This estimate considered the vesting period for the employee stock options and a reasonable assumption about the post-vesting holding period. In anticipation of adopting SFAS No. 123R on January 1, 2006, the Company updated this estimate to reflect more recent historical experience of employee stock option exercises and cancellations. The Company included the updated expected life of option assumption for option grants made during the fourth quarter of 2005.

For the purposes of pro forma disclosures, the estimated fair value of the stock based awards is amortized to expense over the vesting period for options and the offering period for stock purchases under the Employee Stock Purchase Plan.

Stockholder Rights Plan

On July 6, 2001, the Board of Directors adopted a Stockholder Rights Plan. The rights issued pursuant to the plan expire on July 6, 2011 and are exercisable ten days after a person or group either (a) announces the acquisition of 17.5 percent or more of the Company s outstanding common stock or (b) commences a tender offer, which would result in ownership by the person or group of 17.5 percent or more of the Company s outstanding common stock. Upon exercise, all rights holders except the potential acquiror will be entitled to acquire the Company s common stock at a discount. Under certain circumstances, the company s Board of

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Directors may also exchange the rights (other than those owned by the acquiror or its affiliates) for the company s common stock at an exchange ratio of one share of common stock per right. The Company is entitled to redeem the rights at any time on or before the tenth day following acquisition by a person or group of 17.5 percent or more of the Company s common stock.

12. Income Taxes

Income tax provision was $4,000 and $18,000 in 2005 and 2004 due to state income taxes paid for API in 2005 and 2004, respectively, compared with zero in 2003. Prior to 2004, the Company had no provision for income taxes, as the Company incurred losses for all periods presented.

The reconciliation of income tax expenses (benefit) at the statutory federal income tax rate of 34% to net income tax benefit included in the statement of operations for the years ended December 31, 2005, 2004 and 2003 is as follows (in thousands):

	Year Ended December 31,		
	2005	2004	2003
U.S. federal taxes (benefit) at statutory rate	$ (6,162)	$ (9,397)	$ (7,717)
State taxes	4	18	
Unutilized net operating loss	5,884	9,432	7,730
Other	278	(35)	(13)
Total	$ 4	$ 18	$

Deferred tax assets and liabilities reflect the net tax effects of net operating loss and credit carryforwards and the temporary differences between the carrying amounts of assets and liabilities for financial reporting and the amounts used for income tax purposes. Significant components of the Company s deferred tax assets are as follows (in thousands):

	December 31,	
	2005	2004
Deferred tax assets:		

Net operating loss carryforwards	$ 52,471	$ 48,900
Capitalized research and development expenses	3,374	2,970
Deferred revenue	3,688	
Other	5,239	5,140
Total deferred tax assets	64,772	57,010
Valuation allowance for deferred tax assets	(64,772)	(57,010)
Net deferred tax assets	$	$

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $7.8 million and $12.5 million during 2005 and 2004, respectively.

As of December 31, 2005, the Company had net operating loss carryforwards for federal income tax purposes of approximately $142.4 million, which expire in the years 2018 through 2025 and federal research and development tax credits of approximately $1.7 million which expire at various dates beginning in 2018 through 2025, if not utilized.

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DURECT CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

As of December 31, 2005, the Company had net operating loss carryforwards for state income tax purpose of approximately $72.1 million, which expire in the years 2008 through 2015, if not utilized and state research and development tax credits of approximately $1.6 million, which do not expire.

Utilization of the net operating losses may be subject to a substantial annual limitation due to federal and state ownership change limitations. The annual limitation may result in the expiration of net operating losses before utilization.

13. Unaudited Selected Quarterly Financial Data (in thousands, except per share amounts)

	First Quarter		Second Quarter		Third Quarter		Fourth Quarter	
	2005	2004	2005	2004	2005	2004	2005	2004
Revenue, net	$ 5,354	$ 3,385	$ 8,819	$ 3,080	$ 8,622	$ 3,365	$ 5,776	$ 4,023
Net loss	$ (5,427)	$ (5,990)	$ (3,648)	$ (7,433)	$ (3,012)	$ (7,260)	$ (6,041)	$ (6,954)
Basic and diluted net loss per share	$ (0.10)	$ (0.12)	$ (0.07)	$ (0.14)	$ (0.06)	$ (0.14)	$ (0.10)	$ (0.13)

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Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

Not applicable.

Item 9A. Controls and Procedures

See Management s Discussion and Analysis of Financial Condition and Results of Operations Management s Report on Controls and Procedures appearing on page 63 of this annual report.

Item 9B. Other Information

Not applicable.

PART III

The definitive proxy statement for our 2006 annual meeting of stockholders, when filed, pursuant to Regulation 14A of the Securities Exchange Act of 1934, will be incorporated by reference into this Form 10-K pursuant to General Instruction G (3) of Form 10-K and will provide the information required under Part III (Items 10-14), except for the information with respect to our executive officers, which is included in Part I Executive Officers of the Registrant.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) The following documents are filed as part of this report:

(1) *Financial Statements*

See Item 8 of this Form 10-K

(2) *Financial Statement Schedules*

Schedule II Valuation and Qualifying Accounts

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

(3) Exhibits are incorporated herein by reference or are filed in accordance with Item 601 of Regulation S K.

Number	Description
2.1	Agreement and Plan of Merger dated April 18, 2001, among the Company, Target and Magnolia Acquisition Corporation (2).
3.3	Amended and Restated Certificate of Incorporation of the Company (1).
3.5	Amended and Restated Bylaws of the Company (1).
3.6	Certificate of Designation of Rights, Preferences and Privileges of Series B-1 Preferred Stock (1).
3.7	Certificate of Designation of Rights, Preferences and Privileges of Series C Preferred Stock (1).
4.2	Second Amended and Restated Investors Rights Agreement (1).
4.3	Preferred Shares Rights Agreement, dated as of July 6, 2001, between the Company and EquiServe Trust Company, N.A. including the Certificate of Designation, the form of the Rights Certificate and the Summary of Rights attached thereto as Exhibits A, B and C, respectively (3).

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Number	Description
10.1	Form of Indemnification Agreement between the Company and each of its Officers and Directors (1).
10.2	1998 Stock Option Plan (1).
10.3	2000 Stock Plan (1).
10.4	2000 Employee Stock Purchase Plan (1).
10.5	2000 Directors Stock Option Plan (1).
10.6**	Second Amended and Restated Development and Commercialization Agreement between the Company and ALZA Corporation effective April 28,1999 (1).
10.7**	Product Acquisition Agreement between the Company and ALZA Corporation dated as of April 14, 2000 (1).
10.8	Amended and Restated Loan and Security Agreement between the Company and Silicon Valley Bank dated as of October 28, 1998 (1).
10.9**	Manufacturing and Supply Agreement between Neuro-Biometrix, Inc. and Novel Biomedical, Inc. dated as of November 24, 1997 (1).
10.10**	Master Services Agreement between the Company and Quintiles, Inc. dated as of November 1, 1999 (1).
10.11	Modified Net Single Tenant Lease Agreement between the Company and DeAnza Enterprises, Ltd. dated as of February 18, 1999 (1).
10.12	Sublease Amendment between the Company and Ciena Corporation dated as of November 29, 1999 and Sublease Agreement between Company and Lightera Networks, Inc. dated as of March 10, 1999 (1).
10.13**	Project Proposal between the Company and Chesapeake Biological Laboratories, Inc. dated as of October 11, 1999 (1).
10.17	Common Stock Purchase Agreement between the Company and ALZA Corporation dated April 14, 2000 (1).
10.18	Warrant issued to ALZA Corporation dated April 14, 2000 (1).
10.19	Amended and Restated Market Stand-off Agreement between the Company and ALZA Corporation dated as of April 14, 2000 (1).
10.20**	Asset Purchase Agreement between the Company and IntraEAR, Inc. dated as of September 24, 1999 (1).
10.21	Warrant issued to Silicon Valley Bank dated December 16, 1999 (1).
10.22	Amendment to Second Amended and Restated Investors Rights Agreement dated as of April 14, 2000 (1).
10.23**	Master Agreement between the Company and Pacific Data Designs, Inc. dated as of July 6, 2000 (1).
10.24**	Master Services Agreement between the Company and Clinimetrics Research Associates, Inc. dated as of July 11, 2000 (1).
10.25**	Supply Agreement between the Company and Mallinckrodt, Inc. dated as of October 1, 2000 (5).
10.26	Lease between Sobrato Development Companies #850 and the Company (6).
10.27	Southern BioSystems, Inc. 1993 Stock Option Plan (as amended) (4).
10.28	Southern Research Technologies, Inc. 1995 Nonqualified Stock Option Plan (as amended) (4).
10.29**	Feasibility, Development and Commercialization Agreement between Southern BioSystems, Inc., an Alabama corporation and wholly-owned subsidiary of the Company (now merged into the Company), and Voyager Pharmaceutical Corporation dated as of July 22, 2002. (7).

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Number	Description
10.30**	License & Option Agreement and Mutual Release between Southern BioSystems, Inc, an Alabama corporation and wholly-owned subsidiary of the Company (now merged into the Company), and Thorn BioScience LLC dated as of July 26, 2002 (7).
10.31**	Third Amended and Restated Development and Commercialization Agreement between the Company and ALZA Corporation dated as of October 1, 2002 (7).
10.32**	Development and License Agreement between the Company, Southern BioSystems, Inc, an Alabama corporation and wholly-owned subsidiary of the Company (now merged into the Company), and BioPartners, GmbH dated as of October 18, 2002.(8)
10.33**	Development, Commercialization and Supply License Agreement between the Company and Endo Pharmaceuticals Inc. dated as of November 8, 2002.(8)
10.34**++	Development and License Agreement between the Company, Southern BioSystems, Inc., an Alabama corporation and wholly-owned subsidiary of the Company (now merged into the Company), and Pain Therapeutics, Inc. dated as of December 19, 2002.(8)
10.35	Sublease between the Company and Norian Corporation with commencement date of January 1, 2004.(9)
10.36	Lease between the Company and Renault & Handley Employee Investments Co. with commencement date of January 1, 2005.(9)
10.37	Amendment to Development, Commercialization and Supply License Agreement between the Company and Endo Pharmaceuticals Inc. dated as of January 28, 2004.(9)
10.38	Indenture of Lease between the Company and the Board of Trustees of the University of Alabama dated as of May 1, 2004.(10)
10.39**	License and Commercial Agreement between the Company and NeuroSystec Corporation dated as of May 13, 2004. (10)
10.40	Commercial Lease between the Company and EWE, Inc. dated as of September 21, 2004.(11)
10.41**	License agreement between the Company and Endo Pharmaceuticals, Inc. dated as of March 10, 2005.(12)
10.42	Indenture of Lease between the Company and the Board of Trustees of the University of Alabama dated as of April 25, 2005.(13)
10.43	Third Addendum to Lease between the Company and Garaventa Properties dated as of July 8, 2005.(14)
10.44	Lease between the Company and RWC, LLC dated as of September 1, 2005.(14)
10.45+	Amendment dated December 21, 2005 to Development and License Agreement dated December 19, 2002 between the Company and Pain Therapeutics, Inc.
10.46+	Sucrose Acetate Isobutyrate Pharmaceutical Grade Supply Agreement between the Company and Eastman Chemical Company dated as of December 30, 2005.
12.1	Ratio of Earnings to Fixed Charges.
23.1	Consent of Independent Registered Public Accounting Firm
24.1	Power of Attorney (see signature page of this Form 10-K).
31.1	Rule 13a-14(a) Section 302 Certification.
31.2	Rule 13a-14(a) Section 302 Certification.
32.1	Certificate pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certificate pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

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(1) Incorporated by reference to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed with the Securities and Exchange Commission on April 20, 2000.

(2) Incorporated by reference to our Current Report on Form 8-K (File No. 000-31615) filed with the Securities and Exchange Commission on May 15, 2001.

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

(4) Incorporated by reference to our Registration Statement on Form S-8 (File No. 333-61224) filed with the Securities and Exchange Commission on May 18, 2001.

(5) Incorporated by reference to our Annual Report on Form 10-K (File No. 000-31615) filed with the Securities and Exchange Commission on March 30, 2001.

(6) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the Securities and Exchange Commission on November 13, 2001.

(7) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the Securities and Exchange Commission on November 14, 2002.

(8) Incorporated by reference to our Annual Report on Form 10-K (File No. 000-31615) filed with the Securities and Exchange Commission on March 14, 2003.

(9) Incorporated by reference to our Annual Report on Form 10-K (File No. 000-31615) filed with the Securities and Exchange Commission on March 11, 2004.

(10) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the Securities and Exchange Commission on August 4, 2004.

(11) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the Securities and Exchange Commission on November 5, 2004.

(12) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the Securities and Exchange Commission on May 6, 2005.

(13) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the Securities and Exchange Commission on August 4, 2005.

(14) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the Securities and Exchange Commission on October 13, 2005.

** Confidential treatment granted with respect to certain portions of this Exhibit.

+ Confidential treatment requested with respect to certain portions of this Exhibit.

++ Refiled with additional disclosure previously treated as confidential.

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SCHEDULE II VALUATION AND QUALIFYING ACCOUNTS

Year Ended December 31, 2005, 2004 and 2003

(in thousands)

	Balance at beginning of year	Provision	Write Offs	Balance at end of the year
December 31, 2005				
Allowance for doubtful accounts	$ 208	$ 48	$ (128)	$ 128
December 31, 2004				
Allowance for doubtful accounts	$ 141	$ 112	$ (45)	$ 208
December 31, 2003				
Allowance for doubtful accounts	$ 207	$ 70	$ (136)	$ 141

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

DURECT CORPORATION

By: /s/ JAMES E. BROWN

James E. Brown

President and Chief Executive Officer

Date: March 15, 2006

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints James E. Brown and Felix Theeuwes, jointly and severally, his or her attorneys-in-fact, each with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and 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)	March 15, 2006
/s/ FELIX THEEUWES Felix Theeuwes	Chairman and Chief Scientific Officer	March 15, 2006
/s/ JIAN LI Jian Li	Vice President, Finance and Corporate Controller (Principal Financial and Accounting Officer)	March 15, 2006

/s/ Simon Benito	Director	March 15, 2006
Simon Benito		
/s/ Michael D. Casey	Director	March 15, 2006
Michael D. Casey		
/s/ David R. Hoffmann	Director	March 15, 2006
David R. Hoffmann		
/s/ Armand P. Neukermans	Director	March 15, 2006
Armand Neukermans		
/s/ Jon S. Saxe	Director	March 15, 2006
Jon S. Saxe		