

DURECT CORP  
Form 10-K  
March 10, 2009  
Table of Contents

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**Form 10-K**

(Mark One)

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

For the fiscal year ended December 31, 2008

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

Edgar Filing: DURECT CORP - Form 10-K

(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

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

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  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.

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

Large accelerated filer  Accelerated filer  Non-accelerated filer  Smaller reporting company   
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). YES  NO

The aggregate market value of the voting stock held by non-affiliates of the registrant was approximately \$282,473,859 as of June 30, 2008 based upon the closing sale price on the NASDAQ Global 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 82,025,921 shares of the registrant's Common Stock issued and outstanding as of February 27, 2009.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference from the definitive Proxy Statement for the 2009 annual meeting of stockholders, which is expected to be filed not later than 120 days after the Registrant's fiscal year ended December 31, 2008.



**Table of Contents**

**DURECT CORPORATION**  
**ANNUAL REPORT ON FORM 10-K**  
**FOR THE FISCAL YEAR ENDED DECEMBER 31, 2008**

**TABLE OF CONTENTS**

		<b>Page</b>
<b>PART I</b>		
ITEM 1.	<u>Business</u>	1
ITEM 1A.	<u>Risk Factors</u>	26
ITEM 1B.	<u>Unresolved Staff Comments</u>	46
ITEM 2.	<u>Properties</u>	46
ITEM 3.	<u>Legal Proceedings</u>	46
ITEM 4.	<u>Submission of Matters to a Vote of Security Holders</u>	46
<b>PART II</b>		
ITEM 5.	<u>Market for the Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	47
ITEM 6.	<u>Selected Financial Data</u>	49
ITEM 7.	<u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	50
ITEM 7A.	<u>Quantitative and Qualitative Disclosures About Market Risk</u>	70
ITEM 8.	<u>Financial Statements and Supplementary Data</u>	72
ITEM 9.	<u>Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	107
ITEM 9A.	<u>Controls and Procedures</u>	107
ITEM 9B.	<u>Other Information</u>	107
<b>PART III</b>		
ITEM 10.	Directors, Executive Officers and Corporate Governance	109
ITEM 11.	Executive Compensation	109
ITEM 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	109
ITEM 13.	Certain Relationships and Related Transactions, and Director Independence	109
ITEM 14.	Principal Accountant Fees and Services	109
<b>PART IV</b>		
ITEM 15.	<u>Exhibits, and Financial Statement Schedules</u>	109
	<u>Signatures</u>	115

---

**Table of Contents**

**PART I**

**Item 1. Business.  
Overview**

We are an emerging specialty pharmaceutical company focused on the development of pharmaceutical products based on our proprietary drug delivery technology platforms. We are developing 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 as well as, for certain applications, placement of the drug at the intended site of action. Our proprietary drug delivery technology platforms include:

**SABER Delivery System** a patented and versatile depot injectable useful for delivery of small molecules and biologics 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 (POSIDUR), for which we have licensed commercialization rights in Europe and certain other countries to Nycomed Danmark APS (Nycomed) while retaining commercialization rights in the United States, Canada, Asia and other countries. A successful Phase IIb clinical trial in hernia surgery was completed and an end-of-Phase II meeting has been held with the FDA. We are currently in dialogue with the FDA regarding our Phase III program. In parallel with these discussions, we are conducting a 60-patient Phase IIb study in Australia using a 5 mL dose in shoulder surgery in order to confirm aspects of our clinical study design. Additionally, Nycomed is commencing Phase IIb studies in surgical procedures in Europe.

**ORADUR<sup>®</sup> Delivery System** 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). In December 2007, Pain Therapeutics and King reported positive results from the pivotal Phase III trial submitted under an approved Special Protocol Assessment (SPA) with the FDA. The NDA was submitted to the FDA in June 2008, and in August 2008 the NDA was accepted by the FDA and granted priority review. In December 2008, Pain Therapeutics received a Complete Response Letter for its NDA for Remoxy in which the FDA determined that the NDA was not approved. According to Pain Therapeutics, the FDA indicated that additional non-clinical data will be required to support the approval of Remoxy but the FDA has not requested or recommended additional clinical efficacy studies prior to approval. Pain Therapeutics has indicated that they plan to meet with the FDA in the second quarter of 2009 regarding the NDA for Remoxy, and that they believe this FDA meeting will provide them with a more reliable context in which to make projections about Remoxy.

**TRANSDUR Delivery System** a proprietary transdermal patch technology. The advantages of TRANSDUR may include, depending on the application, 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. An end-of-Phase II meeting with the FDA for TRANSDUR-Sufentanil was held on February 19, 2009. As a result of that meeting, we believe we understand the anticipated regulatory pathway for the Phase III

*NOTE: POSIDUR, SABER, TRANSDUR, ORADUR<sup>®</sup>, ELADUR, DURIN, CHRONOGESIC<sup>®</sup>, MICRODUR, ALZET<sup>®</sup> and LACTEL<sup>®</sup> are trademarks of DURECT Corporation. Other trademarks referred to belong to their respective owners.*



---

**Table of Contents**

program and approval, which will follow a 505(b)2 pathway as discussed with the FDA. This pathway allows referencing of third-party data, potentially reducing time and expense. On February 26, 2009, Endo notified us that it was terminating its license agreement for TRANSDUR-Sufentanil and thereby returning to us Endo's rights to develop and commercialize TRANSDUR-Sufentanil in the U.S. and Canada effective August 26, 2009. Endo has committed to assist us in an orderly and rapid transition of this program back to us. Our second application of TRANSDUR is for a transdermal bupivacaine patch (TRANSDUR-Bupivacaine or ELADUR), which we have licensed to Alpharma Ireland Limited, an affiliate of Alpharma Inc. (Alpharma) (now owned by King). We successfully completed a Phase IIa clinical trial with ELADUR in the fourth quarter of 2007.

**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 (Voyager). Voyager has conducted clinical studies for Memryte but future development is pending Voyager's ability to obtain additional financing and is not assured.

**DUROS® System** an osmotic implant technology licensed to us for specified fields from ALZA Corporation, a Johnson & Johnson Company (ALZA). 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.

**MICRODUR Biodegradable Microparticulates** a patented biodegradable microparticulate depot injectable. Sustained release from a few days to many months can be achieved through suitable choice of polymers and processing.

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, when desired, 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 biologics 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, or for certain acute conditions where longer drug dosing is required or advantageous, 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 and biotechnology companies to develop and commercialize proprietary and enhanced pharmaceutical products based on our technologies.

**Table of Contents****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:

<b>Disease/Indication</b>	<b>Product Candidate</b>	<b>Collaborator</b>	<b>Technology Platform</b>	<b>Stage</b>
Post Operative Pain	POSIDUR (Controlled release injection of bupivacaine)	Nycomed (Europe and certain other territories); DURECT retains rights in U.S., Canada, Asia and other countries	SABER	Phase II
Neuropathic Pain associated with Post-Herpetic Neuralgia (PHN)	ELADUR (Transdermal bupivacaine)	King (worldwide)	TRANSDUR	Phase II
Chronic Pain	Remoxy (Oral controlled release oxycodone)	King/Pain Therapeutics (worldwide)	ORADUR	NDA accepted but not approved/ Complete Response Letter received
Pain	Oral controlled release opioid (active agent undisclosed)	King/Pain Therapeutics (worldwide)	ORADUR	Phase I
Pain	Oral controlled release opioid (active agent undisclosed)	King/Pain Therapeutics (worldwide)	ORADUR	Phase I
Chronic Pain	TRANSDUR-Sufentanil (Transdermal sufentanil)	Endo (U.S. & Canada) until August 2009; DURECT retains rights in Europe, Asia and other countries, and worldwide rights as of August 2009	TRANSDUR	Phase II
Alzheimer's Disease	Memryte (Controlled release Leuprolide implant)	Voyager (worldwide)	DURIN	Further development pending financing/ partnering by Voyager
Central Nervous System Disorders/Cardiovascular Disorders/Biologics Programs	Various	DURECT retains worldwide rights	SABER/ DUROS/ DURIN	Preclinical/ Research Stage



---

**Table of Contents***Local Post-Operative Pain*

## POSIDUR

*Market Opportunity.* According to data published by the Center for Disease Control and Prevention, there are approximately 72 million ambulatory and inpatient procedures performed in the United States. Epidemiological studies indicate that up to 100% of surgical patients experience postoperative pain, with 50-75% reporting inadequate pain relief. 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 including drowsiness, constipation, cognitive impairment. Effective pain management can be compromised if patients fail to adhere to recommended dosing regimens because they are sleeping or disoriented. Post-surgical pain can be treated effectively with local anesthetics; however, the usefulness of current conventional medications is limited by their short duration of action.

*Development Strategy.* We are developing POSIDUR, a sustained-release formulation of bupivacaine, using our SABER delivery system for the treatment of post-surgical pain. Bupivacaine is a local anesthetic agent currently used in the hospital for anesthesia and analgesia and for which the patent covering the chemical entity has expired. The physician would administer POSIDUR at the time of surgery 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, thus minimizing side effects. POSIDUR is intended to provide local analgesia for up to 3 days, which we believe coincides with the time period of greatest need for post-surgical pain control in most patients. In November 2006, we entered into a collaboration agreement with Nycomed Danmark, APS. Under the terms of the agreement, we licensed to Nycomed the exclusive commercialization rights to POSIDUR for the European Union (E.U.) and certain other countries. Nycomed paid us an upfront license fee of \$14.0 million in 2006 and an \$8.0 million milestone payment in 2007, with future potential additional milestone payments of up to \$180.0 million upon achievement of defined development, regulatory and sales milestones. We will jointly direct and equally fund with Nycomed a development program for POSIDUR intended to secure regulatory approval in both the U.S. and the E.U. In addition, we will manufacture and supply the product to Nycomed for commercial sale in the territory licensed to Nycomed. Nycomed will pay us blended royalties on sales in the defined territory of 15-40% depending on annual sales, as well as a manufacturing markup. We retain full commercial rights to POSIDUR in the U.S., Canada, Asia and certain other countries.

*Clinical Program.* In 2007, we successfully completed a 122 patient Phase IIb clinical trial of POSIDUR for treatment of post-operative pain in patients undergoing inguinal hernia repair, thereby triggered the \$8.0 million milestone payment from Nycomed. In the Phase IIb trial, POSIDUR at a dose of 5 mL demonstrated statistically significant reductions in pain and in total consumption of supplemental opioid analgesic medications versus placebo. These successful results triggered the \$8.0 million milestone payment by Nycomed to us under our agreement with Nycomed.

*Phase IIb Inguinal Hernia Trial**Design*

The POSIDUR Phase IIb clinical trial was designed to evaluate the tolerability, activity, dose response and pharmacokinetics of POSIDUR in patients undergoing open inguinal hernia repair. The study was conducted in Australia and New Zealand as a multi-center, randomized, double blind, placebo-controlled study in 122 patients. Study patients were randomized into three treatment groups: patients that were treated with POSIDUR 2.5 mL (n=43), POSIDUR 5 mL (n=47) and placebo (n=32). The co-primary efficacy endpoints for the study were Mean Pain Intensity on Movement area under the curve (AUC), a measure of pain over a period of 1-72 hours post-surgery, and the proportion of patients requiring supplemental opioid analgesic medication during the study. Secondary efficacy endpoints included Mean Pain Intensity on Movement AUC over the period 1-48 hours post-surgery, mean total consumption of supplemental opioid analgesic medication, and time to first use of supplemental opioid analgesic medication. The threshold for statistical significance was considered to be at the  $p < 0.05$  level.

---

## **Table of Contents**

### *Results*

#### *Pain Control*

In relation to the co-primary endpoint of pain reduction as measured by Mean Pain Intensity on Movement AUC 1-72 hours post-surgery, the patient group treated with POSIDUR 5 mL reported thirty-one percent (31%) less pain versus placebo ( $p=0.0033$ ). A secondary endpoint measure reported a thirty-five percent (35%) reduction of pain as measured by Mean Pain Intensity on Movement AUC for the period 1-48 hours post-surgery between the POSIDUR 5 mL treatment group versus placebo ( $p=0.0007$ ).

#### *Consumption of Supplemental Opioid Analgesic Medication*

Fifty-three percent (53%) of the study patients in the POSIDUR 5 mL group took supplemental opioid analgesic medications versus seventy-two percent (72%) of the placebo patients ( $p=0.0909$ ). Although this positive trend for this co-primary endpoint in favor of the POSIDUR 5 mL group was not statistically significant, both secondary endpoints measuring opioid analgesic medication consumption were met at a statistically significant level. During the periods of 1-24 hours, 24-48 hours and 48-72 hours after surgery, placebo patients consumed approximately 3.5 ( $p=0.0009$ ), 2.9 ( $p=0.0190$ ) and 3.6 ( $p=0.0172$ ) times more supplemental opioid analgesic medications (mean total daily consumption of opioid analgesic medication in morphine equivalents), respectively, than the POSIDUR 5 mL treatment group. In addition, the median time to first use of supplemental opioid analgesic medication after surgery for the placebo patients was 2.7 hours versus >72 hours for the POSIDUR 5 mL treatment group ( $p=0.0197$ ).

#### *Dose Finding*

POSIDUR administered at the dose of 5 mL showed statistically significant activity relative to placebo whereas POSIDUR administered at 2.5 mL showed a positive trend relative to placebo on certain parameters but the results were not statistically significant.

#### *Safety*

The patient groups treated with POSIDUR 5 mL and POSIDUR 2.5 mL showed comparable safety profiles as the patient groups treated with placebo, and the drug administration appeared well tolerated. The side effects commonly observed with opioid medication use were less frequent in the POSIDUR 5 mL and 2.5 mL treatment groups compared to placebo.

#### *Other Exploratory Phase II studies*

In addition to the Phase IIb study described above, we have also been conducting smaller exploratory Phase II studies in hernia, shoulder arthroscopy and appendectomy surgeries to evaluate different application techniques, clinical design and conduct as well as other investigational factors. These trials have been conducted in multiple cohorts, generally consisting of approximately 6 to 21 patients in each treatment group. Hernia, shoulder and appendectomy studies have been completed. In all the exploratory studies, patient groups treated with POSIDUR 5 mL and POSIDUR 2.5 mL showed comparable safety profiles as the patient groups treated with placebo, and the drug administration appeared well tolerated. Some treatment groups from these exploratory studies utilizing POSIDUR have shown positive activity as measured by reduction of pain or consumption of supplemental opioid analgesic medication versus placebo, while other treatment groups have not. We have evaluated these studies to understand the different results observed, and intend to apply our learnings in the design of our Phase III program.

We have held an end-of-Phase II meeting with the FDA and are in dialogue with the FDA regarding our POSIDUR Phase III program. In parallel with these discussions, we are conducting a 60-patient Phase IIb study in Australia using a 5 mL dose in shoulder surgery in order to confirm aspects of our clinical study design. Additionally, Nycomed is commencing Phase IIb studies in surgical procedures in Europe.

**Table of Contents***Local Pain*

## ELADUR

*Market Opportunity.* Neuropathic pain is pain resulting from a disturbance of the central nervous system (brain and spinal cord) or peripheral nervous system (nerves outside the brain and spinal cord). There are a variety of conditions and diseases that produce neuropathic pain, including trauma and diseases such as multiple sclerosis and stroke. One form of neuropathic pain is a debilitating complication of herpes zoster referred to as Post-Herpetic Neuralgia (PHN or post-shingles pain), which is usually defined as the presence of pain at the site of eruption that lasts more than a month after the onset of zoster eruption. Within the affected skin supplied by the nerve root, patients have a variety of sensory abnormalities in addition to neuropathic pain. Pain can persist for months and occasionally years. The prevalence of PHN (including PHN lasting more than one year) is estimated to be approximately 144,000 people in the U.S.

*Development Strategy.* We are developing a transdermal bupivacaine patch (ELADUR) based on our proprietary TRANSDUR transdermal technology intended to provide continuous delivery of bupivacaine for up to three days from a single application, as compared to a wearing time limited to 12 hours with currently available lidocaine patches. We anticipate that ELADUR will have several potential differentiating attributes compared with currently marketed lidocaine patches, including extended duration of action and better wearability. During 2008, we received Orphan Drug Designation for bupivacaine for relief of persistent pain associated with post-herpetic neuralgia, such that if ELADUR is the first bupivacaine product approved for PHN, ELADUR will receive seven years of market exclusivity following its approval by the FDA. Effective October 2008, we licensed the worldwide development and commercialization rights for ELADUR to Alpharma Ireland, Ltd. (which was acquired by King Pharmaceuticals in December 2008).

*Clinical Program.* In 2007, we successfully completed a 60 patient Phase IIa clinical trial for ELADUR. In this study of patients suffering from PHN, ELADUR showed improved pain control versus placebo during the 3-day continuous treatment period. In addition, ELADUR appeared well tolerated overall, and patients treated with ELADUR and placebo exhibited similar safety profiles. In 2008, we conducted manufacturing scale-up and processing studies to secure additional Phase II and Phase III supplies, and developed our clinical and regulatory strategy for further development of this program.

*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 50 million Americans annually. OxyContin®, a brand name extended-release oral oxycodone-based painkiller, accounted for approximately \$1.6 billion in worldwide sales in 2007, and Duragesic®, a leading transdermal fentanyl product, accounted for approximately \$1.0 billion in worldwide sales in 2008.

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

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;

TRANSDUR-Sufentanil, our proprietary transdermal patch that is intended to provide sufentanil for a period of up to seven days from a single application. The rights to develop and commercialize this drug candidate in the U.S. and Canada were licensed to Endo, but Endo has notified us that it is returning the rights to us effective August 26, 2009, after which we will hold worldwide development and commercialization rights.

---

**Table of Contents**

*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. Subsequently, Pain Therapeutics has 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 extended-release oral painkiller, which achieved annual worldwide sales of approximately \$1.6 billion in 2007. Under the agreement with Pain Therapeutics, we are eligible to receive milestone payments of up to \$9.3 million in the aggregate upon the achievement of predetermined development and regulatory milestones. As of December 31, 2008, we have received \$1.7 million in milestone payments. We also receive reimbursement for our research and development efforts on Remoxy and a manufacturing profit on our supply of key product excipients 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 on the sales volumes.

*Clinical Program.* In December 2007, Pain Therapeutics and King Pharmaceuticals announced that the pivotal Phase III trial for Remoxy successfully met its primary endpoint ( $p < 0.01$ ) that was prospectively defined by the FDA during the Special Protocol Assessment process. In addition, the study achieved statistically significant results in secondary endpoints such as Quality of Analgesia ( $p < 0.01$ ) and Global Assessment ( $p < 0.01$ ).

Pain Therapeutics submitted an NDA for Remoxy to the FDA in June 2008, and in August 2008 the NDA was accepted by the FDA and granted priority review. In December 2008, Pain Therapeutics received a Complete Response Letter for its NDA for Remoxy in which the FDA determined that the NDA was not approved. According to Pain Therapeutics, the FDA indicated that additional non-clinical data will be required to support the approval of Remoxy, but the FDA has not requested or recommended additional clinical efficacy studies prior to approval. Pain Therapeutics has indicated that they plan to meet with the FDA in the second quarter of 2009 regarding the NDA for Remoxy, and they believe this FDA meeting will provide them with a more reliable context in which to make projections about Remoxy.

*Additional ORADUR-Opioid Products in Development*

During 2006, 2007 and 2008, we also worked with Pain Therapeutics and King on the development of additional ORADUR abuse-resistant opioid drug candidates. Phase I clinical trials have been completed for two of these ORADUR-based product. According to Pain Therapeutics, the data from these Phase I trials indicate that these drug candidates are safe and well-tolerated with release profiles that appear well suited to use with a chronic pain population. The active ingredients in these two drug candidates are opioids whose identities have not been publicly disclosed.

*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 two to three days of relief provided by currently available opioid patches. Sufentanil is a highly potent opioid that is currently used in hospitals as an analgesic for which the patent covering the chemical entity has expired. 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, were approximately \$1.0 billion in 2008.

---

**Table of Contents**

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 \$10.0 million in connection with the execution of the Agreement. In February 2009, Endo notified us that it was terminating the license agreement with us, and thereby returning Endo's rights to develop and commercialize TRANSDUR-Sufentanil in the U.S. and Canada to us effective August 26, 2009. Endo has committed to assist in an orderly and rapid transition of this program back to us. Effective August 26, 2009, we will hold worldwide commercialization rights for TRANSDUR-Sufentanil. During 2008, we continued to perform development activities for Endo with respect to TRANSDUR-Sufentanil.

*Clinical Program.* Endo recently successfully completed a Phase II program for TRANSDUR-Sufentanil in which they evaluated the conversion of patients on oral and transdermal opioids to TRANSDUR-Sufentanil. The most recent Phase II study met its primary and secondary objectives of establishing a successful dose-titration regimen and dose potency relationships, demonstrating safety and tolerability at the therapeutic dose, and achieving effective analgesic pain control. The Phase II data, extensive non-clinical data that had been generated by Endo and detailed proposed protocols for Phase III were reviewed with the FDA at an end-of-Phase II meeting on February 19, 2009. As a result of that meeting, we believe we understand the anticipated regulatory pathway for the Phase III program and approval, which will follow a 505(b)2 pathway as discussed with FDA. This pathway would allow us to reference third-party data, potentially reducing time and expense.

*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. It is estimated that Alzheimer's patients and their families spend more than \$200,000 on health care per patient and employers lose approximately \$60 billion per year on lost productivity as adult caregivers are forced to leave their jobs either permanently or temporarily to care for a family member with the 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 has been estimated to be over \$3.5 billion in 2006. It is estimated that over five million Americans suffer from Alzheimer's disease and this number could more than triple by mid-century.

*Development Strategy.* In July 2002, we entered into a development and commercialization agreement with Voyager under which we granted Voyager the exclusive, worldwide rights to develop and commercialize a product, Memryte, using the DURIN implant system to deliver the peptide leuprolide acetate to treat Alzheimer's disease based on Voyager's patented method of treatment. Under the agreement, as amended, we are eligible to receive milestone payments from Voyager of up to \$3.0 million in the aggregate upon the achievement of predetermined development and regulatory milestones. As of December 31, 2008, we have received \$500,000 in milestone payments. Additionally, if the product candidate is commercialized, we will receive royalties of between 10% to 14% of net sales depending on the sales volumes, and we will receive 10% of any upfront, milestone and other fees received by Voyager in the event that the product candidate is sublicensed to a third party.

*Clinical Program.* In October 2005, Voyager initiated a Phase III clinical trial for Memryte, which was truncated by Voyager in order to get an earlier look at potential efficacy. In the second quarter of 2007, Voyager informed its shareholders that it had observed positive outcome trends among women, but no positive effect among men in this truncated Phase III clinical trial. Based on these results, Voyager has stated that it intends to focus its efforts on developing Memryte for the treatment of Alzheimer's disease in women and on seeking a potential collaborative partner for the program. There can be no assurance that Voyager or any other party will continue development of Memryte.

---

## **Table of Contents**

### *Biologics Programs*

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, and advanced drug delivery systems such as we possess are required to realize the full potential of many of these protein and peptide drugs. We have active programs underway to apply our drug delivery systems to various biotechnology drugs and drug candidates, and have entered into a number of feasibility studies with biotechnology and pharmaceutical companies to test their products in our systems.

### *Research Programs in other Therapeutic Categories*

We have underway a number of research programs covering medical diseases and conditions other than pain. Such programs include various diseases and disorders of the central nervous system (CNS), including schizophrenia and attention deficit/hyperactivity disorder. Another area of focus includes cardiovascular disease, including congestive heart failure. In conducting our research programs and determining which particular efforts to prioritize for formal development, we employ a rigorous opportunity assessment process that takes into account the unmet medical need, commercial opportunity, technical feasibility, clinical viability, intellectual property considerations, and the development path including costs to achieve various critical milestones.

## **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 1.7 million deaths, or 70% of all deaths in the U.S. Chronic diseases cause major limitations in daily living for more than 25 million Americans. These diseases account for more than 70% of the \$1 trillion spent on health care each year in America. Demographic trends suggest that, as the U.S. population ages, the cost of treating chronic diseases 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.

---

## **Table of Contents**

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.

*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 systemic 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 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

---

## **Table of Contents**

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.

### **DURECT Pharmaceutical Systems Technology**

Our pharmaceutical systems combine technology innovations from the drug delivery and medical device industries with proprietary pharmaceutical and biologic 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 biologics 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, biocompatible excipients and other additives, the resulting formulation is liquid enough to inject easily with standard syringes and needles. After injection of a SABER formulation, the excipients diffuse 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.



---

## **Table of Contents**

*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 POSIDUR, which is in Phase II clinical trials. 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 for which an end-of-Phase II meeting with the FDA was held in February 2009. The development and commercialization rights in the U.S. and Canada have been licensed to Endo until August 26, 2009, after which we will hold worldwide development and commercialization rights. The TRANSDUR technology is also the basis for ELADUR, which is currently in Phase II testing and which we have licensed worldwide development and commercialization rights to Alpharma Ireland, Ltd. (which was acquired by King in December 2008).

### *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 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 deterrent 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. In December 2007, Remoxy successfully completed a pivotal Phase III study. Pain Therapeutics submitted an NDA for Remoxy to the FDA in June 2008, and in August 2008, the NDA was accepted by the FDA and granted priority review. In December 2008, Pain Therapeutics received a Complete Response Letter for its NDA for Remoxy in which the FDA determined that the NDA was not approved. According to Pain Therapeutics, the FDA indicated that additional non-clinical data will be required to support the approval of Remoxy but the FDA has not requested or recommended additional clinical efficacy studies prior to approval. Pain Therapeutics has indicated that they plan to meet with the FDA in the second quarter of 2009 regarding the NDA for Remoxy, and they believe this FDA meeting will provide them with a more reliable context in which to make projections about Remoxy.

We also have two other ORADUR-based opioid drug candidates for which Phase I clinical trials have been completed. According to Pain Therapeutics, the data from these Phase I trials indicate that these drug candidates are safe and well-tolerated with release profiles that appear well suited to use with a chronic pain population. The active ingredients in these two drug candidates are opioids whose identities have not been publicly disclosed.

### *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<sup>®</sup> 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

---

## **Table of Contents**

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. The DURIN technology is the basis of Memryte for the treatment of Alzheimer's disease, with any future development controlled by Voyager.

### *The DUROS Technology*

The DUROS system is a miniature drug-dispensing pump which can be as small as a wooden matchstick. We have licensed the DUROS system for specified fields of use from ALZA, 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, 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.

### *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 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 in the future, 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 and Certain Local Pain 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. In addition, we have identified certain local and acute pain conditions that we believe can benefit from improved therapeutics. Our initial efforts will focus on using our versatile drug delivery platform technologies to develop products that address these medical conditions.

*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;

---

**Table of Contents**

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 biologics, 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 or reduce the need for multiple injections of these drugs. In addition, through 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.

*Diversify Risk by Pursuing Multiple Programs in Development.* In order to reduce the risks inherent in pharmaceutical product development, we have diversified our product pipeline such that, between our own programs and those we have partnered, we presently have one program for which an NDA has been accepted but not approved by the FDA, and for which a Complete Response Letter has been received, and five different disclosed programs in clinical development, including two oral drug candidates, two transdermal patch candidates and one injectable drug candidate. We believe that having multiple programs in development helps mitigate the negative consequences to us of any setbacks or delays in any one of our programs.

*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, mitigate our risk and enable us to better manage our operating costs. Additionally, such collaborations enable us to leverage investment by our collaborators and reduce our net cash burn, while retaining significant economic rights.

*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 will continue to pursue 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.

---

**Table of Contents****Third-Party Collaborations**

We have entered into the following collaboration agreements:

*Alpharma Ireland Limited (acquired by King Pharmaceuticals in December 2008).* In September 2008, we and Alpharma Ireland Limited, an affiliate of Alpharma Inc. (Alpharma), entered into a development and license agreement granting Alpharma the exclusive worldwide rights to develop and commercialize ELADUR, our investigational transdermal bupivacaine patch currently under development for the treatment of pain associated with post-herpetic neuralgia (PHN). The agreement became effective in October 2008 after clearance under the Hart-Scott-Rodino (HSR) Antitrust Improvements Act of 1976. Under the terms of the agreement, upon closing of the transaction, Alpharma paid us an upfront license fee of \$20 million, with possible additional payments of up to \$93 million upon the achievement of predefined development and regulatory milestones spread over multiple clinical indications and geographical territories as well as possible additional payments of up to \$150 million in sales-based milestones. If ELADUR is commercialized, we would also receive royalties on product sales. Alpharma will control and fund further development of the program. We will perform development activities through completion of Phase II, and formulation and manufacturing scale-up activities for the program, the costs of which shall be reimbursed by Alpharma. The term of the agreement will continue on a jurisdiction-by-jurisdiction basis until the later of fifteen (15) years from the date of first commercial sale of ELADUR or the expiration of patent coverage or data exclusivity in such jurisdiction. During the term of the agreement, subject to specified conditions, neither party nor their affiliates may develop or commercialize a transdermal patch containing bupivacaine. Upon expiration of the term of the agreement, the rights and licenses granted to Alpharma shall convert to fully paid-up, non-royalty bearing, perpetual rights and licenses. The agreement provides each party with specified termination rights, including the right of Alpharma to terminate at any time without cause and each party to terminate the agreement upon material breach of the agreement by the other party. The agreement also contains terms and conditions customary for this type of arrangement, including representations, warranties and indemnities. As a result of the acquisition of Alpharma by King in December 2008, the rights and obligations of the agreement are now controlled by King. As of December 31, 2008, the cumulative aggregate payments received by us under this agreement were \$21.6 million.

*Nycomed Danmark, APS.* In November 2006, we entered into a collaboration agreement with Nycomed. Under the terms of the agreement, we licensed to Nycomed the exclusive commercialization rights to POSIDUR for the European Union (E.U.) and certain other countries. Nycomed paid us an upfront license fee of \$14.0 million in 2006 and an \$8.0 million milestone payment in 2007 triggered by achievement of a clinical development milestone, with future potential additional milestone payments of up to \$180.0 million upon achievement of defined development, regulatory and sales milestones. We will jointly direct and equally fund with Nycomed a development program for POSIDUR intended to secure regulatory approval in both the U.S. and the E.U. In addition, we will manufacture and supply the product to Nycomed for commercial sale in the territory licensed to Nycomed. Nycomed will pay us blended royalties on sales in the defined territory of 15-40% depending on annual sales, as well as a manufacturing markup. We retain full commercial rights to POSIDUR in the U.S., Canada, Asia and certain other countries. 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, Nycomed shall have the right to terminate the agreement after expiry of patents covering POSIDUR in all major market countries in the E.U. and for adverse product events. As of December 31, 2008, the cumulative aggregate payments received by us under this agreement were \$30.0 million. In addition, the cumulative aggregate payments paid by us to Nycomed were \$2.3 million as of December 31, 2008.

*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 certain products developed under the agreement (including Remoxy) to King. In December 2005, we amended our agreement with Pain

**Table of Contents**

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 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. Under the agreement with Pain Therapeutics, we are eligible to receive milestone payments of up to \$9.3 million in the aggregate upon the achievement of predetermined development and regulatory milestones for the four drug candidates currently in development. As of December 31, 2008, we have received \$1.7 million in milestone payments. 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. As of December 31, 2008, the cumulative aggregate payments received by us under this agreement were \$31.3 million.

*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. We have received an initial payment of \$10.0 million in connection with the execution of the Agreement. In February 2009, Endo notified us that it was terminating the license agreement with us, and thereby returning Endo's right to develop and commercialize TRANSDUR-Sufentanil in the U.S. and Canada to us effective August 26, 2009. Endo has committed to assist in an orderly and rapid transition of this program back to us. As of December 31, 2008, the cumulative aggregate payments received by us under this agreement were \$21.4 million.

*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. Under the agreement, as amended, we are eligible to receive milestone payments from Voyager of up to \$3.0 million in the aggregate upon the achievement of predetermined development and regulatory milestones. As of December 31, 2008, we have received \$500,000 in milestone payments. We are also eligible to receive reimbursement for any research and development work we perform. 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. Effective January 2007, we amended our agreement with Voyager. Under the amendment, among other changes to the Agreement, the royalty rate that we will receive on net sales of Memryte, if commercialized, is doubled (to 10-14% of net sales after the amendment), and in addition, we will receive 10% of any upfront, milestone and other fees received by Voyager in the event that the product is sublicensed to a third party. In return, we paid Voyager \$1 million in cash and forgave approximately \$725,000 which was owed to us for previously provided services. As of December 31, 2008, the cumulative aggregate payments received by us under this agreement were \$11.6 million.

*ALZA Corporation.* In April 1998, we entered into a development and commercialization agreement with ALZA, which has been subsequently amended and restated, most recently in October 2002. The agreement provides us with exclusive rights to develop, commercialize and manufacture products using ALZA's patented DUROS technology in selected fields of use, and obligates us to pay ALZA a royalty on the net sales of our DUROS-based products and a percentage of upfront license fees, milestone payments, or any other payments or consideration received by us with respect to such DUROS-based products. In connection with the execution of the Agreement, we 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. We issued an additional 1,000,000 shares of our common stock and a warrant to purchase 1,000,000 shares of common stock to ALZA in connection with an amendment of the Agreement in April 2000. The warrant expired in September 2004. This agreement can be terminated by either party for material breach by the other party and by us without cause.

---

## **Table of Contents**

*EpiCept Corporation.* In December 2006, we entered into a license agreement with EpiCept Corporation (EpiCept) that provides us with the exclusive, worldwide rights to certain of EpiCept's intellectual property for a transdermal patch containing bupivacaine for the treatment of back pain. Pursuant to the agreement, we paid EpiCept \$1.0 million upfront in December 2006 and, subject to our achievement of specified milestones, agreed to pay EpiCept an additional \$9.0 million in milestone payments as well as a royalty on net sales of any product covered by the license. In September 2008, we and EpiCept entered into an amendment to the license agreement. Under the amendment, among other changes, the scope of the license was broadened from the treatment of back pain to all uses covered by the EpiCept intellectual property including myofascial pain and muscle tension pain, and the license was converted to an exclusive, worldwide, fully paid up, royalty-free, perpetual and irrevocable license. In consideration of this amendment, we made a one-time payment of \$2.25 million to EpiCept in full satisfaction of all future payment obligations to EpiCept under the license agreement.

*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 early 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 will remain in effect until the expiration of NeuroSystec's royalty obligations under the agreement, which will occur when the last of our related patent rights expire or are found to be invalid, unless the agreement is otherwise terminated earlier. 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.

## **Commercial Businesses**

### *ALZET®*

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

The ALZET product line consists of miniature, implantable osmotic pumps and accessories 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 line and assets used primarily in the manufacture, sale and distribution of this product line from ALZA in April 2000. We believe that the ALZET business provides us with innovative design and application opportunities for potential new products.

### *LACTEL® Absorbable Polymers*

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-

---

## **Table of Contents**

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 leverage 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 will continue to pursue 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.

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

### **Suppliers**

We purchase sucrose acetate isobutyrate, a raw material for our ORADUR and SABER-based pharmaceutical systems, including POSIDUR, Remoxy and other ORADUR-based opioid drug candidates licensed to Pain Therapeutics, pursuant to a supply agreement with Eastman Chemical Company. We also purchase sufentanil for TRANSDUR-Sufentanil pursuant to a supply agreement with Mallinckrodt, Inc., and we have entered into a supply agreement with Corium International, Inc. for clinical and commercial supplies of ELADUR and a supply agreement with Hospira Worldwide, Inc. for clinical and commercial supplies of POSIDUR.

Our supply agreement with Eastman Chemical Company requires us to purchase a certain portion of our requirements for sucrose acetate isobutyrate from Eastman Chemical and obligates us to pay a small fee per annum if our purchases do not meet specified sales targets. The Agreement may be terminated by either party under certain circumstances, including any material uncured breach by, or the insolvency, liquidation or bankruptcy of, or similar proceedings involving, the other party.

Our supply agreement with Mallinckrodt, Inc. requires us to purchase a certain portion of our requirements for sufentanil from Mallinckrodt, and has no other minimum purchase requirements or exclusivity provisions. The agreement expires on September 30, 2009 and is subject to automatic renewal for additional one-year terms unless either party provides one year notice of its intention not to renew the agreement. In addition, either party may terminate the Mallinckrodt agreement on 30 days notice for any material uncured breach by, or the bankruptcy of or similar proceedings involving, the other party. Finally, we may terminate the Mallinckrodt agreement on 60 days notice if we reasonably determine that the price being charged by Mallinckrodt is higher than the prevailing price for similar quantities of like grade or quality, or if we cease to develop or commercialize any products incorporating the products we purchase from Mallinckrodt.

We believe that these agreements will provide a sufficient supply of these raw materials and drug product to meet our needs for the 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 with acceptable quality, within acceptable time frames or at reasonable cost.

---

## **Table of Contents**

### **Customers**

Our product revenues are derived from sale of the ALZET and LACTEL product lines. 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. In 2008, revenues from our collaborative agreements with Pain Therapeutics, Endo, Alpharma, and Nycomed represented 24%, 15%, 13% and 11% of our total revenues, respectively. In 2007, revenues from our collaborative agreements with Nycomed, Pain Therapeutics, and Endo represented 36%, 16% and 16% of our total revenues, respectively. In 2006, revenues from our collaborative agreements with Pain Therapeutics and Endo represented 34% and 20% of our total revenues, respectively.

At December 31, 2008, Nycomed and Alpharma accounted for 31% and 29% of our net accounts receivable, respectively. At December 31, 2007, Pain Therapeutics, Nycomed and Endo accounted for 36%, 19% and 16% of our net accounts receivable, respectively. At December 31, 2006, Pain Therapeutics, Nycomed and Endo accounted for 22%, 20% and 16% of our net accounts receivable, respectively.

### **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 POSIDUR, Remoxy, TRANSDUR-Sufentanil, ELADUR, and Memryte. 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 line and certain key components for Remoxy at our Vacaville, CA facility and our LACTEL product line at our Pelham, AL 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. In the fourth quarter of 2007 and first quarter of 2008, in two separate tranches, we acquired from a third party a portfolio of worldwide patents relating to drug delivery technologies. This portfolio consists of approximately 22 issued and pending U.S. patents and patent applications as well as their international counterparts. We believe this portfolio will benefit our business by broadening our drug delivery technology base and strengthening our intellectual property position. As of February 27, 2009, we held 55 issued U.S. patents and 356 issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have 99 pending U.S. patent applications and have filed 107 patent applications under the Patent Cooperation Treaty, from which 549 national phase applications are currently pending in Europe, Australia, Japan, Canada and other countries. Our patents expire at various dates starting in 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.



---

## **Table of Contents**

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. 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.

The process required by the FDA under the new drug provisions of the Federal Food, Drug and Cosmetics Act (the 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.



---

**Table of Contents**

Section 505 of the Act describes three types of new drug applications: (1) an application that contains full reports of investigations of safety and effectiveness (section 505(b)(1)); (2) an application that contains full reports of investigations of safety and effectiveness but where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference (section 505(b)(2)); and (3) an application that contains information to show that the proposed product is identical in active ingredient, dosage form, strength, route of administration, labeling, quality, performance characteristics and intended use, among other things, to a previously approved product (section 505(j)). A supplement to an application is a new drug application. We expect that most of our drug candidates will be approved by submission of a new drug application under section 505(b)(2).

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.

---

**Table of Contents**

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 occur after the product reaches the market. Requirements for additional Phase IV studies (post approval marketing 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

**Table of Contents**

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.

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.

On February 6, 2009, the Food and Drug Administration (FDA) sent letters to manufacturers of certain opioid drug products, indicating that these drugs will be required to have a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of the drugs continue to outweigh the risks. The affected opioid drugs include brand name and generic products and are formulated with the active ingredients fentanyl, hydromorphone, methadone, morphine, oxycodone, and oxymorphone. The FDA has authority to require a REMS under the Food and Drug Administration Amendments Act of 2007 (FDAAA) when necessary to ensure that the benefits of a drug outweigh the risks.

According to the FDA, opioid drugs have benefit when used properly and are a necessary component of pain management for certain patients. Opioid drugs have serious risks when used improperly. The FDA, drug manufacturers, and others have taken a number of steps in the past to prevent misuse, abuse and accidental overdose of these drugs, including providing additional warnings in product labeling, implementing risk management plans, conducting inter-agency collaborations, and issuing direct communications to both prescribers and patients. Despite these efforts, the rates of misuse and abuse, and of accidental overdose of opioids, have risen over the past decade. The FDA believes that establishing a REMS for opioids will reduce these risks, while still ensuring that patients with legitimate need for these drugs will continue to have appropriate access.

According to the FDA, it recognizes the need to achieve balance between appropriate access and risk mitigation, and believes an effective strategy would benefit from input from industry, patient advocacy groups, the pain and addiction treatment communities, the general public, and other stakeholders. In the first of a series of meetings with stakeholders, the FDA invited those companies that market the affected opioid drugs to a meeting with the agency on March 3, 2009 to discuss REMS development. Additional steps will include discussions with other federal agencies and non-government institutions, including patient and consumer advocates, representatives of the pain and addiction treatment communities, other health care professionals, and other interested parties. FDA is planning a public meeting in late spring or early summer to allow for broader public input and participation. Through this process, FDA hopes to gain valuable information that will lead to practical and effective solutions for development of a REMS and for appropriate use of these opioid drug products.

Many of our drug candidates including Remoxy, our other ORADUR-opioid drug candidates and TRANSDUR-Sufentanil are subject to the REMS requirement. Until the contours of required REMS programs are established by the FDA and understood by drug developers and marketers such as ourselves and our collaborators, there may be delays in marketing approvals for these drug candidates. In addition, there may be increased cost, administrative burden and potential liability associated with the marketing and sale of these types of drug candidates subject to the REMS requirement, which could negatively impact the commercial benefits to us and our collaborators from the sale of these drug candidates.

---

## **Table of Contents**

*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, and Remoxy and our other ORADUR-based opioid drug candidates, 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. POSIDUR, TRANSDUR-Sufentanil, ELADUR, Remoxy and the other ORADUR- based opioid drug candidates licensed to Pain Therapeutics, if approved, will compete with currently marketed oral opioids, transdermal opioids, local anesthetic patches, and implantable and external infusion pumps which can be used for infusion of opioids and local anesthetics. Products of these types are marketed by Purdue Pharma, King, Knoll, Janssen, Medtronic, Endo Pharmaceuticals, AstraZeneca, Arrow International, Tricumed, I-Flow and others. 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, Pacira Pharmaceuticals, EpiCept, Innocoll, Inovio, Nektar, Anesiva, NeurogesX, Alexza, Focal, I-Flow, Javelin Pharmaceuticals, Cadence Pharmaceuticals 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 Sciele Pharma, Inc. 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.

## **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](http://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 on our website.

**Table of Contents****Employees**

As of February 27, 2009 we had 171 employees, including 103 in research and development, 30 in manufacturing and 38 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 27, 2009 are as follows:

<b>Name</b>	<b>Age</b>	<b>Position</b>
Felix Theeuwes, D.Sc.	71	Chairman, Chief Scientific Officer and Director
James E. Brown, D.V.M.	52	President, Chief Executive Officer and Director
Matthew J. Hogan, M.B.A.	49	Chief Financial Officer
Peter J. Langecker, M.D., Ph.D.	58	Chief Medical Officer
Jean I Liu, J.D., M.S.	40	Senior Vice President, General Counsel and Secretary
Paula Mendenhall, Pharm.D.	65	Executive Vice President, Operations and Administration
Su Il Yum, Ph.D.	69	Executive 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, 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 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.

Matthew J. Hogan, M.B.A. has served as our Chief Financial Officer since September 2006. He was the Chief Financial Officer at CIPHERGEN Biosystems, Inc. from 2000 to 2006, and a consultant from March 2006. Prior to joining CIPHERGEN, Mr. Hogan was the Chief Financial Officer at Avocet Medical, Inc. from 1999 to 2000. From 1996 to 1999, Mr. Hogan was the Chief Financial Officer at Microcide Pharmaceuticals, Inc. From 1986 to 1996, he held various positions in the investment banking group at Merrill Lynch & Co., most recently as a Director focusing on the biotechnology and pharmaceutical sectors. Mr. Hogan holds a B.A. in economics from Dartmouth College and an M.B.A. from the Amos Tuck School of Business Administration.

Peter J. Langecker, M.D., Ph.D. has served as our Chief Medical Officer since May 2006. Prior to joining DURECT, Dr. Langecker served as Chief Medical Officer and Vice President of Clinical Affairs at Intarcia Therapeutics, Inc. from October 1999 to April 2006. Prior to that, Dr. Langecker was Vice President of Clinical Affairs at Sugen, Inc. from 1997 to 1999, Vice President, Clinical Research at Coulter Pharmaceuticals from

---

**Table of Contents**

1995 to 1997 and Director of Clinical Research, Oncology, at Schering-Plough from 1992 to 1995. Previously, Dr. Langecker worked as a Project Physician Central Medical Advisor, Oncology at Ciba-Geigy (now Novartis) in Basel, Switzerland. He received his M.D. degree and his doctorate in medical sciences from the Ludwig-Maximilians University in Munich.

Jean I Liu, J.D., M.S. 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 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, Pharm.D. has served as our Executive Vice President of Operations and Administration since January 2007 and as 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) and the Parenteral Drugs Association.

Su Il Yum, Ph.D. has served as our Executive Vice President of Pharmaceutical Systems Research and Development since January 2007 and as our Senior Vice President of Pharmaceutical Systems Research and Development since January 2006. Previously, Dr. Yum served as our Senior Vice President, Engineering since December 2003 and 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<sup>®</sup>. Prior to joining Amira, he held a number of senior positions in project management and engineering at Alza Corporation for 27 years. 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.

**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;



---

**Table of Contents**

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;

demonstrating through clinical trials that the drug and system combination is safe and effective in patients for the intended indication;  
and

completing the manufacturing development and scale-up to permit manufacture of the pharmaceutical system in commercial quantities and at acceptable prices.

The time frame necessary to achieve these developmental milestones for any individual product is long and uncertain, and we may not successfully complete these milestones for any of our products in development. We have not yet selected the drug dosages nor finalized the formulation or the system design of POSIDUR, TRANSDUR-Sufentanil, ELADUR, our ORADUR-based drug candidates other than Remoxy, and Memryte, 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 or our collaborators 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. 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 and our collaborators may not be able to complete development of any pharmaceutical 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 POSIDUR, TRANSDUR-Sufentanil, ELADUR, Remoxy and our ORADUR-based drug candidates other than Remoxy, Memryte 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, nonclinical (animal) studies and clinical (human) trials that each system is safe and effective for human use for each targeted indication. The clinical development status of our publicly announced development programs is as follows:

**Remoxy** In December 2007, Pain Therapeutics and King reported positive results from the pivotal Phase III trial submitted under an approved Special Protocol Assessment (SPA) with the FDA; the NDA was submitted to the FDA in June 2008, and in August 2008, the NDA was accepted by the FDA and granted priority review. In December 2008, Pain Therapeutics received a Complete Response Letter for its NDA for Remoxy in which the FDA determined that the NDA was not approved. According to Pain Therapeutics, the FDA indicated that additional non-clinical data will be required to support the approval of Remoxy, but the FDA has not requested or recommended additional clinical efficacy studies prior to approval. Pain Therapeutics has indicated that they plan to meet with the FDA in the second quarter of 2009 regarding the NDA for Remoxy, and they believe this FDA meeting will provide them with a more reliable context in which to make projections about Remoxy.

**POSIDUR** A successful Phase IIb clinical trial in hernia surgery was completed and an end-of-Phase II meeting has been held with the FDA. We are currently in dialogue with the FDA regarding our Phase III program. In parallel with these discussions, we are conducting a 60-patient Phase IIb study in



---

**Table of Contents**

Australia in shoulder surgery in order to allow us to confirm aspects of our clinical study design and conduct. Additionally, Nycomed is commencing Phase IIb studies in surgical procedures in Europe.

**TRANSDUR-Sufentanil Patch** Endo recently successfully completed a Phase II program for TRANSDUR-Sufentanil in which they evaluated the conversion of patients on oral and transdermal opioids to TRANSDUR-Sufentanil. The most recent Phase II study met its primary and secondary objectives of establishing a successful dose-titration regimen and dose potency relationships, demonstrating safety and tolerability at the therapeutic dose, and achieving effective analgesic pain control. The Phase II data, extensive non-clinical data that had been generated by Endo and detailed proposed protocols for Phase III were reviewed with the FDA at an end-of-Phase II meeting on February 19, 2009. On February 26, 2009, Endo notified us that it was terminating its license agreement for TRANSDUR-Sufentanil and thereby returning to us Endo's rights to develop and commercialize TRANSDUR-Sufentanil in the U.S. and Canada effective August 26, 2009.

**ELADUR** A Phase IIa clinical trial was completed and positive results were reported in the fourth quarter of 2007. In 2008, we conducted manufacturing scale-up and processing activities to secure additional Phase II and Phase III supplies, and developed our clinical and regulatory strategy for further development of this program. In September 2008, we entered into a development and license agreement with Alpharma Ireland Ltd., an affiliate of Alpharma Inc., granting such party the exclusive worldwide rights to develop and commercialize ELADUR. The agreement became effective in October 2008 upon clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (HSR). Alpharma was acquired by King Pharmaceuticals in December 2008 and, as a result, the rights and obligations of the agreement are now controlled by King.

**Second and third ORADUR-Opioid Drug Candidates under Pain Therapeutics/King alliance** We also have two other ORADUR-based drug candidates for which Phase I clinical trials have been completed. According to Pain Therapeutics, the data from these Phase I trials indicate that these drug candidates are safe and well-tolerated with a release profile that appears well suited to use with a chronic pain population. The active ingredients in these two drug candidates are opioids whose identities have not been publicly disclosed. We are currently in the clinical, 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 and our collaborators 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 or our collaborators 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. For example, according to Pain Therapeutics, the FDA has indicated that additional non-clinical data will be required prior to regulatory approval for Remoxy. This additional data could delay commercialization of such pharmaceutical systems and harm our business and financial condition.

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 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

---

**Table of Contents**

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 are 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.

*Regulatory action or failure to obtain product approvals could delay or limit development and commercialization 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 perform clinical trials, 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. In particular, recent recalls of and reported adverse side effects of marketed drugs have made regulatory agencies, including the FDA, increasingly focus on the safety of drug products. Regulatory agencies are requiring more extensive and ever increasing showings of safety at every stage of drug development and commercialization from initial clinical trials to regulatory approval and beyond. These rigorous and evolving standards may delay and increase the expenses of our development efforts. The FDA or other foreign regulatory agency may, at any time, halt our and our collaborators' development and commercialization activities due to safety concerns, in which case our business will be harmed. In addition, the FDA or other foreign regulatory agency may refuse or delay approval of our or our collaborators' drug candidates for failure to collect sufficient clinical or animal safety data, and require us or our collaborators to conduct additional clinical or animal safety data which may cause lengthy delays and increased costs to our programs. For example, Pain Therapeutics has announced that the FDA indicated that additional non-clinical data will be required to support the approval of Remoxy.

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 trials or on the required clinical or animal 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.

---

**Table of Contents**

The time required to obtain approvals from foreign countries may be shorter or longer than that required for FDA approval, and requirements for foreign licensing may differ from FDA requirements. We or our third-party collaborators, as applicable, may be unable to obtain requisite approvals from the FDA and foreign regulatory authorities, and even if obtained, such approvals may not be on a timely basis, or they may not cover the clinical uses that we specify. If we or our third-party collaborators, as applicable, fail to obtain timely clearance or approval for our development products, we or they will not be able to market and sell our pharmaceutical systems, which will limit our ability to generate revenue.

*Many of our drug candidates under development including Remoxy and TRANSDUR-Sufentanil are subject to mandatory Risk Evaluation and Mitigation Strategy (REMS) programs, a new requirement by the FDA, which could delay the approval of these drug candidates and increase the cost, burden and liability associated with the commercialization of these drug candidates*

On February 6, 2009, the Food and Drug Administration (FDA) sent letters to manufacturers of certain opioid drug products, indicating that these drugs will be required to have a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of the drugs continue to outweigh the risks. The affected opioid drugs include brand name and generic products and are formulated with the active ingredients fentanyl, hydromorphone, methadone, morphine, oxycodone, and oxymorphone. The FDA has authority to require a REMS under the Food and Drug Administration Amendments Act of 2007 (FDAAA) when necessary to ensure that the benefits of a drug outweigh the risks.

According to the FDA, opioid drugs have benefit when used properly and are a necessary component of pain management for certain patients. Opioid drugs have serious risks when used improperly. The FDA, drug manufacturers, and others have taken a number of steps in the past to prevent misuse, abuse and accidental overdose of these drugs, including providing additional warnings in product labeling, implementing risk management plans, conducting inter-agency collaborations, and issuing direct communications to both prescribers and patients. Despite these efforts, the rates of misuse and abuse, and of accidental overdose of opioids, have risen over the past decade. The FDA believes that establishing a REMS for opioids will reduce these risks, while still ensuring that patients with legitimate need for these drugs will continue to have appropriate access.

According to the FDA, it recognizes the need to achieve balance between appropriate access and risk mitigation, and believes an effective strategy would benefit from input from industry, patient advocacy groups, the pain and addiction treatment communities, the general public, and other stakeholders. In the first of a series of meetings with stakeholders, the FDA invited those companies that market the affected opioid drugs to a meeting with the agency on March 3, 2009 to discuss REMS development. Additional steps will include discussions with other federal agencies and non-government institutions, including patient and consumer advocates, representatives of the pain and addiction treatment communities, other health care professionals, and other interested parties. FDA is planning a public meeting in late spring or early summer to allow for broader public input and participation. Through this process, FDA hopes to gain valuable information that will lead to practical and effective solutions for development of a REMS and for appropriate use of these opioid drug products.

Many of our drug candidates including Remoxy, our other ORADUR-opioid drug candidates and TRANSDUR-Sufentanil are subject to the REMS requirement. Until the contours of required REMS programs are established by the FDA and understood by drug developers and marketers such as ourselves and our collaborators, there may be delays in marketing approvals for these drug candidates. In addition, there may be increased cost, administrative burden and potential liability associated with the marketing and sale of these types of drug candidates subject to the REMS requirement, which could negatively impact the commercial benefits to us and our collaborators from the sale of these drug candidates.

---

**Table of Contents**

*We depend to a large extent on third-party collaborators, and we have limited or no control over the development, sales, distribution and disclosure for our pharmaceutical systems which are the subject of third-party collaborative or license agreements*

Our 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 an agreement with Endo related to the development, promotion and distribution of TRANSDUR-Sufentanil in the United States and Canada, which agreement will terminate effective August 26, 2009. In addition, we have entered into agreements with Pain Therapeutics, Nycomed, Alpharma (acquired by King in December 2008) and Voyager under which we granted such third parties the right to develop, apply for regulatory approval for, market, promote or distribute Remoxy and other ORADUR-based products incorporating specified opioids, POSIDUR, ELADUR 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, clinical trial strategy, regulatory approval, 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. They may also conduct their activities in a manner that is different from the manner we would have chosen, had we been developing such pharmaceutical systems ourselves. 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, clinical trials, regulatory approval, manufacture, marketing or sale of these pharmaceutical systems. If any of these events occur, we may not 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.

*Our near-term revenues depend on collaboration agreements with other companies. These agreements subject us to obligations which must be fulfilled and also make our revenues dependent on the performance of such 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 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 relationships with such collaborators and resolving possible issues of contractual interpretation which may detract from time our management would otherwise devote to 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 TRANSDUR-Sufentanil (which will terminate effective August 26, 2009), Pain Therapeutics with respect to Remoxy and other ORADUR-based products incorporating specified opioids, Nycomed with respect to POSIDUR, Alpharma (acquired by King) with respect to ELADUR, 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.

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

---

**Table of Contents**

*Our near-term revenues also depend on milestone payments based on achievements by our third-party collaborators. Failure of such collaborators to attain such milestones would result in our not receiving additional revenues.*

In addition to payments based on our performance of research and development activities, our revenues also depend on the attainment of milestones set forth in our collaboration agreements. Such milestones are typically related to clinical trial developments, regulatory approvals or sales accomplishments. To the extent third-party collaborators do not achieve such milestones, we will not receive the associated revenues, which could harm our financial condition and may cause us to defer or cut-back development activities or forego the exploitation of opportunities in certain geographic territories, any of which could have a material adverse effect on our business.

*Our business strategy includes the entry into additional collaborative agreements. We may not be able to enter into additional collaborative agreements or may not be able to negotiate commercially acceptable terms for these agreements*

Our current business strategy includes the entry into additional collaborative agreements for the development and commercialization of our pharmaceutical systems. The negotiation and consummation of these type of agreements typically involve simultaneous discussions with multiple potential collaborators and require significant time and resources from our officers, business development, legal, and research and development staff. In addition, in attracting the attention of pharmaceutical and biotechnology company collaborators, we compete with numerous other third parties with product opportunities as well the collaborators own internal product opportunities. We may not be able to consummate additional collaborative agreements, or we may not be able to negotiate commercially acceptable terms for these agreements. If we do not consummate additional collaborative agreements, we may have to consume money more rapidly on our product development efforts, defer development activities or forego the exploitation of certain geographic territories, any of which could have a material adverse effect on our business.

*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;

the continuation of our collaborative agreements that provide financial funding for our activities;

success in entering into collaboration agreements and meeting milestones under such agreements;

progress with preclinical studies and clinical trials;

the time and costs involved in obtaining regulatory clearance;

costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;

## Edgar Filing: DURECT CORP - Form 10-K

costs of developing sales, marketing and distribution channels and our ability and that of our collaborators to sell our pharmaceutical systems;



---

**Table of Contents**

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;

costs for recruiting and retaining employees and consultants; and

unexpected legal, accounting and other costs and liabilities related to our business.

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 collaborators 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.

*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 manufacturing processes associated with our pharmaceutical systems are complex. Except with respect to Remoxy, we and our third-party collaborators, where relevant, have not yet completed development of the manufacturing process for any pharmaceutical systems or components including POSIDUR, TRANSDUR-Sufentanil, ELADUR, Memryte, and other ORADUR-based drug candidates. 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 system or component at an acceptable cost, then we and our third-party collaborators may not be able to commercialize that pharmaceutical system or we may be in breach of our supply obligations to our third-party collaborators.

Our manufacturing facility in Cupertino is a multi-disciplinary site that we have used to manufacture only research and clinical supplies of several of our pharmaceutical systems under good manufacturing practices (GMP), including POSIDUR, TRANSDUR-Sufentanil, ELADUR, Remoxy and additional ORADUR-based drug candidates, and Memryte. 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 accomplish these tasks in a timely manner.

---

**Table of Contents**

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 compliance with applicable regulations, the clinical trials and the commercial sale of our pharmaceutical systems and those of our third-party collaborators 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 have entered into a supply agreement with Corium International, Inc. for clinical and commercial supplies of ELADUR and a supply agreement with Hospira Worldwide, Inc. for clinical and commercial supplies of POSIDUR. These third parties are currently our sole source for drug product required for development and commercialization of these drug candidates. Furthermore, we and our third-party collaborators, where relevant, may also need or choose to subcontract with additional third-party contractors to perform manufacturing steps of our pharmaceutical systems or supply required components for our pharmaceutical systems. Where third party contractors perform manufacturing services for us, we will be subject to the schedule, expertise and performance of third parties as well as incur significant additional costs. Failure of third parties to perform their obligations could adversely our operations, development timeline and financial results. 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 collaborators or ourselves or at an acceptable cost, our operating results will be harmed.

*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 or other similar 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

FDA required product withdrawals or warnings arising from identification of serious and unanticipated adverse side effects in our pharmaceutical systems.

Manufacturers of drugs 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

---

**Table of Contents**

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.

*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, 2008, had an accumulated deficit of approximately \$283.6 million. We expect to continue to incur significant operating losses over the next several years as we continue to incur significant costs for research and development, clinical trials, manufacturing, sales, and general and administrative functions. 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 from third parties 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 do so in the near future. Our current product revenues are from the sale of the ALZET product line and the sale of LACTEL biodegradable polymers, and from payments under collaborative research and development agreements with third parties. We do not expect our product revenues to increase significantly in the near future, and we do not expect that collaborative research and development revenues will exceed our actual operating expenses. We do not anticipate meaningful revenues to derive from the 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 develop our own sales force to market POSIDUR but we have limited sales experience and may not be able to do so effectively*

We may choose to develop our own sales force to market POSIDUR in the United States if POSIDUR is 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 limit or materially harm our business.

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

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

fail to satisfy financial or contractual obligations to us;

fail to adequately market our 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



---

**Table of Contents**

build up inventory in excess of demand thereby limiting future purchases of 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. These third parties may not execute their responsibilities and tasks competently or in a timely fashion. We rely on third-parties to manufacture or perform manufacturing steps relating to our pharmaceutical systems or components. 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 competent or 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 POSIDUR, TRANSDUR-Sufentanil, ELADUR, Remoxy and our additional ORADUR-based drug candidates, and Memryte) are currently purchased from a single or a limited number of outside sources. In particular, Eastman Chemicals is the sole supplier, pursuant to a supply agreement entered into in December 2005, of our requirements of sucrose acetate isobutyrate, a necessary component of POSIDUR, Remoxy, our additional ORADUR-opioids and certain other pharmaceuticals systems we have under development. The reliance on a sole or limited number of suppliers could result in:

delays associated with redesigning a pharmaceutical system 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 delivery time.

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

---

**Table of Contents**

*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 27, 2009, we held 55 issued U.S. patents and 356 issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have 99 pending U.S. patent applications and have filed 107 patent applications under the Patent Cooperation Treaty, from which 549 national phase applications are currently pending in Europe, Australia, Japan, Canada and other countries. Our patents expire at various dates starting in 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 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.

The patent laws of the U.S. have recently undergone changes through court decisions which may have significant impact on us and our industry. The recent decisions of the U.S. Supreme Court (e.g., *KSR v. Teleflex*, *EBay v. MercExchange*) and other courts (e.g., *In re Seagate*) with respect to the standards of patentability, enforceability, availability of injunctive relief and damages may make it more difficult for us to procure, maintain and enforce patents. In addition, bills are pending before the U.S. Congress including the Patent Reform Act of 2007 that may fundamentally change the patent laws of the U.S. on issues ranging from priority entitlement, filing and prosecution matters to enforcement and damages. These changes and proposed reforms have introduced significant uncertainty in the patent law landscape and may potentially negatively impact our ability to procure, maintain and enforce patents to provide exclusivity for our products.

We are party to several collaborative agreements. Our third-party collaborators have entered into these agreements based on the exclusivity that our intellectual property rights confer on the products being developed. The loss or diminution 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 and data 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, the decision by the Supreme Court in the case of *MedImmune, Inc. v. Genentech, Inc.* 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

---

**Table of Contents**

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 pharmaceutical systems infringe on their intellectual property rights, particularly because there is substantial uncertainty about the validity and breadth of medical patents*

We and our collaborators 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 or our collaborators 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 or our collaborators, 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. In addition, pursuant to our collaborative agreements, we have provided our collaborators with the right, under specified circumstances, to defend against any claims of infringement of the third party intellectual property rights, and such collaborators may not defend against such claims adequately or in the manner that we would do ourselves. Intellectual property litigation or claims could force us or our collaborators 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

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 may choose to develop may include proprietary drugs to which we do not have commercial rights. 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.

## Table of Contents

*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 as 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. The TRANSDUR-Sufentanil patch, Remoxy and our additional ORADUR-based drug candidates, and other pharmaceutical systems we have under development contain active ingredients which are classified as 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 extensive and include regulations governing manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, record keeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs and the expense associated with development and commercialization of drug candidates including controlled substances. 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 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. For example, we had a \$13.5 million non-cash write down of deferred royalties and commercial rights related to CHRONOGESIC in the fourth quarter of 2008, which impacted our financial statements. We are required to perform periodic impairment reviews of our goodwill at least annually.





---

**Table of Contents**

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 2008 and determined that goodwill was not impaired as of December 31, 2008. 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 123(R)), *Share-Based Payment*, which was originally effective for annual or interim periods beginning after June 15, 2005. SFAS 123(R) 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 123(R) using the modified prospective basis on January 1, 2006. Our adoption of SFAS 123(R) has and will continue to have a material adverse impact on our results of operations and will adversely impact or delay our profitability.

*Global credit and financial market conditions could negatively impact the value of our current portfolio of cash equivalents or short-term investments and our ability to meet our financing objectives.*

Our cash and cash equivalents are maintained in highly liquid investments with remaining maturities of 90 days or less at the time of purchase. Our short-term investments consist primarily of readily marketable debt securities with remaining maturities of more than 90 days and less than one year at the time of purchase. While as of the date of this filing, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents or short-term investments since December 31, 2008, no assurance can be given that further deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or short-term investments or our ability to meet our financing objectives.

*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. 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 company through varying business cycles*

Our success will depend on properly sizing our company through growth and contraction cycles caused in part by changing business conditions, which places a significant strain on our management and on our administrative, operational and financial resources. To manage through such cycles, we must expand or contract our facilities, our operational, financial and management systems and our personnel. If we were unable to manage growth and contractions effectively our business would be harmed.

---

## **Table of Contents**

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

Our corporate headquarters, primary 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, development and manufacturing efforts, could be destroyed.

## **Risks Related To Our Industry**

### *The market for our pharmaceutical systems is 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.

We may face competition from other companies in numerous industries including pharmaceuticals, medical devices and drug delivery. POSIDUR, TRANSDUR-Sufentanil, ELADUR, Remoxy and other ORADUR-based opioids, and Memryte, if approved, will compete with currently marketed oral opioids, transdermal opioids, local anesthetic patches, and implantable and external infusion pumps which can be used for infusion of opioids and local anesthetics. Products of these types are marketed by Purdue Pharma, King, Knoll, Janssen, Medtronic, Endo Pharmaceuticals, AstraZeneca, Arrow International, Tricumed, I Flow and others. 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, Pacira Pharmaceuticals, EpiCept, Innocoll, Inovio, Nektar, Focal, I-Flow, Anesiva, NeurogesX, Alexza, Cadence Pharmaceuticals, Javelin Pharmaceuticals 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. Many of these entities have significantly greater research and development

---

**Table of Contents**

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 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 POSIDUR, TRANSDUR-Sufentanil, ELADUR, Remoxy and other ORADUR-based drug candidates, and Memryte. 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.

---

**Table of Contents**

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 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.

*Potential new accounting pronouncements and legislative actions are likely to impact our future financial position or results of operations*

Future changes in financial accounting standards 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 Global Market rules, are creating uncertainty for companies such as ours and insurance, accounting and auditing costs are increasing as a result of

## **Table of Contents**

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.

### **Risks Related To Our Common Stock**

#### *Our operating history makes evaluating our stock difficult*

Our quarterly and annual results of operations have historically fluctuated and we expect will continue to 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*

Investors may experience dilution of their investment if we raise capital through the sale of additional equity securities or convertible debt securities or grant additional stock options to employees and consultants. Any sales in the public market of the common stock issuable upon such conversion could adversely affect prevailing market prices for our common 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, Pain Therapeutics or its commercialization sublicensee King Pharmaceuticals, Nycomed, Alpharma (now owned by King) or Voyager) to develop and commercialize successfully the respective pharmaceutical systems they are developing;

adverse results (including adverse events) or delays in our clinical and non-clinical trials of POSIDUR, TRANSDUR-Sufentanil, ELADUR, Remoxy, our additional ORADUR-based drug candidates, Memryte 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, clinical trials, manufacturing processes or sales and marketing activities, or those of our third party collaborators;

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

regulatory developments in the United States and foreign countries;

## Edgar Filing: DURECT CORP - Form 10-K

any lawsuit involving us or our pharmaceutical systems including intellectual property infringement or product liability suits;

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

**Table of Contents**

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 or directors or sales of substantial amounts of common stock by others;

changes in accounting principles; and

loss of any of our key scientific or management personnel.

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 common stock.

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.

*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 principal stockholders 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



## Edgar Filing: DURECT CORP - Form 10-K

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;

**Table of Contents**

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.**

The following chart indicates the facilities that we lease, the location and size of each such facility and their designated use.

<b>Location</b>	<b>Approximate Square Feet</b>	<b>Operation</b>	<b>Expiration</b>
Cupertino, CA	30,000 sq. ft.	Office, Laboratory and Manufacturing	Lease expired February 2009 (an option to renew for an additional five years has been exercised by us and the terms of the renewal period are under negotiation between us and the landlord)
Cupertino, CA	20,000 sq. ft.	Office and Laboratory	Lease expires 2014 (with an option to renew for an additional five years)
Cupertino, CA	40,560 sq. ft.	Office	Lease expires 2012 (with an option to renew for an additional six years)
Vacaville, CA	24,634 sq. ft.	Manufacturing	Lease expires 2013 (with an option to renew for an additional five years)
Pelham, AL	9,400 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2010 (with an option to renew for an additional 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.**

No matters were submitted during the fourth quarter of the year ended December 31, 2008.



**Table of Contents****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 traded on the NASDAQ Global Market under the symbol DRRX since our initial public offering on September 28, 2000. The following table sets forth, for the periods indicated, the high and low sales prices for our common stock as reported by the NASDAQ Global Market.

	Common Stock Price	
	Low	High
<b>Year ended December 31, 2007</b>		
First Quarter	\$ 3.89	\$ 4.59
Second Quarter	3.78	4.87
Third Quarter	3.68	5.66
Fourth Quarter	5.00	6.90
<b>Year ended December 31, 2008</b>		
First Quarter	\$ 4.07	\$ 6.43
Second Quarter	3.67	5.41
Third Quarter	3.66	5.96
Fourth Quarter	2.87	5.38

The closing sale price of our common stock as reported on the NASDAQ Global Market on February 27, 2009 was \$1.99 per share. As of that date there were approximately 142 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.

**Table of Contents****STOCK PERFORMANCE GRAPH**

The following graph compares the cumulative total stockholder return data for our stock with the cumulative return of (i) The NASDAQ Stock Market (U.S.) Index and (ii) the NASDAQ Biotechnology Index since December 31, 2003. The graph assumes that \$100 was invested on December 31, 2003. The stock price performance on the following graph is not necessarily indicative of future stock price performance.

\* \$100 Invested on 12/31/03 in stock or index including reinvestment of dividends. Fiscal year ending December 31.

**DURECT CORPORATION**

	Cumulative Total Return					
	12/31/03	12/31/04	12/31/05	12/31/06	12/31/07	12/31/08
DURECT CORPORATION	100.00	131.20	202.80	177.60	257.20	135.60
NASDAQ STOCK MARKET (U.S.)	100.00	108.59	110.08	120.56	132.39	78.72
NASDAQ BIOTECHNOLOGY	100.00	106.13	109.14	110.25	115.30	100.75

**Purchases of Equity Securities by the Issuer and Affiliated Purchasers**

None.

**Table of Contents****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 financial statements and related notes, which are included in this Form 10-K. The statement of operations data for the years ended December 31, 2008, 2007 and 2006 and the balance sheet data at December 31, 2008 and 2007 are derived from, and are qualified by reference to, the audited financial statements included elsewhere in this Form 10-K. The statement of operations data for the years ended December 31, 2005 and 2004, and the balance sheet data at December 31, 2006, 2005 and 2004 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 financial statements for an explanation of the determination of the shares used in computing net loss per share.

	2008	Year Ended December 31,			2004
		2007	2006	2005	
		(in thousands, except per share data)			
<b>Statement of Operations Data:</b>					
Collaborative research and development and other revenue	\$ 18,336	\$ 22,417	\$ 13,786	\$ 20,032	\$ 7,437
Product revenue, net	8,765	8,258	8,108	6,939	6,416
Revenue from sale of intellectual property rights				1,600	
<b>Total revenue</b>	<b>27,101</b>	<b>30,675</b>	<b>21,894</b>	<b>28,571</b>	<b>13,853</b>
Operating expenses:					
Cost of revenue	3,365	3,225	3,248	2,815	2,730
Research and development	39,411	38,342	37,241	29,141	24,390
Selling, general and administrative	15,462	13,618	12,417	11,034	9,793
Write down of deferred royalties and commercial rights	13,480				
Amortization of intangible assets	48	31	424	1,209	1,249
<b>Total operating expenses</b>	<b>71,766</b>	<b>55,216</b>	<b>53,330</b>	<b>44,199</b>	<b>38,162</b>
Loss from operations	(44,665)	(24,541)	(31,436)	(15,628)	(24,309)
Other income (expense):					
Interest income and other	1,547	3,545	3,832	2,270	1,236
Interest expense	(789)	(2,625)	(3,436)	(4,363)	(4,546)
Debt conversion expense		(718)	(2,287)	(403)	
Net other income (expense)	758	202	(1,891)	(2,496)	(3,310)
Loss before income taxes	(43,907)	(24,339)	(33,327)	(18,124)	(27,619)
Income tax provision				4	18
<b>Net loss</b>	<b>\$ (43,907)</b>	<b>\$ (24,339)</b>	<b>\$ (33,327)</b>	<b>\$ (18,128)</b>	<b>\$ (27,637)</b>
Basic and diluted net loss per share	\$ (0.56)	\$ (0.35)	\$ (0.51)	\$ (0.34)	\$ (0.54)
Shares used in computing basic and diluted net loss per share	78,332	70,483	65,961	53,719	51,507
	<b>2008</b>	<b>2007</b>	<b>As of December 31,</b>		<b>2004</b>
			<b>2006</b>		
			<b>(in thousands)</b>		
<b>Balance Sheet Data:</b>					
Cash, cash equivalents and investments	\$ 52,692	\$ 62,016	\$ 81,607	\$ 90,997	\$ 61,813
Working capital	43,401	25,700	63,100	84,202	42,082
Total assets	74,874	84,020	102,485	117,414	85,468
Convertible subordinated notes		23,559	37,337	57,337	60,000
Other long-term liabilities	656	1,083	910	832	1,589
Stockholders' equity	37,564	34,581	37,032	43,352	18,390



---

## **Table of Contents**

### **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, 2008, 2007 and 2006 should be read in conjunction with our 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.*

*Forward-looking statements made in this report include, for example, statements about:*

the progress of our third-party collaborations, including estimated milestones;

the progress and results of our research and development programs;

the results and timing of clinical trials and the commencement of future clinical trials;

submission and timing of applications for regulatory approval;

the impact of FDA and other government regulation on our business;

uncertainties associated with obtaining and protecting patents and other intellectual property rights;

products and companies that will compete with the products we license to third-party collaborators;

our intention to commercialize our own products and to build up our commercial, sales and marketing capabilities and other required infrastructure in focused specialty areas; and

future performance, sufficiency of our cash resources, anticipated capital requirements and our need for additional financing.

*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 seek to 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.



## Edgar Filing: DURECT CORP - Form 10-K

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 six disclosed on-going product candidates in development. The following are our publicly announced product candidates in development:

**Table of Contents***POSIDUR (SABER -Bupivacaine)*

Our post-operative pain relief depot, POSIDUR, is a sustained release injectable using our SABER delivery system to deliver bupivacaine, an off-patent anesthetic agent. 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. POSIDUR is designed to be administered to a surgical site at the time of surgery for post-operative pain relief and is intended to provide local analgesia for up to 3 days, which we believe coincides with the time period of the greatest need for post surgical pain control in most patients.

In November 2006, we entered into a collaboration agreement with Nycomed Danmark, APS. Under the terms of the agreement, we licensed to Nycomed the exclusive commercialization rights to POSIDUR for the European Union (E.U.) and certain other countries. Nycomed paid us an upfront license fee of \$14.0 million in 2006 and an \$8.0 million milestone payment in 2007, with future potential additional milestone payments of up to \$180.0 million upon achievement of defined development, regulatory and sales milestones. We jointly direct and equally fund with Nycomed a development program for POSIDUR intended to secure regulatory approval in both the U.S. and the E.U. In addition, we will manufacture and supply the product to Nycomed for commercial sale in the territory licensed to Nycomed. Nycomed will pay us blended royalties on sales in the defined territory of 15-40% depending on annual sales, as well as a manufacturing markup. We retain full commercial rights to POSIDUR in the U.S., Canada, Asia and certain other countries.

In 2007, we successfully completed a 122 patient Phase IIb clinical trial of POSIDUR for treatment of post-operative pain in patients undergoing inguinal hernia repair. In the Phase IIb trial, POSIDUR at a dose of 5 mL demonstrated statistically significant reductions in pain and in total consumption of supplemental opioid analgesic medications versus placebo. These successful results triggered the \$8.0 million milestone payment by Nycomed to us under our agreement with Nycomed.

We continue to be in dialogue with the FDA regarding the Phase III program for POSIDUR and believe we are making progress in defining that program. In parallel with these discussions, we and Nycomed continue to advance development of this drug candidate. Our proposed studies for regulatory approval will include an orthopedic surgical model. Toward that end, we are conducting a 60-patient Phase IIb study in Australia using a 5 mL dose in shoulder surgery in order to confirm aspects of our clinical study design. Additionally, Nycomed is commencing Phase IIb studies in surgical procedures in Europe. These studies will contribute to the total number of patient exposures that will ultimately be required by the FDA and the European Medicines Agency (EMA) as part of the product approval process in the U.S. and Europe.

*Remoxy and other ORADUR-based opioid products licensed to Pain Therapeutics*

In December 2002, we entered into an agreement with 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. In November 2005, Pain Therapeutics and King entered into collaboration and license agreements for the development and commercialization of Remoxy by King.

In December 2007, Pain Therapeutics and King reported positive results from the pivotal Phase III trial submitted under an approved Special Protocol Assessment (SPA) with the FDA. The NDA was submitted to the FDA in June 2008, and in August 2008 the NDA was accepted by the FDA and granted priority review. In

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

---

## Table of Contents

December 2008, Pain Therapeutics received a Complete Response Letter for its NDA for Remoxy in which the FDA determined that the NDA was not approved. According to Pain Therapeutics, the FDA indicated that additional non-clinical data will be required to support the approval of Remoxy, but the FDA has not requested or recommended additional clinical efficacy studies prior to approval. Pain Therapeutics has indicated that they plan to meet with the FDA in the second quarter of 2009 regarding the NDA for Remoxy, and they believe this FDA meeting will provide them with a more reliable context in which to make projections about Remoxy.

During 2008, we began to manufacture commercial lots of certain key components that are included in Remoxy to meet the anticipated requirements for these components. In addition, during the second, third and fourth quarters of 2008 we made our first shipments of these materials to meet the production requirements of King, which has rights to commercialize Remoxy upon approval by the FDA. Revenue attributable to these arrangements aggregating \$1.3 million and cost of goods sold aggregating \$562,000 in the year ended December 31, 2008 has been deferred pending the execution of a final supply agreement with King Pharmaceuticals.

We have also worked with King and Pain Therapeutics on the development of ORADUR-based abuse-resistant opioid drug candidates in addition to Remoxy. Phase I clinical trials have been completed for two of these ORADUR-based drug candidates. According to Pain Therapeutics, the data from these Phase I trials indicate that these drug candidates are safe and well-tolerated with a release profile that appears well suited to use with a chronic pain population. The active ingredients in these two drug candidates are opioids whose identities have not been publicly disclosed.

### *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 two to three days of relief provided with currently available opiate patches. We anticipate that the small size of our sufentanil patch (potentially as small as 1/5<sup>th</sup> the size of currently marketed transdermal fentanyl patches for a therapeutically equivalent dose) may offer improved convenience and compliance for patients. In 2005, we successfully completed a Phase II clinical trial of TRANSDUR-Sufentanil in chronic pain.

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 \$10.0 million in connection with the execution of the Agreement. In February 2009, Endo notified us that it was terminating the license agreement, and thereby returning to us Endo's right to develop and commercialize TRANSDUR-Sufentanil in the U.S. and Canada effective August 26, 2009. Endo has committed to assist in an orderly and rapid transition of this program back to DURECT. Effective August 26, 2009, we will hold worldwide commercialization rights for TRANSDUR-Sufentanil. Endo recently successfully completed a Phase II program for TRANSDUR-Sufentanil in which they evaluated the conversion of patients on oral and transdermal opioids to TRANSDUR-Sufentanil. The most recent Phase II study met its primary and secondary objectives of establishing a successful dose-titration regimen and dose potency relationships, demonstrating safety and tolerability at the therapeutic dose, and achieving effective analgesic pain control. The Phase II data, extensive non-clinical data that had been generated by Endo and detailed proposed protocols for Phase III were reviewed with the FDA at an end-of-Phase II meeting on February 19, 2009. As a result of that meeting, we understand the anticipated regulatory pathway for the Phase III program and approval, which will follow a 505(b)2 pathway as discussed with FDA. This pathway would allow us to reference third-party data, potentially reducing time and expense.

### *ELADUR (TRANSDUR -Bupivacaine)*

Our transdermal bupivacaine patch (ELADUR) uses our proprietary TRANSDUR transdermal technology and is intended to provide continuous delivery of bupivacaine for up to three days from a single application, as compared to a wearing time limited to 12 hours with currently available lidocaine patches.

---

## **Table of Contents**

In 2007, we successfully completed a 60 patient Phase IIa clinical trial for ELADUR. In this study of patients suffering from post-herpetic neuralgia, ELADUR showed improved pain control versus placebo during the 3-day continuous treatment period. In addition, ELADUR appeared well tolerated overall, and patients treated with ELADUR and placebo exhibited similar safety profiles. During 2008, we continued to develop our clinical and regulatory strategy, and to conduct manufacturing scale-up and processing activities to secure additional Phase II and Phase III supplies. In June 2008, the FDA granted to us orphan drug designation for bupivacaine for relief of persistent pain associated with post-herpetic neuralgia (PHN). If ELADUR is the first bupivacaine product approved for PHN, under the 1983 Orphan Drug Act, ELADUR will receive seven years of market exclusivity following the approval of the product by the FDA. There can be no assurance that ELADUR will be the first bupivacaine product approved for PHN, and therefore ELADUR may not be entitled to the seven year exclusivity for orphan drugs.

In September 2008, we entered into a development and license agreement with Alharma granting Alharma the exclusive worldwide rights to develop and commercialize ELADUR. The agreement became effective in October 2008 after clearance under the Hart-Scott-Rodino (HSR) Antitrust Improvements Act of 1976. Under the terms of the agreement, upon closing of the transaction, Alharma paid us an upfront license fee of \$20 million in October 2008. Alharma was acquired by King in December 2008 and, as a result, the rights and obligations of the agreement are now controlled by King.

### *Other Programs*

#### *Biologics Programs*

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, and advanced drug delivery systems such as we possess are required to realize the full potential of many of these protein and peptide drugs. We have active programs underway to apply our drug delivery systems to various biotechnology drugs and drug candidates, and have entered into a number of feasibility studies with biotechnology and pharmaceutical companies to test their products in our systems.

#### *Memryte*

In July 2002, we entered into a development and commercialization agreement with Voyager under which we granted Voyager the exclusive, worldwide rights to develop and commercialize a product, Memryte, using the DURIN implant system to deliver the peptide leuprolide acetate to treat Alzheimer's disease based on Voyager's patented method of treatment. Effective January 2007, we amended our agreement with Voyager. Under the amendment, among other changes to the agreement, the royalty rate that we will receive on net sales of Memryte, if commercialized, was doubled (to 10-14% of net sales after the amendment), and in addition, we will receive 10% of any upfront, milestone and other fees received by Voyager in the event that the product is sublicensed to a third party. In return, we paid Voyager \$1.0 million in cash and forgave approximately \$725,000 which was owed to us for previously provided services.

In October 2005, Voyager initiated a Phase III clinical trial for Memryte, but the Phase III trial was truncated by Voyager in order to get an early look at potential efficacy. In the second quarter of 2007, Voyager informed its shareholders that it had observed positive outcome trends among women, but no positive effect among men in this truncated Phase III clinical trial. Based on these results, Voyager has stated that it intends to focus its efforts on developing Memryte for the treatment of Alzheimer's disease in women and on seeking a potential collaborative partner for the program. There can be no assurance that Voyager or any other party will continue development of Memryte.

---

**Table of Contents**

*Research Programs in Other Therapeutic Categories*

We have underway a number of research programs covering medical diseases and conditions other than pain. Such programs include various diseases and disorders of the central nervous system (CNS), including schizophrenia and attention deficit/hyperactivity disorder. Another area of focus includes cardiovascular disease, including congestive heart failure. In conducting our research programs and determining which particular efforts to prioritize for formal development, we employ a rigorous opportunity assessment process that takes into account the unmet medical need, commercial opportunity, technical feasibility, clinical viability, intellectual property considerations, and the development path including costs to achieve various critical milestones.

*Collaborative Research and Development Revenues*

Collaborative research and development revenues consist of three broad categories: (a) the amortization of upfront license payments on a straight-line basis over the period of our continuing involvement with the third party, (b) the reimbursement of qualified research expenses by third parties, and (c) milestone payments in connection with our collaborative agreements. During the last several years, we generated collaborative research and development revenues from collaborative agreements related to TRANSDUR-Sufentanil (collaboration with Endo), Remoxy and other specified ORADUR-based oral opioids (collaboration with Pain Therapeutics), POSIDUR (collaboration with Nycomed), ELADUR (collaboration with Alpharma) and several feasibility agreements. In contrast to our other collaborations, due to the terms and nature of the Nycomed collaboration, we do not recognize revenue from the reimbursement of qualified research expenses by Nycomed. Rather, we record research and development expense equal to our net share of the joint research and development expenses undertaken under the product development plan.

*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. 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 partners to develop product candidates based on our drug delivery technologies.

Since our inception in 1998, we have had a history of operating losses. At December 31, 2008, we had an accumulated deficit of \$283.6 million and our net losses were \$43.9 million, \$24.3 million and \$33.3 million for the years ended December 31, 2008, 2007 and 2006, respectively. These losses have resulted primarily from costs incurred to research and develop our product candidates 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 nonclinical studies, clinical trials and other research and development activities as well as to incur additional stock-based compensation costs related to research and development personnel under SFAS 123(R). We expect selling, general and administrative expenses to increase in the near future due to expected increases in employee related costs to support our business activities and in stock-based compensation cost related to selling, general and administrative personnel under SFAS 123(R). We also expect to incur non-cash expenses relating to amortization of intangible assets. We do not anticipate meaningful revenues from our pharmaceutical systems, should they be approved, for at least the next twelve months. Therefore, we expect to incur continuing losses and negative cash flow from operations for the foreseeable future.

---

## **Table of Contents**

### **Critical Accounting Policies and Estimates**

#### *General*

The preparation of financial statements in conformity with 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, 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 when there is persuasive evidence that an arrangement exists, the product is shipped and title transfers to customers, provided no continuing obligation exists, the price is fixed or determinable and the collectibility of the amounts owed is reasonably assured. We recognize revenue from the sale of our products and license and collaboration agreements pursuant to Staff Accounting Bulletin No. 104, *Revenue Recognition*, and Emerging Issues Task Force (EITF) Issue 00-21 *Revenue Arrangements with Multiple Deliverables*. Multiple element agreements entered into are evaluated under the provision of EITF 00-21. We evaluate whether there is stand-alone value for the delivered elements and objective and reliable evidence of fair value to allocate revenue to each element in multiple element agreements. When the delivered element does not have stand-alone value or there is insufficient evidence of fair value for the undelivered element(s), we recognize the consideration for the combined unit of accounting in the same manner as the revenue is recognized for the final deliverable, which is generally ratably over the longest period of involvement. Returns or credits related to the sale of products have not had a material impact on our revenues or net loss.

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 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 and the collectibility of the amounts owed is reasonably assured. 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. Of note, in regard to our collaboration with Nycomed, in contrast to our other collaborations, because we and Nycomed jointly control and fund the development of POSIDUR, we will not recognize revenue from the reimbursement of qualified research expenses from Nycomed but instead those reimbursements receivable from Nycomed will be recorded as a reduction in research and development expense.

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

---

## **Table of Contents**

### *Research and Development Expenses*

Research and development expenses are primarily comprised of salaries, benefits, stock based compensation and other compensation cost 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 expense as the related services are performed, generally ratably over the period of service. In addition, reimbursements by Nycomed for research and development expenses incurred by us are recorded as a reduction to research and development expenses. Research and development expenses incurred by Nycomed and reimbursable by us are recorded as an addition to our research and development expenses.

### *Intangible Assets and Goodwill*

We record intangible assets when we acquire other companies and intellectual property rights. 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 technologies 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.

---

## **Table of Contents**

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, 2008. 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 pre-clinical studies, clinical trials, contract manufacturing, validation, testing, and other research and development-related services. We are required to estimate periodically the cost of services rendered but unbilled based on management's estimates of project status. If these good faith estimates are inaccurate, actual expenses incurred could materially differ from our estimates.

### *Stock-Based Compensation*

Under the provisions of FAS 123(R), *Share Based Payment* (FAS 123R), employee stock-based compensation is estimated at the date of grant based on the employee stock award's fair value using the Black-Scholes option-pricing model and is recognized as expense ratably over the requisite period in a manner similar to other forms of compensation paid to employees.

We estimate the volatility of our common stock at the date of grant based on the historical volatility of our common stock, consistent with SFAS 123(R) and SAB 107. We base the risk-free rate that we use in the Black-Scholes option valuation model on the implied yield in effect at the time of option grant on U.S. Treasury zero-coupon issues with equivalent remaining terms. We have never paid any cash dividends on our common stock and we do not anticipate paying any cash dividends in the foreseeable future. Consequently, we use an expected dividend yield of zero in the Black-Scholes option valuation model. SFAS 123(R) requires us to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from those estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. For options granted before January 1, 2006, we amortize the fair value on an accelerated basis. For options granted on or after January 1, 2006, we amortize the fair value on a straight-line basis. All options are amortized over the requisite service periods of the awards, which are generally the vesting periods. We may elect to use different assumptions under the Black-Scholes option valuation model in the future, which could materially affect our net income or loss and net income or loss per share.

### *Recent Accounting Pronouncements*

In February 2008, the FASB issued FASB Staff Position No. FSP 157-2, *Effective Date of FASB Statement No. 157*, which provides a one year deferral of the effective date of SFAS 157 for non-financial assets and non-financial liabilities, except for those items that are recognized or disclosed in the financial statements at fair value at least annually. Therefore, we have adopted the provisions of SFAS 157 with respect to our financial assets and liabilities only. The FSP deferred the effective date of FAS 157 for non-financial assets and non-financial liabilities until our fiscal year beginning on January 1, 2009. We do not expect the adoption of FAS 157 for non-financial assets and non-financial liabilities to have a material effect on our financial statements.

In December 2007, the Emerging Issues Task Force of the FASB issued a consensus on Issue No. 07-1 ( EITF 07-1 ), *Accounting for Collaborative Arrangements*. The scope of EITF 07-1 is limited to collaborative arrangements where no separate legal entity exists and in which the parties are active participants and are exposed to significant risks and rewards that depend on the success of the activity. The Task Force concluded that revenue transactions with third parties and associated costs incurred should be reported in the appropriate line item in each company's financial statements pursuant to the guidance in EITF 99-19, *Reporting Revenue Gross as a Principal versus Net as an Agent*. The Task Force also concluded that the equity method of



**Table of Contents**

accounting under Accounting Principles Board Opinion 18, *The Equity Method of Accounting for Investments in Common Stock*, should not be applied to arrangements that are not conducted through a separate legal entity. The Task Force also concluded that the income statement classification of payments made between the parties in an arrangement should be based on a consideration of the following factors: the nature and terms of the arrangement; the nature of the entities' operations; and whether the partners' payments are within the scope of existing GAAP. To the extent such costs are not within the scope of other authoritative accounting literature, the income statement characterization for the payments should be based on an analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. The provisions of EITF 07-1 are effective for fiscal years beginning on or after December 15, 2008, and companies will be required to apply the provisions through retrospective application to all collaborative arrangements existing at adoption as a change in accounting principle. We do not believe that the adoption of EITF 07-1 will have a material impact on our financial statements.

In December 2007, the FASB issued SFAS No. 141R, *Business Combinations* ( SFAS No. 141R ). SFAS No. 141R amends SFAS 141 and provides revised guidance for recognizing and measuring identifiable assets and goodwill acquired, liabilities assumed, and any noncontrolling interest in the acquiree. It also provides disclosure requirements to enable users of the financial statements to evaluate the nature and financial effects of the business combination. It is effective for fiscal years beginning on or after December 15, 2008 and will be applied prospectively. The effect of the adoption of FAS 141R will depend upon the nature of any future business combinations we undertake.

In May 2008, the FASB issued Staff Position No APB 14-1, *Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement)* ( FSP APB 14-1 ). FSP APB 14-1 requires the issuer of certain convertible debt instruments that may be settled in cash or other assets on conversion, either in part or in full, to separately account for the liability (debt) and equity (conversion option) components of the instrument in a manner that results in the recognition of interest expense equal to the issuer's nonconvertible debt borrowing rate. This FSP is effective for financial statements issued for fiscal years beginning after December 15, 2008 and interim periods within those fiscal years. This FSP must be applied retrospectively to all periods presented. We do not believe that the adoption of FSP APB 14-1 will have a material impact on our financial statements.

**Results of Operations***Comparison of years ended December 31, 2008, 2007 and 2006*

**Revenues.** Net revenues were \$27.1 million in 2008 compared to \$30.7 million in 2007. We recognized \$850,000 of milestone revenue in 2008 from our Pain Therapeutics collaboration as compared to \$8.0 million recognized in 2007 from our Nycomed collaboration related to POSIDUR. Excluding the milestone revenue, total revenue in 2008 increased compared to 2007 primarily due to higher collaborative research and development revenue recognized from our agreements with Alphasigma and Pain Therapeutics as well as higher product revenue from our ALZET and LACTEL product lines, partially offset by lower collaborative research and development revenue from Endo and from feasibility agreements with various third parties.

Net revenues were \$30.7 million in 2007 compared to \$21.9 million in 2006. The increase in total revenues in 2007 is primarily attributable to milestone revenue of \$8.0 million recognized in 2007 from our Nycomed collaboration related to POSIDUR as well as increased collaborative research and development revenue from Endo, from feasibility agreements with third parties and from the amortization of the Nycomed upfront fee, partially offset by decreased collaborative research and development revenue from Pain Therapeutics and Voyager.

---

**Table of Contents**

*Collaborative research and development and other revenue*

We recognize revenues from collaborative research and development activities and service contracts. Collaborative research and development revenue primarily 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, amortization of upfront fees and milestone payments associated with the license agreements.

We recorded \$18.3 million of collaborative research and development and other revenue in 2008 compared to \$22.4 million in 2007. The decrease in collaborative research and development and other revenue in 2008 was primarily attributable to our recognition in 2007 of \$8.0 million of milestone revenue from our Nycomed collaboration related to POSIDUR. Excluding the impact of milestone revenue, collaborative research and development revenue increased in 2008 due to higher revenue recognized in connection with our agreement for ELADUR (collaboration with Alharma), Remoxy and other ORADUR-based opioid drug candidates (collaboration with Pain Therapeutics), partially offset by lower collaborative research and development revenue recognized in connection with our agreement for TRANSDUR-Sufentanil (collaboration with Endo) and from feasibility agreements compared with 2007.

We recorded \$22.4 million of collaborative research and development and other revenue in 2007 compared to \$13.8 million in 2006. The increase in collaborative research and development and other revenue in 2007 was primarily attributable to \$8.0 million of milestone revenue recognized in 2007 from our Nycomed collaboration related to POSIDUR, higher revenue recognized from amortization of the upfront fee received from Nycomed and, and higher collaborative research and development revenue recognized in connection with increased development activities associated with TRANSDUR-Sufentanil and feasibility agreements, partially offset by decreased development activities for Remoxy and other opioids and Memryte (collaboration with Voyager) compared with 2006. We ceased to recognize collaborative research and development revenue related to Memryte after August 2006 because the collectibility of the amounts owed was not reasonably assured.

We received a \$10.0 million upfront fee in connection with the license agreement signed with Endo in March 2005 relating to TRANSDUR-Sufentanil. The \$10.0 million upfront fee is recognized as collaborative research and development revenue ratably over the term of our continuing involvement with Endo with respect to TRANSDUR-Sufentanil. We recognized \$3.0 million in 2008, \$2.2 million in 2007 and \$2.2 million in 2006 from amortization of the upfront fee. The term of the continuing involvement has been estimated based on the product development plan pursuant to the agreement. Our estimate of the remaining term of our continuing involvement was adjusted in the fourth quarter of 2008 as a result of Endo's termination notice received by us in February 2009.

We also received a \$14.0 million upfront fee in connection with the development and license agreement signed with Nycomed in November 2006 relating to POSIDUR. The \$14.0 million upfront fee is recognized as collaborative research and development revenue ratably over the term of our continuing involvement with Nycomed with respect to POSIDUR. The amount recognized in 2008, 2007 and 2006 as collaborative research and development revenue from the amortization of the upfront fee was \$3.1 million, \$3.1 million and \$271,000, respectively. The term of the continuing involvement has been estimated based on the product development plan pursuant to that agreement.

We also received a \$20.0 million upfront fee in connection with the development and license agreement signed with Alharma in September 2008 relating to ELADUR. The \$20.0 million upfront fee is recognized as collaborative research and development revenue ratably over the term of our continuing involvement with Alharma with respect to ELADUR. The amount recognized in 2008, 2007 and 2006 as collaborative research and development revenue from the amortization of the upfront fee was \$752,000, zero and zero, respectively. The term of the continuing involvement has been estimated based on the product development plan pursuant to that agreement.

**Table of Contents**

We expect our collaborative research and development revenue to fluctuate in future periods pending our efforts to enter into potential new collaborations and our existing third party collaborators' commitment to and progress in the research and development programs. The collaborative research and development and other revenues associated with our major collaborators are as follows (in thousands):

Collaborator	Year ended December 31,		
	2008	2007	2006
Pain Therapeutics, Inc. (Pain Therapeutics)(1)	\$ 6,410	\$ 4,864	\$ 7,477
Endo Pharmaceuticals, Inc. (Endo)(2)	3,934	4,818	4,438
Alpharma Ireland Limited (Alpharma)(3)	3,412		
Nycomed Danmark, APS (Nycomed)(4)	3,051	11,051	271
Voyager Pharmaceutical Corporation (Voyager)			777
Others	1,529	1,684	823
Total collaborative research and development and other revenue	\$ 18,336	\$ 22,417	\$ 13,786

- (1) Amounts related to milestone revenue recognized in connection with the Pain Therapeutics collaboration were \$850,000 in 2008 and zero in 2007 and 2006.
- (2) Amounts related to the amortization of upfront fees were \$3.0 million in 2008 and \$2.2 million in both 2007 and 2006. Our agreement with Endo will terminate effective August 26, 2009.
- (3) Amounts related to the amortization of upfront fees were \$752,000 in 2008 and zero in both 2007 and 2006. Alpharma is now owned by King.
- (4) Amounts related to the amortization of upfront fees were \$3.1 million in 2008 and 2007, and \$271,000 in 2006. Research and development expenses incurred by us in conjunction with the Nycomed collaboration and reimbursable by Nycomed are recorded as a reduction to total research and development expense. The 2007 figure also includes \$8.0 million of milestone revenue recognized in connection with the Nycomed agreement.

We amortize upfront 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.

Milestone payments under collaborative arrangements are recognized as revenue upon achievement of the milestone events, which represent the culmination of the earnings process related to that milestone. Milestone payments are triggered 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. We recorded \$850,000 of milestone revenue from our Pain Therapeutics collaboration related to the achievement of clinical and regulatory milestones in 2008, \$8.0 million of milestone revenue from our Nycomed collaboration due to the achievement of a clinical development milestone for POSIDUR in 2007 and \$100,000 of milestone revenue from our collaboration with Pain Therapeutics in 2006.

We recognized \$87,000 in revenue from service contracts in 2008 compared to zero in both 2007 and 2006. Service contract revenues recognized in 2008 were related to certain polymer-related service activities performed for customers. We currently do not expect to increase our effort to generate significant revenue from such polymer-related service contracts in the future.



---

**Table of Contents**

*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 LACTEL biodegradable polymer products. Net product revenues were \$8.8 million in 2008 compared with \$8.3 million in 2007. The increase was primarily due to higher average selling prices for our ALZET mini pump and LACTEL polymers in 2008 compared with 2007. Product revenues attributable to the shipments of key components of REMOXY in 2008 aggregating \$1.3 million in 2008 have been deferred pending the execution of a final supply agreement with King Pharmaceuticals.

Net product revenues were \$8.3 million in 2007 compared with \$8.1 million in 2006. The increase was primarily due to higher LACTEL polymer sales in 2007 compared with 2006. Alzet mini pump product sales remained comparable in both years.

*Cost of revenues.* Cost of revenues was \$3.4 million in 2008, compared to \$3.2 million in 2007. Cost of revenues includes cost of product revenue from our ALZET mini pump product line and our LACTEL polymer products. The increase in the cost of product revenue in 2008 was primarily the result of higher product revenue by our ALZET and LACTEL product lines in 2008. Cost of goods sold aggregating \$562,000 in 2008 has been deferred pending the execution of a final supply agreement with King Pharmaceuticals. Cost of service revenue was \$29,000 in 2008 compared to zero in 2007 due to an increase in our service contract revenue related to our polymer business in 2008. Stock based compensation expense related to cost of revenue was \$135,000 recognized under SFAS 123(R) in 2008 compared with \$130,000 in 2007.

Cost of revenues was \$3.2 million in 2007, essentially unchanged from \$3.2 million in 2006. Stock based compensation expense related to cost of revenue was \$130,000 recognized under SFAS 123(R) in 2007 compared with \$75,000 in 2006.

As of December 31, 2008, 2007 and 2006, we had 31, 23 and 22 manufacturing employees, respectively.

*Research and Development.* Research and development expenses are primarily comprised of salaries, benefits, stock based compensation and other compensation cost 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. In addition, research and development expenses incurred by us and reimbursed by Nycomed are recorded as a reduction to research and development expenses. Research and development expenses incurred by Nycomed and reimbursed by us are recorded as additional research and development expenses.

Research and development expenses were \$39.4 million in 2008 and \$38.3 million in 2007. The increase in 2008 was primarily attributable to higher development costs associated with ELADUR, Remoxy and other ORADUR-based opioid drug candidates, and our biologics programs, partially offset by decreased clinical trial expenses for POSIDUR, decreased development costs associated with CHRONOGESIC, TRANSDUR-Sufentanil and other research programs as more fully discussed below. In addition, we paid \$2.25 million to EpiCept in the third quarter of 2008 under the amended agreement with EpiCept and recorded this amount as a research and development expense for the year ended December 31, 2008. Stock-based compensation expense related to research and development personnel increased to \$5.6 million in 2008 from \$4.3 million in 2007.

Research and development expenses were \$38.3 million in 2007 and \$37.2 million in 2006. The increase in 2007 was primarily attributable to higher development expenses for TRANSDUR-Sufentanil, our biologics programs and other research programs, partially offset by lower development expenses for Remoxy and other ORADUR-based opioid product candidates, POSIDUR (due largely to the sharing of various research and development costs with Nycomed after signing our license agreement on November 29, 2006), ELADUR and CHRONOGESIC. In 2007, we recorded a net reduction of \$5.0 million in research and development expenses related to POSIDUR compared with \$426,000 in 2006. The net reduction in research and development expenses represents a net reimbursement from Nycomed reflecting that both parties bore 50% of the development expenses defined under the collaboration

**Table of Contents**

agreement for POSIDUR. The 2007 research and development figures include our recording \$1.0 million in research and development expense associated with our payment of \$1.0 million to Voyager in connection with our amended agreement with Voyager related to Memryte in the first quarter of 2007. The 2006 research and development figures include our recording \$1.0 million as research and development expense associated with our payment of an upfront fee upon execution of a license agreement with EpiCept. Stock-based compensation expense related to research and development personnel increased from \$2.9 million in 2006 to \$4.3 million in 2007.

*ELADUR*

Our research and development expenses for ELADUR increased to \$11.9 million in 2008 from \$5.1 million in 2007. The increases were primarily due to higher employee costs and contract manufacturing expenses related to manufacturing scale-up and processing activities to secure additional Phase II and Phase III supplies for this drug candidate in 2008. In addition, we paid \$2.25 million to EpiCept in the third quarter of 2008 related to certain intellectual property relevant to ELADUR under the amended agreement with EpiCept.

Our research and development expenses for ELADUR decreased to \$5.1 million in 2007 from \$6.9 million in 2006 primarily due to lower contract manufacturing expenses, partially offset by higher clinical trials expenses for a Phase II clinical trial in 2007.

*POSIDUR*

Our research and development expenses for POSIDUR decreased to \$8.1 million in 2008 from \$10.9 million in 2007. The decrease was primarily due to lower costs associated with clinical trial expenses and contract manufacturing development activities. Research and development expenses for POSIDUR incurred by us but reimbursable by Nycomed under the terms of our agreement with Nycomed were \$3.6 million in 2008 compared to \$6.2 million in 2007, which are accounted for as a reduction of research and development expenses. Research and development expenses for POSIDUR incurred by Nycomed but reimbursable by us under the terms of our agreement with Nycomed were \$2.2 million in 2008 compared to \$1.2 million in 2007, which are accounted for as additional research and development expenses. As a result of the collaboration agreement with Nycomed, our net research and development expenses for POSIDUR were reduced by \$1.4 million in 2008 compared to \$5.0 million in 2007. The net reduction in research and development expenses represents a net reimbursement from Nycomed reflecting that both parties bore 50% of the development expenses defined under the collaboration agreement for POSIDUR.

Our research and development expenses for POSIDUR decreased to \$10.9 million in 2007 from \$12.0 million in 2006 due to a higher net reduction in research and development expense related to POSIDUR under our agreement with Nycomed, partially offset by an increase in costs associated with the Phase II clinical program and contract manufacturing development activities. Research and development expenses for POSIDUR incurred by us but reimbursable by Nycomed under the terms of our agreement with Nycomed were \$6.2 million in 2007 compared with \$426,000 in 2006, which was accounted for as a reduction of research and development expenses. Research and development expenses for POSIDUR incurred by Nycomed but reimbursable by us under the terms of our agreement with Nycomed were \$1.2 million in 2007 compared with zero in 2006, which was accounted for as additional research and development expenses. As a result of the collaboration agreement with Nycomed, our net research and development expenses for POSIDUR were reduced by \$5.0 million in 2007 compared to \$426,000 in 2006. The net reduction in research and development expenses represents a net reimbursement from Nycomed reflecting that both parties bore 50% of the development expenses defined under the collaboration agreement for POSIDUR.

*Remoxy and other ORADUR-based opioid products*

Our research and development expenses for Remoxy and other opioids partnered with Pain Therapeutics increased to \$5.3 million in 2008 from \$4.4 million in 2007. The increase was primarily due to increased NDA support activities for Remoxy as well as additional formulation and clinical manufacturing activities for other ORADUR-based opioid drug candidates in 2008.

## **Table of Contents**

Our research and development expenses for Remoxy and other opioids partnered with Pain Therapeutics decreased to \$4.4 million in 2007 from \$6.0 million in 2006 due to reduced formulation and clinical manufacturing activities for Remoxy and other ORADUR-based opioid drug candidates performed by us in 2007 compared with 2006.

### *Biologics Programs*

Our research and development expenses for biologics programs increased to \$4.6 million in 2008 from \$3.2 million in 2007. The increase was primarily due to higher external costs and employee related costs in support of these programs in 2008.

Our research and development expenses for biologics programs increased to \$3.2 million in 2007 from \$2.8 million in 2006 due to higher external costs and employee related costs in support of these programs in 2007.

### *TRANSDUR-Sufentanil*

Our research and development expenses for TRANSDUR-Sufentanil decreased to \$1.4 million in 2008 from \$2.8 million in 2007. The decrease was primarily due to lower development support activities performed in support of this drug candidate in 2008.

Our research and development expenses for TRANSDUR-Sufentanil increased to \$2.8 million in 2007 from \$2.2 million in 2006 due to slightly higher clinical manufacturing related activities performed in support of this drug candidate in 2007.

### *CHRONOGESIC® (sufentanil) Pain Therapy System*

Our research and development expenses for CHRONOGESIC decreased to \$89,000 in 2008 from \$1.7 million in 2007. The decrease was primarily due to lower employee related costs and external development expenses in 2008.

Our research and development expenses for CHRONOGESIC decreased to \$1.7 million in 2007 from \$2.1 million in 2006. The decrease was primarily due to lower external development expenses in 2007.

### *Memryte*

Our research and development expenses for Memryte decreased to zero in 2008 from \$1.3 million in 2007. The reported research and development expense in 2007 includes a one-time cash payment of \$1.0 million which we made in January 2007 as part of the amendment of our license agreement with Voyager.

Our research and development expenses for Memryte were \$1.3 million in 2007 and \$1.2 million in 2006. The reported research and development expense in 2007 includes a one-time cash payment of \$1.0 million which we made in January 2007 in accordance with our amended license agreement with Voyager.

### *Other DURECT Research Programs*

Our research and development expenses for all other activities decreased to \$8.1 million from \$8.9 million in 2007. The decrease was primarily due to lower employee related costs, offset by increased formulation and clinical development activities for these programs.

Our research and development expenses for all other activities increased to \$8.9 million in 2007 from \$4.0 million in 2006 primarily due to higher employee related costs and increased formulation development activities for these programs.

**Table of Contents**

As of December 31, 2008, 2007 and 2006, we had 104, 117 and 116 research and development employees respectively. We expect research and development expenses to increase in the near future as we continue product development efforts for our internal and partnered product candidates and incur additional stock-based compensation cost under SFAS 123(R) related to research and development personnel.

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

	Year Ended December 31,		
	2008	2007	2006
ELADUR(1)	\$ 11,852	\$ 5,132	\$ 6,946
POSIDUR(2)	8,081	10,924	12,005
Remoxy and other ORADUR-based opioid products licensed to Pain Therapeutics	5,274	4,372	5,987
Biologics Programs	4,614	3,193	2,782
TRANSDUR-Sufentanil	1,365	2,843	2,189
CHRONOGESIC	89	1,719	2,104
Memryte(3)		1,271	1,213
Others	8,136	8,888	4,015
<b>Total research and development expenses(4)</b>	<b>\$ 39,411</b>	<b>\$ 38,342</b>	<b>\$ 37,241</b>

- (1) The reported research and development expense in 2008 includes a one-time cash payment of \$2.25 million which we made in September 2008 as part of the amendment of the license agreement with EpiCept. The reported research and development expense in 2006 includes a one-time cash payment of \$1.0 million which we made in December 2006 as part of the license agreement with EpiCept.
- (2) Research and development expenses for POSIDUR incurred by us but reimbursable by Nycomed under the terms of our agreement with Nycomed were \$3.6 million, \$6.2 million and \$426,000 in 2008, 2007 and 2006, respectively, which were accounted for as a reduction of research and development expenses. Research and development expenses for POSIDUR incurred by Nycomed but reimbursable by us under the terms of our agreement with Nycomed were \$2.2 million, \$1.2 million and zero in 2008, 2007 and 2006, respectively, which were accounted for as additional research and development expenses. The agreement with Nycomed was signed in November 2006.
- (3) The reported research and development expense in 2007 includes a one-time cash payment of \$1.0 million which we made in January 2007 as part of the amendment of the license agreement with Voyager.
- (4) Includes stock-based compensation expenses of \$5.6 million, \$4.3 million and \$2.9 million in 2008, 2007 and 2006, respectively. We cannot reasonably estimate the timing and 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 to and progress in 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.



---

**Table of Contents**

*Selling, General and Administrative.* Selling, general and administrative expenses are primarily comprised of salaries, benefits and stock-based compensation 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 \$15.5 million in 2008 compared with \$13.6 million in 2007. The increase in selling, general and administrative expenses was primarily attributable to higher employee related costs (which in turn were largely a function of increased stock-based compensation) as well as increased patent related expenses in 2008 compared with 2007. Stock-based compensation expense recognized under SFAS 123(R) related to selling, general and administrative personnel was \$2.8 million in 2008 compared with \$2.3 million in 2007.

Selling, general and administrative expenses were \$13.6 million in 2007 compared with \$12.4 million in 2006. The increase in selling, general and administrative expenses was primarily attributable to higher employee related costs (which in turn were largely a function of increased stock-based compensation) as well as increased patent related expenses in 2007 compared with 2006. Stock based compensation expense recognized under SFAS 123(R) related to selling, general and administrative personnel was \$2.3 million in 2007 compared with \$1.4 million in 2006.

As of December 31, 2008, 2007 and 2006, we had 38, 36 and 34 selling, general and administrative personnel, respectively. We expect selling, general and administrative expenses to increase in the near future due to expected increases in patent related costs, in employee related costs to support our business activities and in stock-based compensation costs related to selling, general and administrative personnel under SFAS 123(R).

*Write down of deferred royalties and commercial rights.* Write down of deferred royalties and commercial rights was \$13.5 million in 2008 compared with zero in 2007. In 2000, we recorded the fair value of common stock and a warrant that we issued to Alza Corporation in connection with an amended agreement related to CHRONOGESIC. The amounts were recorded in stockholders' equity as additional paid-in capital and as a contra-equity account referred to as deferred royalties and commercial rights. At the end of 2008, we made the strategic decision that other research and development programs would take priority over CHRONOGESIC and recorded a \$13.5 million non-cash write down of deferred royalties and commercial rights given the fact that there are no plans in the foreseeable future to actively attempt to develop CHRONOGESIC.

*Amortization of intangible assets.* Amortization of intangible assets was \$48,000 in 2008 compared with \$31,000 in 2007. The amortization of intangible assets increased in 2008 compared with 2007 as we acquired additional patents in the fourth quarter of 2007 and the first quarter of 2008.

Amortization of intangible assets was \$31,000 in 2007 compared with \$424,000 in 2006. The amortization of intangible assets decreased in 2007 as certain intangible assets became fully amortized in 2006.

We continue to amortize the existing intangible assets at a constant rate over their estimated useful lives. In the fourth quarter of 2008, 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 would be required to record an impairment charge to write the goodwill down to its estimated fair value.

In December 2007 and January 2008, in two separate tranches, we acquired from a third party a portfolio of worldwide patents and patent applications relating to drug delivery technologies. We paid \$100,000 and \$25,000, respectively, to this third party upon execution of the agreements. We recorded \$100,000 and \$25,000 as intangible assets on our balance sheet as of December 31, 2007 and December 31, 2008, respectively, and amortize these patents over a useful life of 7 years.

The net amount of intangible assets at December 31, 2008 was \$157,000, which will be amortized as follows: \$48,700 in 2009, \$37,000 in 2010, \$17,600 in each of the years from 2011 to 2014, and \$900 in 2015. Should any intangible assets become impaired, we will write them down to their estimated fair value.

---

**Table of Contents**

*Other Income (Expense).* Interest and other income was \$1.5 million in 2008 compared with \$3.5 million in 2007. The decrease in interest income was primarily the result of lower yields on our investments as well as lower average cash and investment balances in 2008 compared with 2007.

Interest and other income was \$3.5 million in 2007 compared with \$3.8 million in 2006. The decrease in interest income was primarily the result of lower average cash and investment balances in 2007 compared with 2006, partially offset by higher yields on our investments in 2007.

Interest expense was \$789,000 in 2008 compared with \$2.6 million in 2007. The decrease in interest expense in 2008 was primarily due to lower outstanding balances on our convertible notes in 2008 compared with 2007 due to the conversion of the remaining \$23.6 million in aggregate principal amount of convertible notes in June 2008.

Interest expense was \$2.6 million in 2007 compared with \$3.4 million in 2006. The decrease in interest expense in 2006 was primarily due to lower remaining balances on our convertible notes in 2007 compared with 2006 due to the conversion of \$13.7 million in aggregate principal amount of convertible notes in 2007.

Debt conversion expense was zero in 2008 compared with \$718,000 in 2007. The debt conversion expense in 2007 was recorded in connection with the conversion of \$13.7 million in aggregate principal amount of the 6.25% convertible notes into 4.4 million shares of our common stock.

Debt conversion expense was \$718,000 in 2007 compared with \$2.3 million in 2006. The debt conversion expense in 2007 was recorded in connection with the conversion of \$13.7 million in aggregate principal amount of the 6.25% convertible notes into 4.4 million shares of our common stock. The debt conversion expense in 2006 was recorded in connection with the conversion of \$20.0 million in aggregate principal amount of the 6.25% convertible notes into 6.3 million shares of our common stock.

*Income taxes.* Income tax provision was zero in 2008, 2007 and 2006. As of December 31, 2008, we had net operating loss carryforwards for federal income tax purposes of approximately \$187.0 million, which expire in the years 2018 through 2028, and federal research and development tax credits of approximately \$3.6 million, which expire at various dates beginning in 2018 through 2028, if not utilized. As of December 31, 2008, we had net operating loss carryforwards for state income tax purpose of approximately \$93.4 million, which expire in the years 2008 through 2018 and state research and development tax credits of approximately \$4.0 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, 2008 and 2007, we had net deferred tax assets of \$96.4 million and \$86.0 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.

Because realization of such tax benefits is uncertain, we provided a 100% valuation allowance as of December 31, 2008 and December 31, 2007. Utilization of the NOL and R&D credits carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future provided by Sections 382 and 383 of the Internal Revenue Code of 1986, as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and R&D credits carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period. Since our formation, we have raised capital through the issuance of capital stock on several occasions

---

## **Table of Contents**

which, combined with the purchasing shareholders' subsequent disposition of those shares, may have resulted in a change of control, as defined by Section 382, or could result in a change of control in the future upon subsequent disposition. In addition, we issued \$60.0 million of convertible notes in 2003 and subsequently all of these notes had been converted as of December 31, 2008 into our common stock. These transactions may also have resulted in a change of control or could result in a change of control in the future upon the subsequent disposition of the shares.

We have not currently completed a study to assess whether a change in control has occurred or whether there have been multiple changes of control since our formation due to the significant complexity and cost associated with such a study and the fact that there could be additional changes in the future. If we have experienced a change of control at any time since our formation, utilization of our NOL or R&D credits carryforwards would be subject to an annual limitation under Sections 382 and 383 which is determined by first multiplying the value of our stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the NOL or R&D credits carryforwards before utilization. Further, until a study is completed and any limitation known, no amounts are being presented as an uncertain tax position under FIN 48. Interest and penalties related to uncertain tax positions will be reflected in income tax expense. Tax years 1998 to 2008 remain subject to future examination by the major tax jurisdictions in which we are subject to tax.

### **Liquidity and Capital Resources**

We had cash, cash equivalents, and investments totaling \$52.7 million and \$62.0 million at December 31, 2008 and 2007, respectively. This includes \$1.0 million of interest-bearing marketable securities classified as restricted investments on our balance sheet as of December 31, 2008 and 2007, 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 deposit of the leased facilities and the SBS bonds will expire in December 2012 and November 2009, respectively.

The decrease in cash, cash equivalents and investments from 2007 to 2008 was primarily the result of ongoing operating expenses, partially offset by a \$20.0 million milestone payment from Alpharma and other payments received from our customers and third-party collaborators. The decrease in cash, cash equivalents and investments from 2006 to 2007 was primarily attributable to increased operating and capital expenditures, partially offset by an \$8.0 million milestone payment from Nycomed and other payments received from our customers and third-party collaborators.

Working capital was \$43.4 million, \$25.7 million and \$63.1 million at December 31, 2008, 2007 and 2006, respectively. The increase in working capital from 2007 to 2008 was primarily attributable to the exchange of the \$23.6 million in aggregate principal amount of convertible notes at maturity in June 2008 into approximately 7.5 million shares of common stock, partially offset by cash used for operations in 2008. The decrease in working capital from 2006 to 2007 was primarily attributable to the reclassification of convertible notes due June 2008 from a long term liability at December 31, 2006 to a current liability at December 31, 2007 as well as cash used in operating activities in 2007.

We used \$9.4 million, \$18.3 million and \$9.5 million of cash in operating activities in the years ended December 31, 2008, 2007 and 2006, respectively. The decrease in cash used in operating activities in 2008 was primarily due to a \$20.0 million milestone payment received from Alpharma in 2008 and increases in accounts receivable and inventory balances in 2008 compared with 2007. The increase in cash used in operating activities in 2007 was primarily due to higher operating expenses in our development programs and lower payments received from our collaborators compared with 2006, partially offset by an \$8.0 million milestone payment received from Nycomed in 2007.

---

**Table of Contents**

We generated \$289,000 and \$13.1 million of cash from investing activities in the years ended December 31, 2008 and 2007, respectively, and used \$16.7 million of cash from investing activities in the year ended December 31, 2006. The decrease in cash proceeds from investing activities in 2008 was primarily due to lower net proceeds received from maturing investments, offset by reduced purchases of property and equipment compared with 2007. The increase in cash provided by investing activities in 2007 was primarily due to higher net proceeds received from maturing investments, partially offset by increased purchases of property and equipment as well as expenditures to acquire patents in 2007 compared with 2006.

We generated \$1.0 million, \$1.3 million and \$2.1 million of cash from financing activities in the years ended December 31, 2008, 2007 and 2006, respectively. The decrease in cash provided by financing activities in 2008 was primarily due to lower proceeds from exercises of stock options and a higher principal payment on the SBS bonds compared with 2007. The decrease in cash provided by financing activities in 2007 compared with 2006 was primarily due to lower proceeds from exercises of stock options.

In November 2008, we filed a new shelf registration statement on Form S-3 with the SEC, which, upon being declared effective by the SEC, 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 June and July 2003, we completed a private placement of an aggregate of \$60.0 million in convertible subordinated notes and received net proceeds of approximately \$56.7 million after deducting underwriting fees of \$3.0 million and related expenses of \$300,000. The notes bore interest at a fixed rate of 6.25% per annum and were due on June 15, 2008. The notes were 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, or \$3.15 per share. Interest on the notes was payable semi-annually in arrears in June and December. From the third quarter of 2005 through October 2007, we exchanged an aggregate of approximately \$36.4 million in principal amount of our 6.25% convertible subordinated notes in individually negotiated transactions with note holders, pursuant to which we issued approximately 11.6 million shares of our common stock, and made cash payments in the aggregate amount of approximately \$3.8 million. In June 2008, the remaining \$23.6 million in aggregate principal amount of convertible notes were converted into approximately 7.5 million shares of our common stock. As of December 31, 2008, the remaining principal balance of our convertible subordinated notes was zero.

In conjunction with the acquisition of SBS in April 2001, we assumed the SBS Bonds with remaining principal payments of \$1.7 million as of April 30, 2001, and an interest rate of 6.35% increasing each year up to 7.20% at 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 on the SBS Bonds are due semi-annually and principal payments are due annually. Principal payments on the SBS Bonds increase in annual increments from \$150,000 to \$240,000 over the term of the bonds until the principal is fully paid 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, 2008, the remaining principal balance of the bonds was \$240,000.

**Table of Contents**

The cash used in our operating activities is heavily influenced by the timing and structure of new corporate collaborations. While one feature of our business strategy is seeking new corporate collaborations, assuming no new collaborations and no milestone payments, 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	2009	2010	2011	2012	2013	2014 and thereafter	Total
Short-term debt(1)	\$ 254	\$	\$	\$	\$	\$	\$ 254
Capital lease(1)	52	52	12				116
Purchase commitments	350	500	500	500	500	2,500	4,850
Operating lease obligations	1,534	1,456	1,419	1,374	494	83	6,360
<b>Total contractual cash obligations</b>	<b>\$ 2,190</b>	<b>\$ 2,008</b>	<b>\$ 1,931</b>	<b>\$ 1,874</b>	<b>\$ 994</b>	<b>\$ 2,583</b>	<b>\$ 11,580</b>

(1) Includes principal and interest payments.

We also anticipate incurring capital expenditures of approximately \$500,000 over the next 12 months. 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 the next 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 significant revenues from our pharmaceutical systems currently under development for at least the next twelve months, if at all. Depending on whether we enter into additional collaborative agreements in the near term and the extent to which we earn milestone revenues, we may be required to raise additional capital through a variety of sources, including:

the public equity markets;

private equity financings;

collaborative arrangements; and/or

public or private debt.

There can be no assurance that we will enter into additional collaborative agreements in the near term, will earn milestone revenues or 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.

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.

**Off-Balance Sheet Arrangements**

We have not utilized off-balance sheet arrangements to fund our operations or otherwise manage our financial position.

**Table of Contents****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 and corporate bonds. The diversity of our portfolio helps us to achieve our investment objectives. As of December 31, 2008, approximately 97% of our investment portfolio is composed of investments with original maturities of one year or less and approximately 54% of our investment portfolio matures less than 90 days from the date of purchase.

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, 2008 by year of maturity (dollars in thousands):

	2009	2010	Total
Cash equivalents:			
Fixed rate	\$ 4,798	\$	\$ 4,798
Average fixed rate	1.53%		1.53%
Variable rate	\$ 22,092		\$ 22,092
Average variable rate	0.64%		0.64%
Short-term investments:			
Fixed rate	\$ 20,836	\$	\$ 20,836
Average fixed rate	2.34%		2.34%
Long-term investments:			
Fixed rate	\$	\$ 1,362	\$ 1,362
Average fixed rate		3.42%	3.42%
Restricted investments:			
Fixed rate	\$ 1,049	\$	\$ 1,049
Average fixed rate	1.99%		1.99%
Total investment securities	\$ 48,775	\$ 1,362	\$ 50,137
Average rate	2.01%	3.42%	2.07%

**Table of Contents**

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, 2007 by year of maturity (dollars in thousands):

	2008	2009	2010	Total
<b>Cash equivalents:</b>				
Fixed rate	\$ 33,272	\$	\$	\$ 33,272
Average fixed rate	5.83%			5.83%
Variable rate	\$ 74			\$ 74
Average variable rate	4.63%			4.63%
<b>Short-term investments:</b>				
Fixed rate	\$ 19,710	\$		\$ 19,710
Average fixed rate	4.96%			4.96%
<b>Long-term investments:</b>				
Fixed rate	\$	\$ 3,697	\$	\$ 3,697
Average fixed rate		4.71%		4.71%
<b>Restricted investments:</b>				
Fixed rate	\$ 626	\$	\$ 394	\$ 1,020
Average fixed rate	5.11%		2.62%	3.45%
<b>Total investment securities</b>	<b>\$ 53,682</b>	<b>\$ 3,697</b>	<b>\$ 394</b>	<b>\$ 57,773</b>
<b>Average rate</b>	<b>5.13%</b>	<b>4.71%</b>	<b>2.62%</b>	<b>4.72%</b>



**Table of Contents**

**Item 8. Financial Statements and Supplementary Data.**

**DURECT CORPORATION**

**INDEX TO FINANCIAL STATEMENTS**

	<b>Page No.</b>
<u>Report of Independent Registered Public Accounting Firm</u>	73
<u>Balance Sheets</u>	74
<u>Statements of Operations</u>	75
<u>Statements of Stockholders' Equity</u>	76
<u>Statements of Cash Flows</u>	78
<u>Notes to Financial Statements</u>	79

**Table of Contents**

**Report of Independent Registered Public Accounting Firm**

To the Board of Directors and Stockholders of

DURECT Corporation

We have audited the accompanying balance sheets of DURECT Corporation as of December 31, 2008 and 2007, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2008. Our audits also included the financial statement schedule listed in the Index at Item 15(a). 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 financial statements referred to above present fairly, in all material respects, the financial position of DURECT Corporation at December 31, 2008 and 2007, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2008, 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), DURECT Corporation's internal control over financial reporting as of December 31, 2008, 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, 2009 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California

March 9, 2009

**Table of Contents****DURECT CORPORATION****BALANCE SHEETS**

(in thousands, except per share amounts)

	December 31,	
	2008	2007
<b><u>ASSETS</u></b>		
Current assets:		
Cash and cash equivalents	\$ 29,445	\$ 37,589
Short-term investments	20,836	19,710
Short-term restricted investments	624	
Accounts receivable (net of allowances of \$113 in 2008 and \$49 in 2007)	4,055	3,622
Inventories	3,474	1,963
Prepaid expenses and other current assets	1,850	1,904
<b>Total current assets</b>	<b>60,284</b>	<b>64,788</b>
Property and equipment, net	5,971	7,658
Goodwill	6,399	6,399
Intangible assets, net	157	180
Long-term investments	1,362	3,697
Long-term restricted investments	425	1,020
Other long-term assets	276	278
<b>Total assets</b>	<b>\$ 74,874</b>	<b>\$ 84,020</b>
<b><u>LIABILITIES AND STOCKHOLDERS EQUITY</u></b>		
Current liabilities:		
Accounts payable	\$ 1,018	\$ 1,834
Accrued liabilities	5,204	5,499
Contract research liabilities	995	1,946
Deferred revenue, current portion	9,235	5,728
Convertible subordinated notes, current portion		23,599
Other short-term liabilities	431	482
<b>Total current liabilities</b>	<b>16,883</b>	<b>39,088</b>
Deferred revenue, non-current portion	19,771	9,268
Other long-term liabilities	656	1,083
Commitments (Note 7)		
Stockholders' equity:		
Common stock, \$0.0001 par value: 110,000 shares authorized; 82,018 and 74,107 shares issued and outstanding at December 31, 2008 and 2007, respectively	8	7
Additional paid-in capital	321,067	287,689
Deferred royalties and commercial rights		(13,480)
Accumulated other comprehensive income	81	50
Accumulated deficit	(283,592)	(239,685)
<b>Stockholders' equity</b>	<b>37,564</b>	<b>34,581</b>
<b>Total liabilities and stockholders' equity</b>	<b>\$ 74,874</b>	<b>\$ 84,020</b>

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



**Table of Contents****DURECT CORPORATION****STATEMENTS OF OPERATIONS****(in thousands, except per share amounts)**

	Year ended December 31,		
	2008	2007	2006
Collaborative research and development and other revenue	\$ 18,336	\$ 22,417	\$ 13,786
Product revenue, net	8,765	8,258	8,108
<b>Total revenues</b>	<b>27,101</b>	<b>30,675</b>	<b>21,894</b>
Operating expenses:			
Cost of revenues(1)	3,365	3,225	3,248
Research and development(1)	39,411	38,342	37,241
Selling, general and administrative(1)	15,462	13,618	12,417
Write down of deferred royalties and commercial rights	13,480		
Amortization of intangible assets	48	31	424
<b>Total operating expenses</b>	<b>71,766</b>	<b>55,216</b>	<b>53,330</b>
<b>Loss from operations</b>	<b>(44,665)</b>	<b>(24,541)</b>	<b>(31,436)</b>
Other income (expense):			
Interest and other income	1,547	3,545	3,832
Interest expense	(789)	(2,625)	(3,436)
Debt conversion expense		(718)	(2,287)
<b>Net other income (expense)</b>	<b>758</b>	<b>202</b>	<b>(1,891)</b>
<b>Net loss</b>	<b>\$ (43,907)</b>	<b>\$ (24,339)</b>	<b>\$ (33,327)</b>
<b>Net loss per share, basic and diluted</b>	<b>\$ (0.56)</b>	<b>\$ (0.35)</b>	<b>\$ (0.51)</b>
<b>Shares used in computing basic and diluted net loss per share</b>	<b>78,332</b>	<b>70,483</b>	<b>65,961</b>

(1) Includes stock-based compensation related to the following:

Cost of revenues	\$ 135	\$ 130	\$ 75
Research and development	5,575	4,286	2,885
Selling, general and administrative	2,790	2,273	1,431
	<b>\$ 8,500</b>	<b>\$ 6,689</b>	<b>\$ 4,391</b>

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

**Table of Contents**

**DURECT CORPORATION**  
**STATEMENT OF STOCKHOLDERS EQUITY**

(in thousands)

	Common Stock		Additional Paid-In Capital	Deferred Royalties And Commercial Rights	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders Equity
	Shares	Amount					
Balance at December 31, 2005	61,609	\$ 6	\$ 239,057	\$ (13,480)	\$ (212)	\$ (182,019)	\$ 43,352
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	1,105		2,428				2,428
Issuance of common stock in connection with acquisition of Absorbable Polymer Technologies, Inc.	150		500				500
Stock-based compensation expense from stock options and ESPP shares			4,431				4,431
Conversion of subordinated convertible notes	6,349	1	19,480				19,481
Net change in unrealized gain on available-for-sale securities					167		167
Net loss						(33,327)	(33,327)
Total comprehensive net loss							(33,160)
Balance at December 31, 2006	69,213	\$ 7	\$ 265,896	\$ (13,480)	\$ (45)	\$ (215,346)	\$ 37,032

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

**Table of Contents****DURECT CORPORATION****STATEMENT OF STOCKHOLDERS EQUITY (Continued)**

(in thousands)

	Common Stock		Additional Paid-In Capital	Deferred Royalties And Commercial Rights	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders Equity
	Shares	Amount					
Balance at December 31, 2006 (carried forward)	69,213	\$ 7	\$ 265,896	\$ (13,480)	\$ (45)	\$ (215,346)	\$ 37,032
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	533		1,498				1,498
Stock-based compensation expense from stock options and ESPP shares			6,687				6,687
Conversion of subordinated convertible notes	4,361		13,608				13,608
Net change in unrealized gain on available-for-sale securities					95		95
Net loss						(24,339)	(24,339)
<b>Total comprehensive net loss</b>							<b>(24,244)</b>
Balance at December 31, 2007	74,107	\$ 7	\$ 287,689	\$ (13,480)	\$ 50	\$ (239,685)	\$ 34,581
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	419		1,264				1,264
Stock-based compensation expense from stock options and ESPP shares			8,516				8,516
Conversion of subordinated convertible notes	7,492	1	23,598				23,599
Write down of deferred royalties and commercial rights				13,480			13,480
Net change in unrealized gain on available-for-sale securities					31		31
Net loss						(43,907)	(43,907)
<b>Total comprehensive net loss</b>							<b>(43,876)</b>
Balance at December 31, 2008	82,018	\$ 8	\$ 321,067	\$	\$ 81	\$ (283,592)	\$ 37,564

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

**Table of Contents**

**DURECT CORPORATION**  
**STATEMENTS OF CASH FLOWS**

(in thousands)

	Year ended December 31,		
	2008	2007	2006
<b>Cash flows from operating activities</b>			
Net loss	\$ (43,907)	\$ (24,339)	\$ (33,327)
Adjustments to reconcile net loss to net cash used in operating activities:			
Write down of deferred royalties and commercial rights	13,480		
Depreciation	2,580	2,287	2,039
Amortization	48	31	424
Stock-based compensation	8,500	6,689	4,391
Loss on impairment and disposal of fixed assets	4	31	34
Inventory write-off	529	167	100
Changes in assets and liabilities:			
Accounts receivable	(433)	(1,470)	2,336
Inventories	(2,024)	(82)	(64)
Prepaid expenses and other assets	56	402	2,411
Accounts payable	(816)	970	(971)
Accrued liabilities	(449)	1,591	1,522
Contract research liability	(951)	322	206
Interest payable on convertible notes	(61)	(35)	(52)
Deferred revenue	14,010	(4,859)	11,472
<b>Total adjustments</b>	<b>34,473</b>	<b>6,044</b>	<b>23,848</b>
Net cash used in operating activities	(9,434)	(18,295)	(9,479)
<b>Cash flows from investing activities</b>			
Purchase of property and equipment	(897)	(2,545)	(2,220)
Purchase of intangible assets	(25)	(100)	
Purchase of available-for-sale securities	(21,487)	(33,458)	(56,254)
Proceeds from sales of available-for-sale securities		1,032	
Proceeds from maturities of available-for-sale securities	22,698	48,147	41,823
Net cash provided by (used in) investing activities	289	13,076	(16,651)
<b>Cash flows from financing activities</b>			
Payments on term loan and equipment financing obligations	(38)	(34)	(86)
Payment on long term debt	(225)	(210)	(200)
Net proceeds from issuances of common stock and stockholders' notes	1,264	1,498	2,428
Net cash provided by financing activities	1,001	1,254	2,142
Net decrease in cash and cash equivalents	(8,144)	(3,965)	(23,988)
Cash and cash equivalents at beginning of year	37,589	41,554	65,542
Cash and cash equivalents at end of year	\$ 29,445	\$ 37,589	\$ 41,554
<b>Supplemental disclosure of cash flow information</b>			
Cash paid for income taxes	\$	\$	\$
Cash paid for interest	\$ 785	\$ 2,236	\$ 2,413



Edgar Filing: DURECT CORP - Form 10-K

Cash paid upon debt conversion	\$	\$ 718	\$ 2,287
<b>Supplemental disclosure of noncash investing and financing activities</b>			
Issuance of common stock for acquisition of APT	\$	\$	\$ 500
Conversion of convertible subordinated notes for common stock	\$ 23,599	\$ 13,738	\$ 20,000

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

---

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO 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 based on its proprietary drug formulations and delivery platform technologies. The Company has several products under development by itself and with third party collaborators. 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.

***Use of Estimates***

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 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. Management makes estimates when preparing the financial statements including those related to revenue recognition, accrued but unbilled expenses for clinical trials and other services and stock-based compensation.

***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 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.

The Company invests its excess cash in debt instruments of government agencies 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

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

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, 2008, Nycomed and Alpharma accounted for 31% and 29% of the Company's net accounts receivable. At December 31, 2007, Pain Therapeutics, Nycomed and Endo accounted for 36%, 19% and 16% of the Company's net accounts receivable.

**Customer and Product Line Concentrations**

A portion of the Company's revenue is derived from its ALZET mini pump product line, which accounted for 25%, 21%, and 29% of total revenues in 2008, 2007 and 2006, respectively.

In 2008, Pain Therapeutics, Endo, Alpharma, and Nycomed accounted for 24%, 15%, 13% and 11% of the Company's total revenues, respectively. In 2007, Nycomed, Pain Therapeutics and Endo accounted for 36%, 16% and 16% of the Company's total revenues, respectively. In 2006, Pain Therapeutics and Endo accounted for 34% and 20% of the Company's total revenues, respectively.

Total revenue by geographic region for the years 2008, 2007 and 2006 is as follows (in thousands):

	Year ended December 31,		
	2008	2007	2006
United States	\$ 20,664	\$ 16,589	\$ 18,535
Europe	4,811	12,344	1,382
Japan	1,032	1,111	1,236
Other	594	631	741
<b>Total</b>	<b>\$ 27,101</b>	<b>\$ 30,675</b>	<b>\$ 21,894</b>

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

**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,	
	2008	2007
Raw materials	\$ 765	\$ 161
Work in-process	1,188	747
Finished goods	1,521	1,055
<b>Total inventories</b>	<b>\$ 3,474</b>	<b>\$ 1,963</b>



---

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

***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 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

a significant change in our market capitalization relative to net book value.

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, 2008, there have been no material impairment losses.

***Stock-Based Compensation***

The Company accounts for share-based payment under FAS 123R, *Share Based Payment*, which requires the recognition of compensation expense, using a fair-value based method, for costs related to all share-based payments, including stock options and stock issued under our employee stock purchase plan (ESPP). FAS 123R requires companies to estimate the fair value of share based payment awards on the date of

## Edgar Filing: DURECT CORP - Form 10-K

grant using an option-pricing model. See Note 8 for further information regarding stock-based compensation.

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

***Revenue Recognition***

Revenue from the sale of products is recognized when there is persuasive evidence that an arrangement exists, the product is shipped and title transfers to customers, provided no continuing obligation exists, the price is fixed or determinable and the collectability of the amounts owed is reasonably assured. The Company recognizes revenue from the sale of its products and license and collaboration agreements pursuant to Staff Accounting Bulletin No. 104, *Revenue Recognition*, and Emerging Issues Task Force (EITF) Issue 00-21, *Revenue Arrangements with Multiple Deliverables*. Multiple element agreements entered into are evaluated under the provision of EITF 00-21. The Company evaluates whether there is stand-alone value for the delivered elements and objective and reliable evidence of fair value to allocate revenue to each element in multiple element agreements. When the delivered element does not have stand-alone value or there is insufficient evidence of fair value for the undelivered element(s), the Company recognizes the consideration for the combined unit of accounting in the same manner as the revenue is recognized for the final deliverable, which is generally ratably over the longest period of involvement. Returns or credits related to the sale of products have not had a material impact on our revenues or net loss.

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.

Milestone payments under collaborative arrangements are recognized as collaborative research and development revenue upon achievement of the milestone events, which represent the culmination of the earnings process related to that milestone as defined in the agreement. Milestone payments are triggered 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 revenue is only recognized upon the achievement of a milestone event if we have no future performance obligations related to that milestone payment.

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

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

<b>Collaborator</b>	<b>Year ended December 31,</b>		
	<b>2008</b>	<b>2007</b>	<b>2006</b>
Pain Therapeutics, Inc. (Pain Therapeutics)(1)	\$ 6,410	\$ 4,864	\$ 7,477
Endo Pharmaceuticals, Inc. (Endo)(2)	3,934	4,818	4,438
Alpharma Ireland Limited (Alpharma)(3)	3,412		
Nycomed Danmark, APS (Nycomed)(4)	3,051	11,051	271
Voyager Pharmaceutical Corporation (Voyager)			777
Others	1,529	1,684	823
<b>Total collaborative research and development and other revenue</b>	<b>\$ 18,336</b>	<b>\$ 22,417</b>	<b>\$ 13,786</b>

- (1) Amounts related to milestone revenue recognized in connection with the Pain Therapeutics collaboration were \$850,000 in 2008 and zero in both 2007 and 2006.
- (2) Amounts related to amortization of upfront fees were \$3.0 million in 2008 and \$2.2 million in both 2007 and 2006. The Company's agreement with Endo will terminate effective August 26, 2009.
- (3) Amounts related to amortization of upfront fees were \$752,000 in 2008 and zero in both 2007 and 2006.
- (4) Amounts related to amortization of upfront fees were \$3.1 million in both 2008 and 2007, and \$271,000 in 2006. Research and development expenses incurred by us in conjunction with the Nycomed collaboration and reimbursable by Nycomed are recorded as a reduction to total research and development expense. The 2007 figure also includes \$8.0 million of milestone revenue recognized in connection with the Nycomed agreement.

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. Revenue on cost-plus-fee contracts, such as under contracts to perform research and development for others, is recognized as the related services are rendered as determined by the extent of reimbursable costs incurred plus estimated fees thereon.

**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. In addition, reimbursements by Nycomed for research and development expenses incurred by the Company are recorded as a reduction to research and development expenses. Research and development expenses incurred by Nycomed and reimbursed by the Company are recorded as additional research and development expenses.





**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

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

	Year Ended December 31,		
	2008	2007	2006
ELADUR(1)	\$ 11,852	\$ 5,132	\$ 6,946
POSIDUR(2)	8,081	10,924	12,005
Remoxy and other ORADUR-based opioid products licensed to Pain Therapeutics	5,274	4,372	5,987
Biologics Programs	4,614	3,193	2,782
TRANSDUR-Sufentanil	1,365	2,843	2,189
CHRONOGESIC	89	1,719	2,104
Memryte(3)		1,271	1,213
Others	8,136	8,888	4,015
<b>Total research and development expenses(4)</b>	<b>\$ 39,411</b>	<b>\$ 38,342</b>	<b>\$ 37,241</b>

- (1) The reported research and development expense in 2008 includes a one-time cash payment of \$2.25 million which the Company made in September 2008 as part of the amendment of its license agreement with EpiCept. The reported research and development expense in 2006 includes a one-time cash payment of \$1.0 million which the Company made in December 2006 as part of the license agreement with EpiCept.
- (2) Research and development expenses for POSIDUR incurred by us but reimbursable by Nycomed under the terms of our agreement with Nycomed were \$3.6 million, \$6.2 million and \$426,000 in 2008, 2007 and 2006, respectively, which were accounted for as a reduction of research and development expenses. Research and development expenses for POSIDUR incurred by Nycomed but reimbursable by us under the terms of our agreement with Nycomed were \$2.2 million, \$1.2 million and zero in 2008, 2007 and 2006, respectively, which were accounted for as additional research and development expenses. The agreement with Nycomed was signed in November 2006.
- (3) The reported research and development expense in 2007 includes a one-time cash payment of \$1.0 million which the Company made in January 2007 as part of the amendment of its license agreement with Voyager.
- (4) Includes stock-based compensation expenses of \$5.6 million, \$4.3 million and \$2.9 million in 2008, 2007 and 2006, respectively.

**Comprehensive Loss**

Components of other comprehensive income (loss), comprised entirely of unrealized gains and losses on the Company's available-for-sale securities for all periods presented, are included in total comprehensive loss as follows.

	Year Ended December 31,		
	2008	2007	2006
Net loss	\$ (43,907)	\$ (24,339)	\$ (33,327)

## Edgar Filing: DURECT CORP - Form 10-K

Net change in unrealized gain on available-for-sale investments, net of tax	31	95	167
<b>Comprehensive loss</b>	<b>\$ (43,876)</b>	<b>\$ (24,244)</b>	<b>\$ (33,160)</b>

Accumulated other comprehensive income (loss) as of December 31, 2008 and 2007 is entirely comprised of unrealized gains, net of taxes.

**Table of Contents****DURECT CORPORATION****NOTES TO 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):

	<b>Year ended December 31,</b>		
	<b>2008</b>	<b>2007</b>	<b>2006</b>
Net loss	\$ (43,907)	\$ (24,339)	\$ (33,327)
Basic and diluted weighted average shares:			
Weighted-average shares of common stock outstanding and used in computing basic and diluted net loss per share	78,332	70,483	65,961
Basic and diluted net loss per share	\$ (0.56)	\$ (0.35)	\$ (0.51)

The computation of diluted net loss per share for the fiscal year ended December 31, 2008 excludes the impact of options to purchase 14.0 million shares of common stock, a warrant to purchase 770 shares of common stock at December 31, 2008 and 3.4 million shares of common stock prior to their conversion at June 15, 2008, as such impact would be antidilutive.

The computation of diluted net loss per share for the fiscal year ended December 31, 2007 excludes the impact of options to purchase 11.6 million shares of common stock, a warrant to purchase 770 shares of common stock and 10.2 million shares of common stock issuable upon conversion of the subordinated notes at December 31, 2007, as such impact would be antidilutive.

The computation of diluted net loss per share for the fiscal year ended December 31, 2006 excludes the impact of options to purchase 9.5 million shares of common stock, a warrant to purchase 770 shares of common stock and 14.5 million shares of common stock issuable upon conversion of the subordinated notes at December 31, 2006, as such impact would be antidilutive.

**Shipping and Handling**

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

---

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO 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 balance sheets and amortizes the deferred rent over the terms of the lease to rent expense on the statements of operations.

***Recent Accounting Pronouncements***

In February 2008, the FASB issued FASB Staff Position No. FSP 157-2, *Effective Date of FASB Statement No. 157*, which provides a one year deferral of the effective date of SFAS 157 for non-financial assets and non-financial liabilities, except for those items that are recognized or disclosed in the financial statements at fair value at least annually. Therefore, the Company has adopted the provisions of SFAS 157 with respect to its financial assets and liabilities only. The FSP deferred the effective date of FAS 157 for non-financial assets and non-financial liabilities until our fiscal year beginning on January 1, 2009. The Company does not expect the adoption of FAS 157 for non-financial assets and non-financial liabilities to have a material effect on its financial statements.

In December 2007, the Emerging Issues Task Force of the FASB issued a consensus on Issue No. 07-1 ( EITF 07-1 ), *Accounting for Collaborative Arrangements*. The scope of EITF 07-1 is limited to collaborative arrangements where no separate legal entity exists and in which the parties are active participants and are exposed to significant risks and rewards that depend on the success of the activity. The Task Force concluded that revenue transactions with third parties and associated costs incurred should be reported in the appropriate line item in each company's financial statements pursuant to the guidance in EITF 99-19, *Reporting Revenue Gross as a Principal versus Net as an Agent*. The Task Force also concluded that the equity method of accounting under Accounting Principles Board Opinion 18, *The Equity Method of Accounting for Investments in Common Stock*, should not be applied to arrangements that are not conducted through a separate legal entity. The Task Force also concluded that the income statement classification of payments made between the parties in an arrangement should be based on a consideration of the following factors: the nature and terms of the arrangement; the nature of the entities' operations; and whether the partners payments are within the scope of existing GAAP. To the extent such costs are not within the scope of other authoritative accounting literature, the income statement characterization for the payments should be based on an analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. The provisions of EITF 07-1 are effective for fiscal years beginning on or after December 15, 2008, and companies will be required to apply the provisions through retrospective application to all collaborative arrangements existing at adoption as a change in accounting principle. The adoption of EITF 07-1 will not have a material impact on the Company's financial statements.

In December 2007, the FASB issued SFAS No. 141R, *Business Combinations* ( SFAS No. 141R ). SFAS No. 141R amends SFAS 141 and provides revised guidance for recognizing and measuring identifiable assets and goodwill acquired, liabilities assumed, and any noncontrolling interest in the acquiree. It also provides disclosure requirements to enable users of the financial statements to evaluate the nature and financial effects of the business combination. It is effective for fiscal years beginning on or after December 15, 2008 and will be applied prospectively. The effect of the adoption of FAS 141R will depend upon the nature of any future business combinations the Company undertakes.

In May 2008, the FASB issued Staff Position No APB 14-1, *Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement)* ( FSP APB 14-1 ). FSP APB 14-1 requires the issuer of certain convertible debt instruments that may be settled in cash or other assets on

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

conversion, either in part or in full, to separately account for the liability (debt) and equity (conversion option) components of the instrument in a manner that results in the recognition of interest expense equal to the issuer's nonconvertible debt borrowing rate. This FSP is effective for financial statements issued for fiscal years beginning after December 15, 2008 and interim periods within those fiscal years. This FSP must be applied retrospectively to all periods presented. The Company does not believe that the adoption of FSP APB 14-1 will have a material impact on its financial statements.

**2. Strategic Agreements*****Agreement with Alharma***

In September 2008, the Company and Alharma, entered into a development and license agreement granting Alharma the exclusive worldwide rights to develop and commercialize ELADUR, DURECT's investigational transdermal bupivacaine patch currently under development for the treatment of pain associated with post-herpetic neuralgia (PHN). The agreement became effective in October 2008 after clearance under the Hart-Scott-Rodino (HSR) Antitrust Improvements Act of 1976.

Under the terms of the agreement, upon closing of the transaction, Alharma paid the Company an upfront license fee of \$20 million, with possible additional payments of up to \$93 million upon the achievement of predefined development and regulatory milestones spread over multiple clinical indications and geographical territories as well as possible additional payments of up to \$150 million in sales-based milestones. If ELADUR is commercialized, the Company would also receive royalties on product sales. Alharma will control and fund further development of the program. The Company will perform development activities through completion of Phase 2, and formulation and manufacturing scale-up activities for the program, the costs of which shall be reimbursed by Alharma. The term of the agreement will continue on a jurisdiction-by-jurisdiction basis until the later of fifteen (15) years from the date of first commercial sale of ELADUR or the expiration of patent coverage or data exclusivity in such jurisdiction. During the term of the agreement, subject to specified conditions, neither party nor their affiliates may develop or commercialize a transdermal patch containing bupivacaine. Upon expiration of the term of the agreement, the rights and licenses granted to Alharma shall convert to fully paid-up, non-royalty bearing, perpetual rights and licenses. The agreement provides each party with specified termination rights, including the right of Alharma to terminate at any time without cause and each party to terminate the agreement upon material breach of the agreement by the other party. The agreement also contains terms and conditions customary for this type of arrangement, including representations, warranties and indemnities. As a result of the acquisition of Alharma by King Pharmaceuticals in December 2008, the agreement is effectively controlled by King.

The Company recognized \$752,000 in 2008 as collaborative research and development revenue from the amortization of the \$20.0 million upfront fee received and \$2.7 million as collaborative research and development revenue from research expenses that are qualified as reimbursement by Alharma. Total collaborative research and development revenue recognized under this arrangement was \$3.4 million for the year ended December 31, 2008. The cumulative aggregate payments received by the Company as of December 31, 2008 were \$21.6 million under this agreement.

***Agreement with Nycomed***

In November 2006, the Company entered into a collaboration agreement (the Agreement) with Nycomed. Under the terms of the agreement, the Company licensed to Nycomed the exclusive commercialization rights to POSIDUR for the European Union (E.U.) and certain other countries. Nycomed paid an upfront license fee of \$14.0 million in 2006 and a milestone payment of \$8.0 million in 2007, with future potential additional milestone

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

payments of up to \$180.0 million upon achievement of defined development, regulatory and sales milestones. The Company will jointly direct and equally fund with Nycomed a development program for POSIDUR intended to secure regulatory approval in both the U.S. and the E.U. In addition, the Company will manufacture and supply the product to Nycomed for commercial sale in the territory licensed to Nycomed. Nycomed will pay the Company blended royalties on sales in the defined territory of 15-40% depending on annual sales, as well as a manufacturing markup. The Company retains full commercial rights to POSIDUR in the U.S., Canada, Asia and other countries. 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, Nycomed shall have the right to terminate the agreement after expiry of patents covering POSIDUR in all major market countries in the E.U. and for adverse product events.

In contrast to the Company's other collaborations, because the Company and Nycomed jointly control, fund, and benefit the development of POSIDUR, the Company does not recognize revenue from the reimbursement of qualified research expenses by Nycomed. Rather, the Company records research expense equal to its share of the joint expenses incurred under the product development plan. The Company recorded a net reduction in research and development expenses of \$1.4 million, \$5.0 million and \$427,000, respectively, for 2008, 2007 and 2006, respectively. This represents a net reimbursement from Nycomed in order that both parties bear 50% of the development expenses under the collaboration agreement for POSIDUR. The Company recognized \$3.1 million, \$3.1 million and \$271,000 in the years ended December 31, 2008, 2007 and 2006, respectively, as collaborative research and development revenue from the amortization of the \$14.0 million upfront fee received in 2006. In addition, the Company recognized an additional \$8.0 million as collaborative research and development revenue, triggered by the achievement of a clinical development milestone under its Nycomed collaboration in 2007. The cumulative aggregate payments received by the Company as of December 31, 2008 were \$30.0 million under this agreement. In addition, the cumulative aggregate payments paid by the Company to Nycomed were \$2.3 million as of December 31, 2008.

***Agreement with Endo Pharmaceuticals***

On March 10, 2005, the Company entered into a license agreement with Endo under which the Company granted to Endo the exclusive right to develop, market and commercialize TRANSDUR-Sufentanil in the U.S. and Canada. The Company received an initial payment of \$10.0 million in connection with the execution of the Agreement. In February 2009, Endo notified the Company that it was terminating the license agreement with the Company, and thereby returning to the Company Endo's right to develop and commercialize TRANSDUR-Sufentanil in the U.S. and Canada effective August 26, 2009. Endo has committed to assist in an orderly and rapid transition of this program back to DURECT.

The \$10.0 million upfront fee is recognized as revenue ratably over the term of the Company's obliged continuing involvement with Endo with respect to TRANSDUR-Sufentanil. The term of the continuing involvement has been estimated based on the product development plan pursuant to the agreement. The Company's estimate of the remaining term of its continuing involvement was adjusted in the fourth quarter of 2008 as a result of Endo's termination notice received by the Company in February 2009.

The Company recognized \$3.0 million, \$2.2 million and \$2.2 million, respectively as collaborative research and development revenue from the amortization of the \$10.0 million upfront fee for the years ended December 31, 2008, 2007 and 2006. Total collaborative research and development revenue recognized under this arrangement was \$3.9 million, \$4.8 million and \$4.4 million for the years ended December 31, 2008, 2007 and 2006, respectively. The cumulative aggregate payments received by the Company as of December 31, 2008 were \$21.4 million under this agreement.

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)*****Agreement with Pain Therapeutics, Inc.***

In December 2002, the Company entered into an exclusive agreement with Pain Therapeutics, Inc. ( 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. Under the agreement with Pain Therapeutics, the Company is eligible to receive milestone payments of up to \$9.3 million in the aggregate upon the achievement of predetermined development and regulatory milestones for the four drug candidates currently in development. As of December 31, 2008, the Company has received \$1.7 million in milestone payments. 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 for 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 \$6.4 million, \$4.9 million and \$7.5 million in 2008, 2007 and 2006, respectively. The Company deferred recognizing approximately \$1.3 million of product revenue for the year ended December 31, 2008 related to its shipments to King Pharmaceuticals of key components that are included in Remoxy pending the execution of a final supply agreement with King Pharmaceuticals. The cumulative aggregate payments received by the Company as of December 31, 2008 were \$31.3 million under this agreement.

***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. Under the agreement, as amended, the Company is eligible to receive milestone payments from Voyager of up to \$3.0 million in the aggregate upon the achievement of predetermined development and regulatory milestones. As of December 31, 2008, the Company has received \$500,000 in milestone payments. 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. Under the agreement, Voyager reimbursed the Company for qualified expenses incurred by the Company in connection with the development program for Memryte. The Company recognized collaborative research and development revenue related to research and development activities for Memryte based on reimbursement of qualified expenses as defined in the agreement, until August 2006 when the Company determined that the collectability of amounts owed was not reasonably assured.

Effective January 2007, the Company entered into an amendment to the agreement with Voyager. Under the amendment, among other changes to the Agreement, the royalty rate that the Company will receive on net sales of Memryte, if commercialized, was doubled (to 10-14% of net sales after the amendment), and in addition, the



---

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

Company will now receive 10% of any upfront, milestone and other fees received by Voyager in the event that the product rights are sublicensed to a third party. As a part of the amendment, for year ended December 31, 2007, the Company paid Voyager \$1.0 million in cash and forgave approximately \$725,000 which was owed to the Company for previously provided services. The collaborative research and development revenue was recognized under the agreement with Voyager was zero, zero and \$777,000 in 2008, 2007 and 2006, respectively. The cumulative aggregate payments received by the Company as of December 31, 2008 were \$11.6 million under this agreement.

***Agreement with EpiCept Corporation***

In December 2006, the Company entered into a license agreement with EpiCept which provided the Company with the exclusive, worldwide rights to certain of EpiCept's intellectual property for a transdermal patch containing bupivacaine for the treatment of back pain. Pursuant to the agreement, the Company paid EpiCept a \$1.0 million upfront fee in 2006 and subject to the Company's achievement of specified milestones, agreed to pay EpiCept an additional \$9.0 million in milestone payments as well as an undisclosed royalty on net sales of any product covered by the license. The \$1.0 million fee was recognized as research and development expense at the execution of the agreement since the rights purchased had not yet reached technological feasibility and such rights also had no future alternative uses.

In September 2008, the Company and EpiCept entered into an amendment to the license agreement. Under the amendment, among other changes, the scope of the license was broadened from the treatment of back pain to all uses covered by the EpiCept intellectual property including myofascial pain and muscle tension pain, and the license was converted to an exclusive, worldwide, fully paid up, royalty-free, perpetual and irrevocable license. In consideration of this amendment, the Company made a one-time payment of \$2.25 million to EpiCept in full satisfaction of all future payment obligations to EpiCept under the license agreement. The Company recorded the payment of \$2.25 million as a research and development expense in the third quarter of 2008 since the rights purchased had not yet reached technological feasibility and such rights also had no future alternative uses.

***Agreement with ALZA Corporation***

In April 1998, the Company entered into a development and commercialization agreement with ALZA, which has been subsequently amended and restated, most recently in October 2002. 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, and obligates the Company to pay ALZA a royalty on the net sales of the Company's DUROS-based products and a percentage of upfront license fees, milestone payments, or any other payments or consideration received by the Company with respect to such DUROS-based products. In connection with the execution of the Agreement, 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 the Company's initial public offering in 2000. The Company issued an additional 1,000,000 shares of its common stock and a warrant to purchase 1,000,000 shares of its common stock to ALZA in connection with an amendment of the Agreement in April 2000. The Company recorded the fair value of the common stock and the warrant in the amount of \$13.5 million as additional paid-in capital and as a contra-equity account referred to as deferred royalties and commercial rights. The warrant expired in September 2004. At the end of 2008, the Company made the strategic decision that other research and development programs would take priority over CHRONOGESIC and recorded a \$13.5 million non-cash write down of deferred royalties and commercial rights associated with CHRONOGESIC given the fact that there are no plans in the foreseeable future to actively attempt to develop CHRONOGESIC (See Note 9). This agreement can be terminated by either party for material breach by the other party and by the Company without cause.

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)****3. Intangible Assets and Goodwill**

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

	<b>Gross Intangibles</b>	<b>December 31, 2008 Accumulated Amortization</b>	<b>Net Intangibles</b>
Developed technology	\$ 3,600	\$ (3,563)	\$ 37
Patents	591	(471)	120
Other intangible assets	3,260	(3,260)	
<b>Total</b>	<b>\$ 7,451</b>	<b>\$ (7,294)</b>	<b>\$ 157</b>

	<b>Gross Intangibles</b>	<b>December 31, 2007 Accumulated Amortization</b>	<b>Net Intangibles</b>
Developed technology	\$ 3,600	\$ (3,540)	\$ 60
Patents	566	(446)	120
Other intangible assets	3,260	(3,260)	
<b>Total</b>	<b>\$ 7,426</b>	<b>\$ (7,246)</b>	<b>\$ 180</b>

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

In December 2007 and January 2008, the Company entered patent assignment agreements and acquired from a third party two portfolios of worldwide patents and patent applications relating to drug delivery technologies. The Company paid \$100,000 and \$25,000 to this third party upon execution of the agreements. In connection with these agreements, the Company recorded \$100,000 and \$25,000 as intangible assets on its balance sheet as of December 31, 2007 and December 31, 2008, respectively and amortizes these patents over an estimated useful life of 7 years.

The net amount of intangible assets at December 31, 2008 was \$157,000, which will be amortized as follows: \$48,700 in 2009, \$37,000 in 2010, \$17,600 in each of the years from 2011 to 2014, and \$900 in 2015. 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, 2008. The Company evaluates goodwill for impairment at least annually. In 2008, 2007 and 2006 goodwill was evaluated and no indicators of impairment were noted. Should goodwill become impaired, the Company may be required to record an impairment charge to write the goodwill down to its estimated fair value.

**4. Financial Instruments**

The carrying amount of 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 debt agreements approximate their fair values. As of December 31, 2008 and 2007, the fair value of the Company's convertible notes was zero and \$49.1 million, respectively, compared with the carrying value of zero and \$23.6 million, respectively. The fair value of the convertible notes was obtained through quoted market prices.



**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

As of January 1, 2008, the Company adopted FASB Statement No. 157, Fair Value Measurements (SFAS 157). In February 2008, the FASB issued FASB Staff Position No. FAS 157-2, Effective Date of FASB Statement No. 157, which provides a one year deferral of the effective date of SFAS 157 for non-financial assets and non-financial liabilities, except those that are recognized or disclosed in the financial statements at fair value at least annually. Therefore, the Company has adopted the provisions of SFAS 157 with respect to its financial assets and liabilities only. SFAS 157 defines fair value, establishes a framework for measuring fair value under generally accepted accounting principles and enhances disclosures about fair value measurements. Fair value is defined under SFAS 157 as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value under SFAS 157 must maximize the use of observable inputs and minimize the use of unobservable inputs. The standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value. These levels of inputs are the following:

Level 1 Quoted prices in active markets for identical assets or liabilities.

Level 2 Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The adoption of SFAS 157 did not have a material effect on the Company's financial position and results of operations, but SFAS 157 introduced new disclosures about how we value certain assets and liabilities. Much of the disclosure is focused on the inputs used to measure fair value, particularly in instances where the measurement uses significant unobservable (Level 3) inputs. The Company's financial instruments are valued using quoted prices in active markets or based upon other observable inputs. The following table sets forth the fair value of our financial assets that were measured on a recurring basis as of December 31, 2008 (in thousands):

	Level 1	Level 2	Level 3	Total
Money market funds	\$	\$ 22,092	\$	\$ 22,092
Certificates of deposit		425		425
Commercial paper		8,716		8,716
Corporate debt		6,378		6,378
U.S. Government agencies		12,526		12,526
Total	\$	\$ 50,137	\$	\$ 50,137

The fair value of the Level 2 assets is estimated using pricing models using current observable market information for similar securities. There is a small degree of variation in the pricing sources for these securities, however the potential differences in the estimate of fair value for the Company's available-for-sale securities are insignificant.

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

The following is a summary of available-for-sale securities as of December 31, 2008 and 2007 (in thousands):

	December 31, 2008			Estimated Fair Value
	Amortized Cost	Unrealized Gain	Unrealized Loss	
Money market funds	\$ 22,092	\$	\$	\$ 22,092
Certificates of deposit	425			425
Commercial paper	8,705	11		8,716
Corporate debt	6,363	31	(16)	6,378
U.S. Government agencies	12,471	55		12,526
	\$ 50,056	\$ 97	\$ (16)	\$ 50,137
Reported as:				
Cash and cash equivalents	\$ 26,884	\$ 6	\$	\$ 26,890
Short-term investments	20,745	91		20,836
Short-term restricted investments	624			624
Long-term investments	1,378		(16)	1,362
Long-term restricted investments	425			425
	\$ 50,056	\$ 97	\$ (16)	\$ 50,137

	December 31, 2007			Estimated Fair Value
	Amortized Cost	Unrealized Gain	Unrealized Loss	
Money market funds	\$ 74	\$	\$	\$ 74
Certificates of deposit	394			394
Commercial paper	8,992		(1)	8,991
Corporate debt	7,948	32		7,980
U.S. Government agencies	40,315	19		40,334
	\$ 57,723	\$ 51	\$ (1)	\$ 57,773
Reported as:				
Cash and cash equivalents	\$ 33,338	\$ 9	\$ (1)	\$ 33,346
Short-term investments	19,688	22		19,710
Long-term investments	3,677	20		3,697
Long-term restricted investments	1,020			1,020
	\$ 57,723	\$ 51	\$ (1)	\$ 57,773

The following is a summary of the cost and estimated fair value of available-for-sale securities at December 31, 2008, by contractual maturity (in thousands):

	<b>2008</b>	
	<b>Amortized Cost</b>	<b>Estimated Fair Value</b>
Mature in one year or less	\$ 48,678	\$ 48,775
Mature after one year through five years	1,378	1,362
	<b>\$ 50,056</b>	<b>\$ 50,137</b>

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

The following is a summary of unrealized losses for available-for-sale securities at December 31, 2008 (in thousands):

	<b>Fair Value</b>	<b>Unrealized Loss for Less than 12 Months Unrealized Loss</b>
Corporate debt	\$ 2,361	\$ (16)
	\$ 2,361	\$ (16)

The following is a summary of unrealized losses for available-for-sale securities at December 31, 2007 (in thousands):

	<b>Fair Value</b>	<b>Unrealized Loss for Less than 12 Months Unrealized Loss</b>
Commercial paper	\$ 5,309	\$ (1)
	\$ 5,309	\$ (1)

There were no securities that have had an unrealized loss for more than 12 months as of December 31, 2008 and 2007.

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.

**5. Property and Equipment**

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

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
Equipment	\$ 14,123	\$ 13,469
Leasehold improvement	9,415	9,042
Construction-in-progress	166	327
	23,704	22,838
Less accumulated depreciation and amortization	(17,733)	(15,180)
Property and equipment, net	\$ 5,971	\$ 7,658

## Edgar Filing: DURECT CORP - Form 10-K

Depreciation expense was \$2.6 million, \$2.3 million and \$2.0 million in 2008, 2007 and 2006, respectively. At December 31, 2008 and 2007, no equipment was collateralized as security for equipment financing facilities. Depreciation expense was \$39,580, \$39,580 and \$34,035 in 2008, 2007 and 2006 for capital lease assets, respectively.



---

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

**6. Restricted Investments**

In July 2001, the Company deposited \$2.4 million in investment grade securities with an institution to guarantee bonds assumed in the acquisition of SBS (see Note 7). 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 2008, as allowed under the guarantee agreement, a total of approximately \$1.8 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 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.

In January 2006, the Company deposited \$61,000 in the form of a certificate of deposit with a financial institution as a letter of credit to secure a lease signed in December 2005 for capital equipment from a third party vendor for a phone system at the Cupertino facilities. The installation was completed in April 2006. The restriction on these funds will be released upon termination of the lease in January 2011.

As of December 31, 2008 and 2007, the Company had \$1.0 million recorded as restricted investments in connection with the above items.

**7. 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 were 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 were 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, or \$3.15 per share, subject to adjustment in certain circumstances. Interest on the notes was payable semi-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 was included in other long-term assets on the balance sheet and was amortized to interest expense using the effective interest rate method over the duration of the notes, which was 5 years. The notes were unsecured obligations of the Company and were 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.

---

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

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.

In May 2006, a holder of \$20.0 million in principal amount of the Company's 6.25% convertible subordinated notes converted such notes into 6,349,206 shares of common stock, at the conversion rate originally set forth in the Notes. Under the terms of the Exchange Agreement between the Company and the holder, the company made a cash payment to such holder of \$2,860,000. As a result of the conversion, the Company recorded \$2,287,000 in debt conversion expense in its statement of operations in the second quarter of 2006. The debt conversion expense represented the difference between our cash payment of \$2,860,000 to the holder and the interest expense accrued on the \$20.0 million of notes converted from the last interest payment date to the date of conversion. The conversion was recorded as a reduction of \$20.0 million of convertible subordinated notes, a reduction of other long term assets of \$519,000 attributable to the related unamortized debt issuance costs and an increase of \$19.5 million to shareholder's equity.

In September and October 2007, the Company entered into privately negotiated transactions with holders of the Company's 6.25% convertible subordinated notes, pursuant to which such holders elected to convert \$13.7 million in principal amount of such notes into an aggregate of 4,361,265 shares of common stock, at the conversion rate originally set forth in the indenture for such notes. The Company made cash payments to such holders of \$981,890, which amount satisfied the future interest payments due on such notes until maturity of \$858,625 plus a small premium for early conversions.

As a result of these conversions, the Company recorded \$718,000 in debt conversion expense in its statement of operations in 2007. The debt conversion expense represented the difference between our cash payment of \$981,890 to the holders and the interest expense accrued on the \$13.7 million of notes converted from the last interest payment date to the dates of conversions. The conversions were recorded as a reduction of \$13.7 million of short-term liabilities, a reduction of other short-term assets of \$130,000 attributable to the related unamortized debt issuance costs and an increase of \$13.7 million to shareholders' equity.

In June 2008, the holders of the Company's remaining \$23.6 million in aggregate principal amount of convertible subordinated notes converted all remaining notes into 7,491,745 shares of our common stock at a conversion rate of 317.4603 shares per \$1,000 principal amount of notes as set forth in the original indenture.

***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 2008, as allowed under the guarantee agreement, a total of approximately \$1.8 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, 2008, the remaining principal balance totaled \$240,000.

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)****Operating Leases**

The following chart indicates the facilities that we lease, the location and size of each such facility and their designated use.

<b>Location</b>	<b>Approximate Square Feet</b>	<b>Operation</b>	<b>Expiration</b>
Cupertino, CA	30,000 sq. ft.	Office, Laboratory and Manufacturing	Lease expired February 2009 (an option to renew for an additional five years has been exercised by us and the terms of the renewal period are under negotiation between us and the landlord)
Cupertino, CA	20,000 sq. ft.	Office and Laboratory	Lease expires 2014 (with an option to renew for an additional five years)
Cupertino, CA	40,560 sq. ft.	Office	Lease expires 2012 (with an option to renew for an additional six years)
Vacaville, CA	24,634 sq. ft.	Manufacturing	Lease expires 2013 (with an option to renew for an additional five years)
Pelham, AL	9,400 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2010 (with an option to renew for an additional five years)

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 \$2.0 million, \$2.0 million and \$2.5 million, for the years ended December 31, 2008, 2007 and 2006, respectively.

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

<b>Year ending December 31,</b>	<b>Bond Maturities</b>	<b>Operating Leases</b>
2009	254	1,534
2010		1,456
2011		1,419
2012		1,374
Thereafter		577
	\$ 254	\$ 6,360

**8. Stockholders Equity****Common Stock**

In October 2005, the Company filed a shelf registration statement on Form S-3 with the SEC, which allowed 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. In October 2008, this shelf registration expired and in November 2008, we filed a new shelf registration statement on Form S-3 with the SEC, which, upon being declared effective by the SEC, 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.



---

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

***Warrants***

As of December 31, 2008, the Company had an outstanding exercisable warrant to purchase its 770 shares of common stock at \$8.50 per share. The warrant was issued in connection with an Exclusive Trademark License and Assignment Agreement. The value of the warrant was insignificant as of December 31, 2008. The warrant expires in 2011.

***Description of Stock-Based Compensation Plans***

***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 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 the 1998 Stock Option Plan. As of December 31, 2008, options to purchase 2,000 shares of common stock were outstanding under this plan. In addition, all of such options were exercisable and vested as of that date.

***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 19,796,500 shares of common stock have been reserved for issuance under this plan.

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

---

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

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.

As of December 31, 2008, 4,313,231 shares of common stock were available for future grant and options to purchase 13,088,894 shares of common stock were outstanding under the 2000 Stock Plan.

***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<sup>1</sup>/<sub>3</sub>% 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.

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, 2008, 314,000 shares of common stock were available for future grant and options to purchase 569,000 shares of common stock were outstanding 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 the 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 were reserved for issuance under this plan at the time the Company assumed the 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, 2008, there were no shares of common stock available for future grant and options to purchase 98,076 shares of common stock were outstanding under the 1993 SBS Plan.

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)****2000 Employee Stock Purchase Plan**

In August 2000, the Company adopted the 2000 Employee Stock 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. A total of 1,500,000 shares of common stock have been reserved for issuance under this plan. As of December 31, 2008, 395,638 shares of common stock were available for future grant and 1,104,362 shares of common stock have been issued under the employee stock purchase plan.

As of December 31, 2008, shares of common stock reserved for future issuance consisted of the following:

	<b>December 31, 2008</b>
Warrants outstanding	770
Stock options outstanding	13,757,970
Stock options available for grant	4,627,231
Employee Stock Purchase Plan	395,638
	<b>18,781,609</b>

A summary of stock option activity under all stock-based compensation plans during the year ended December 31, 2008 is as follows:

	<b>Number of Options</b>	<b>Weighted Average Exercise Price Per Share</b>	<b>Weighted Average Remaining Contractual Term (in Years)</b>	<b>Aggregate Intrinsic Value (in millions)</b>
Outstanding at December 31, 2005	7,571,146	\$ 3.92		
Options granted	3,778,705	\$ 4.88		
Options exercised	(909,453)	\$ 2.24		
Options forfeited	(738,929)	\$ 3.36		
Options expired	(182,871)	\$ 9.46		
Outstanding at December 31, 2006	9,518,598	\$ 4.40	7.37	\$ 8.8
Options granted	2,853,346	\$ 4.37		
Options exercised	(353,110)	\$ 2.40		
Options forfeited	(406,052)	\$ 4.32		
Options expired	(130,815)	\$ 8.33		
Outstanding at December 31, 2007	11,481,967	\$ 4.41	7.09	\$ 26.4
Options granted	2,976,645	\$ 5.66		
Options exercised	(210,679)	\$ 2.46		
Options forfeited	(419,163)	\$ 4.84		
Options expired	(70,800)	\$ 8.13		

Edgar Filing: DURECT CORP - Form 10-K

Outstanding at December 31, 2008	13,757,970	\$ 4.68	6.61	\$ 2.9
Exercisable at December 31, 2008	7,414,408	\$ 4.40	5.32	\$ 2.5
Vested and expected to vest at December 31, 2008	11,742,017	\$ 4.63	6.35	\$ 2.8



---

**Table of Contents**

**DURECT CORPORATION**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

The aggregate intrinsic value in the table above represents the total pretax intrinsic value (i.e., the difference between the Company's closing stock price on the last trading day of 2008 and the exercise price, multiplied by the number of in-the-money options) that would have been received by the option holders had all option holders exercised their options on December 31, 2008. This amount changes based on the fair market value of the Company's common stock. The total intrinsic value of options exercised was \$455,000, \$890,000 and \$2.1 million for the years ended December 31, 2008, 2007 and 2006, respectively.

The weighted-average grant-date fair value of all options granted with exercise price equal to fair market value was \$4.02 in 2008, \$3.35 in 2007 and \$3.84 in 2006. There were no options granted with exercise prices lower than fair market value in 2008, 2007 and 2006.

In 2008, 2007 and 2006, the Company issued options to purchase 28,500, 1,500 and 3,000 shares of common stock to several third party consultants in exchange for services, respectively. In connection with these options to purchase common stock, the Company recorded non-cash charges of \$48,700, \$6,000 and \$10,000 in its statement of operations for the years ended December 31, 2008, 2007 and 2006. The Company has no non-cash charges related to the modification of non-employee stock options in its statement of operations for the year ended December 31, 2008, 2007 and 2006, respectively.

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.

As of December 31, 2008, the Company had five stock-based employee compensation plans, which are described below. The employee stock-based compensation cost that has been included in the statements of operations was \$8.5 million, \$6.7 million and \$4.4 million for the year ended December 31, 2008, 2007 and 2006. Stock-based compensation cost capitalized as part of inventory for the year ended December 31, 2008 was \$124,000.

Because we had a net operating loss carryforward as of December 31, 2008, no excess tax benefits for the tax deductions related to stock-based compensation expense were recognized in our statement of operations. Additionally, no incremental tax benefits were recognized from stock options exercised during 2008, which would have resulted in a reclassification to reduce net cash provided by operating activities with an offsetting increase in net cash provided by financing activities.

*Determining Fair Value*

*Valuation and Amortization Method.* The Company estimates the fair value of stock options granted using the Black-Scholes option valuation model. For options granted before January 1, 2006, the Company amortizes the fair value on an accelerated basis. For options granted on or after January 1, 2006, the Company amortizes the fair value on a straight-line basis. All options are amortized over the requisite service periods of the awards, which are generally the vesting periods.

*Expected Term.* The expected term of options granted represents the period of time that the options are expected to be outstanding. In 2008, the Company determined the expected life using historical option experience under Staff Accounting Bulletin (SAB) No. 110. This develops the expected life by taking the weighted average of the actual life of options exercised and cancelled and assumes that outstanding options are exercised uniformly from the current holding period through the end of the contractual life.

Prior to 2008, based on the limited historical exercise and post-vesting termination of options granted under the Company's plans, the Company did not believe that it was able to rely on its historical employee exercise behavior to provide accurate data for estimating the Company's expected term for use in determining the fair

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

value of these options. Therefore, as allowed by Staff Accounting Bulletin (SAB) No. 107, Share-Based Payment, the Company opted to use the simplified method for estimating its expected term equal to the midpoint between the vesting period and the contractual term of the stock options.

*Expected Volatility.* The Company estimates the volatility of its common stock at the date of grant based on the historical volatility of the Company's common stock, consistent with SFAS 123(R), SAB 107 and SAB 110.

*Risk-Free Rate.* The Company bases the risk-free rate that it uses in the Black-Scholes option valuation model on the implied yield in effect at the time of option grant on U.S. Treasury zero-coupon issues with equivalent remaining terms.

*Dividends.* The Company has never paid any cash dividends on its common stock and the Company does not anticipate paying any cash dividends in the foreseeable future. Consequently, the Company uses an expected dividend yield of zero in the Black-Scholes option valuation model.

The Company used the following assumptions to estimate the fair value of options granted and shares purchased under its employee stock plans and stock purchase plan for the years ended December 31, 2008, 2007 and 2006:

	Year ended December 31,		
	2008	2007	2006
<b>Stock Options</b>			
Risk-free rate	1.7-3.5%	3.6-5.0%	4.3-5.1%
Expected dividend yield			
Expected term (in years)	6.0	6.25	6.25
Volatility	81-85%	81-89%	90-94%
Forfeiture rate	12.9%	14.7%	17.2%
	Year ended December 31,		
	2008	2007	2006
<b>Employee Stock Purchase Plan</b>			
Risk-free rate	1.1-4.0%	3.8-5.0%	4.7-5.1%
Expected dividend yield			
Expected term (in years)	1.25	1.25	1.25
Volatility	51-95%	50-59%	54-82%

All employee stock options under the Company's stock compensation plans were granted with exercise prices equal to the fair market value of the Company's common stock on the date of grant during the years ended December 31, 2008, 2007 and 2006. The estimated weighted average fair value of the stock options granted during the years ended December 31, 2008, 2007 and 2006 was \$4.02, \$3.35 and \$3.84 per share, respectively. The total fair value of options vested during the year ended December 31, 2008 was \$9.7 million.

There were 222,009, 179,567 and 194,492 shares granted under our employee stock purchase plan during the years ended December 31, 2008, 2007 and 2006, respectively. Included in the statement of operations for the year ended December 31, 2008 was \$462,000 in stock-based compensation expense related to the amortization of expenses related to shares granted under the Company's employee stock purchase plan.

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

As of December 31, 2008, \$11.2 million of total unrecognized compensation costs related to nonvested awards is expected to be recognized over the respective vesting terms of each award through 2011. The weighted average term of the unrecognized stock-based compensation expense is 2.3 years.

The following table summarizes information about stock options outstanding at December 31, 2008:

Range of Exercise Price		Options Outstanding		Options Exercisable		
		Number of Options Outstanding	Weighted- Average Remaining Contractual Life (In years)	Weighted- Average Exercise Price	Number of Options Exercisable	Weighted- Average Exercise Price
\$0.35	2.51	1,707,752	4.30	\$ 1.98	1,537,638	\$ 2.02
\$2.57	3.20	1,497,423	5.72	\$ 3.13	1,424,326	\$ 3.14
\$3.22	3.87	1,394,845	6.15	\$ 3.51	1,122,970	\$ 3.48
\$3.92	4.31	429,000	7.94	\$ 4.02	156,375	\$ 3.96
\$4.34	4.34	2,125,759	7.90	\$ 4.34	543,789	\$ 4.34
\$4.35	5.26	994,700	7.58	\$ 4.80	453,627	\$ 4.77
\$5.27	5.27	1,787,483	6.81	\$ 5.27	907,520	\$ 5.27
\$5.38	5.86	118,500	7.60	\$ 5.59	48,500	\$ 5.66
\$5.89	5.89	2,342,245	8.95	\$ 5.89		\$
\$5.90	13.00	1,360,263	3.28	\$ 8.68	1,219,663	\$ 8.96
\$0.35	13.00	13,757,970	6.60	\$ 4.68	7,414,408	\$ 4.40

The Company received \$518,000, \$849,000 and \$2.0 million in cash from option exercises under all stock-based compensation plans for the years ended December 31, 2008, 2007 and 2006, respectively.

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 options 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 123(R) 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.

**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% 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% or more of the Company's outstanding common stock. Upon exercise, all rights holders except the potential acquirer will be entitled to acquire the Company's common stock at a discount. Under certain circumstances, the Company's Board of Directors may



**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

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% or more of the Company's common stock.

**9. Write down of deferred royalties and commercial rights**

In December 2008, the Company recorded a \$13.5 million write down of the carrying value of deferred royalties and commercial rights associated with CHRONOGESIC. In 2000, the Company recorded the fair value of common stock and a warrant issued to Alza Corporation in connection with an amended agreement related to CHRONOGESIC as additional paid-in capital and a contra-equity account referred to as deferred royalties and commercial rights. At the end of 2008, the Company made the strategic decision that other research and development programs would take priority over CHRONOGESIC and recorded this write down given the fact that the Company has no plans in the foreseeable future to actively attempt to develop CHRONOGESIC.

**10. Income Taxes**

Income tax provision was zero in 2008, 2007 and 2006.

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, 2008, 2007 and 2006 is as follows (in thousands):

	Year Ended December 31,		
	2008	2007	2006
U.S. federal taxes (benefit) at statutory rate	\$ (14,928)	\$ (8,275)	\$ (11,331)
State taxes			
Unutilized net operating loss	8,763	6,556	9,956
Non-deductible stock compensation	1,513	1,310	1,008
Write down of deferred royalties and commercial rights	4,583		
Other	69	409	367
Total	\$	\$	\$

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

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,	
	2008	2007
Deferred tax assets:		
Net operating loss carryforwards	\$ 68,782	\$ 66,913
Research and other credits	6,396	5,937
Capitalized research and development expenses	4,060	3,758
Deferred revenue	11,527	5,762
Other	5,658	3,659
<b>Total deferred tax assets</b>	<b>96,423</b>	<b>86,029</b>
Valuation allowance for deferred tax assets	(96,423)	(86,029)
<b>Net deferred tax assets</b>	<b>\$</b>	<b>\$</b>

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 \$10.4 million, \$10.0 million and \$11.3 million during 2008, 2007 and 2006, respectively.

As of December 31, 2008, the Company had net operating loss carryforwards for federal income tax purposes of approximately \$187.0 million, which expire in the years 2018 through 2028 and federal research and development tax credits of approximately \$3.6 million which expire at various dates beginning in 2018 through 2028, if not utilized.

As of December 31, 2008, the Company had net operating loss carryforwards for state income tax purpose of approximately \$93.4 million, which expire in the years 2012 through 2028, if not utilized, and state research and development tax credits of approximately \$4.0 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.

Effective January 1, 2007, the Company adopted the provisions of FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes* an interpretation of FASB Statement No. 109 (FIN 48). FIN 48 prescribes a recognition threshold and a measurement attribute for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more-likely-than-not to be sustained upon examination by taxing authorities. There was not a material impact on the Company's financial position and results of operations as a result of the adoption of the provisions of FIN 48. At December 31, 2007 and December 31, 2008, the Company had unrecognized tax benefits of approximately \$3.0 million and \$3.3 million, respectively (none of which, if recognized, would favorably affect the Company's effective tax rate). The Company does not believe there will be any material changes in its unrecognized tax positions over the next twelve months.

**Table of Contents****DURECT CORPORATION****NOTES TO FINANCIAL STATEMENTS (Continued)**

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	December 31,	
	2008	2007
Balance at beginning of the year	\$ 2,990	\$ 2,462
Increases (decrease) related to prior year tax positions	(153)	
Increases related to current year tax positions	423	528
Settlements		
Reductions due to lapse of applicable statute of limitations		
Balance at end of the year	\$ 3,260	\$ 2,990

Interest and penalty costs related to unrecognized tax benefits, if any, are classified as a component of interest income and other income (expense), net in the accompanying Statements of Operations. The Company, however, did not recognize any interest and penalty expense related to unrecognized tax benefits for the year ended December 31, 2008.

The Company files income tax returns in the U.S. federal jurisdiction and various state jurisdictions. The Company is subject to U.S. federal and state income tax examination for calendar tax years ending 1998 through 2008.

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

	First Quarter		Second Quarter		Third Quarter		Fourth Quarter	
	2008	2007	2008	2007(1)	2008	2007	2008(2)	2007
Revenue	\$ 6,438	\$ 5,726	\$ 6,303	\$ 13,432	\$ 6,634	\$ 4,932	\$ 7,726	\$ 6,585
Net loss	\$ (7,795)	\$ (8,767)	\$ (8,599)	\$ (479)	\$ (9,161)	\$ (7,882)	\$ (18,352)	\$ (7,211)
Basic and diluted net loss per share	\$ (0.11)	\$ (0.13)	\$ (0.11)	\$ (0.01)	\$ (0.11)	\$ (0.11)	\$ (0.22)	\$ (0.10)

Note:

- (1) The net loss figure includes the effects of \$8.0 million of milestone revenue recognized in connection with the Company's collaboration with Nycomed.
- (2) The net loss figure includes the effects of a one-time \$13.5 million write down of deferred royalties and commercial rights.

**13. Subsequent Event**

In February 2009, Endo notified the Company that it was terminating the license agreement with the Company, and thereby returning Endo's right to develop and commercialize TRANSDUR-Sufentanil in the U.S. and Canada effective August 26, 2009. Endo has committed to assist in an orderly and rapid transition of this program back to DURECT. Effective August 26, 2009, the Company will hold worldwide commercialization rights for TRANSDUR-Sufentanil. As a result of Endo's termination notice received by the Company in February 2009, the Company revised the term of continuing involvement with respect to the Endo agreement and recognized \$3.0 million of collaborative research

Edgar Filing: DURECT CORP - Form 10-K

and development revenue in 2008 from amortization of the upfront fee of \$10.0 million received from Endo in 2005.



---

**Table of Contents**

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

Not applicable.

**Item 9A. Controls and Procedures.**

**Disclosure Controls and Procedures**

As required by paragraph (b) of Exchange Act Rules 13a-15 or 15d-15, DURECT's management, including our Chief Executive Officer and Chief Financial Officer, conducted an evaluation as of the end of the period covered by this report, of the effectiveness of DURECT's disclosure controls and procedures as defined in Exchange Act Rule 13a-15(e) and 15d-15(e). Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that DURECT's disclosure controls and procedures were effective as of the end of the period covered by this report.

**Management's Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Under the supervision of our Chief Executive Officer and Chief Financial Officer and with the participation of our management, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2008 based on the framework in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on that evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2008.

Our independent registered public accountants, Ernst & Young LLP, audited the financial statements included in this Annual Report on Form 10-K and have issued an audit report on our internal control over financial reporting. The report on the audit of internal control over financial reporting appears below.

**Item 9B. Other Information.**

*Adjustment of Certain Items included in our Preliminary Unaudited Financial Statements and Earnings Release.* Subsequent to the issuance of our preliminary unaudited financial statements in conjunction with our earnings announcement on February 9, 2009, as a result of the termination notice received from Endo Pharmaceuticals on February 26, 2009, the Company increased its collaborative research and development and other revenue by \$1,144,000 for the three months ended December 31, 2008 and for the year ended December 31, 2008. The effects of this adjustment decreased our net loss from \$(19,496,000) to \$(18,352,000) for the three months ended December 31, 2008 and from \$(45,051,000) to \$(43,907,000) for the year ended December 31, 2008. Our net loss per share decreased by \$0.02 from \$(0.24) to \$(0.22) for the three months ended December 31, 2008 and by \$0.02 from \$(0.58) to \$(0.56) for the year ended December 31, 2008.

The effect on the Balance Sheet was to increase Deferred Revenue - Current Portion by \$202,000, decrease Deferred Revenue - Non Current portion by \$1,346,000 and decrease Accumulated Deficit in Stockholders' Equity by \$1,144,000. The adjustment had no effect on the previously reported Total Assets. In addition, the adjustment had no effect on our net cash used in operating activities as presented in the Consolidated Statements of Cash Flows.

---

**Table of Contents**

**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the Board of Directors and Stockholders of DURECT Corporation

We have audited Durect Corporation's internal control over financial reporting as of December 31, 2008, 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 included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on 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, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, 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, Durect Corporation maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Durect Corporation as of December 31, 2008 and 2007, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2008 of Durect Corporation and our report dated March 9, 2009 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California

March 9, 2009

**Table of Contents**

**Changes in Internal Control Over Financial Reporting**

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by paragraph (d) of Exchange Act Rules 13a-15 or 15d-15 that occurred during our last fiscal quarter that have materially affected or are reasonably likely to materially affect, our internal control over financial reporting.

**Item 9B. Other Information.**

None

**PART III**

The definitive proxy statement for our 2009 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.

<b>Number</b>	<b>Description</b>
2.1	Agreement and Plan of Merger dated April 18, 2001, among the Company, Target and Magnolia Acquisition Corporation(2).
2.2	Agreement and Plan of Merger dated August 15, 2003, among the Company, Birmingham Polymers, Inc., Absorbable Polymer Technologies, Inc. and the Principal Shareholders of Absorbable Polymer Technologies, Inc.(19)
3.3	Amended and Restated Certificate of Incorporation of the Company(1).

## Edgar Filing: DURECT CORP - Form 10-K

- 3.5 Amended and Restated Bylaws of the Company(1).
- 3.6 Certificate of Designation of Rights, Preferences and Privileges of Series A Participating Preferred Stock of Durect Corporation(20).
- 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 form of Certificate of Designation, the form of the Rights Certificate and the Summary of Rights attached thereto as Exhibits A, B and C, respectively(3).

**Table of Contents**

<b>Number</b>	<b>Description</b>
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).

**Table of Contents**

<b>Number</b>	<b>Description</b>
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).
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.(15)
10.46**	Sucrose Acetate Isobutyrate Pharmaceutical Grade Supply Agreement between the Company and Eastman Chemical Company dated as of December 30, 2005.(15)
10.47	Indenture of Lease between the Company and the Board of Trustees of the University of Alabama dated as of October 17, 2006.(16)
10.48**	Development and License Agreement between the Company and NYCOMED Danmark ApS dated as of November 29, 2006.(16)

**Table of Contents**

<b>Number</b>	<b>Description</b>
10.49**	License Agreement between the Company and EpiCept Corporation dated as of December 20, 2006.(16)
10.50	Lease between the Company and KLP Properties dated as of April 23, 2008.(17)
10.51	Amendment No. 1 to License Agreement between the Company and EpiCept Corporation dated as of September 12, 2008.(18)
10.52**	Development and License Agreement between the Company and Alpharma Ireland Limited dated as of September 19, 2008.(18)
10.53*	Amendment to Commercial Lease between the Company and EWE, Inc. effective December 23, 2008.
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.

- (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.

## Edgar Filing: DURECT CORP - Form 10-K

- (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.



**Table of Contents**

- (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.
- (15) Incorporated by reference to our Annual Report on Form 10-K (File No. 000-31615) filed with the Securities and Exchange Commission on March 16, 2006.
- (16) Incorporated by reference to our Annual Report on Form 10-K (File No. 000-31615) filed with the Securities and Exchange Commission on March 15, 2007.
- (17) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the Securities and Exchange Commission on August 8, 2008.
- (18) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the Securities and Exchange Commission on November 4, 2008.
- (19) Incorporated by reference to Exhibit 2.2 to our Registration Statement on Form S-3 (File No. 333-108396) filed with the Securities and Exchange Commission on August 29, 2003.
- (20) Incorporated by reference to Exhibit 3.3 to our Registration Statement on Form S-3 (File No. 333-128979) initially filed with the Securities and Exchange Commission on October 13, 2005.

\* Filed herewith.

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

++ Refiled with additional disclosure previously treated as confidential.

**Table of Contents****SCHEDULE II VALUATION AND QUALIFYING ACCOUNTS****Year Ended December 31, 2008, 2007 and 2006****(in thousands)**

	<b>Balance at beginning of the year</b>	<b>Provision</b>	<b>Write- Offs</b>	<b>Balance at end of the year</b>
December 31, 2008				
Allowance for doubtful accounts	\$ 49	\$ 74	\$ (10)	\$ 113
December 31, 2007				
Allowance for doubtful accounts	\$ 1	\$ 58	\$ (10)	\$ 49
December 31, 2006				
Allowance for doubtful accounts	\$ 128	\$ (36)	\$ (91)	\$ 1

**Table of Contents****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 10, 2009

**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.

<b>Signature</b>	<b>Title</b>	<b>Date</b>
<i>/s/</i> JAMES E. BROWN  James E. Brown	President, Chief Executive Officer and Director (Principal Executive Officer)	March 10, 2009
<i>/s/</i> FELIX THEEUWES  Felix Theeuwes	Chairman and Chief Scientific Officer	March 10, 2009
<i>/s/</i> MATTHEW J. HOGAN  Matthew J. Hogan	Chief Financial Officer (Principal Accounting Officer)	March 10, 2009
<i>/s/</i> SIMON X. BENITO  Simon X. Benito	Director	March 10, 2009
<i>/s/</i> TERRENCE F. BLASCHKE  Terrence F. Blaschke	Director	March 10, 2009
<i>/s/</i> MICHAEL D. CASEY  Michael D. Casey	Director	March 10, 2009

Edgar Filing: DURECT CORP - Form 10-K

/s/ DAVID R. HOFFMANN

Director

March 10, 2009

David R. Hoffmann

115

**Table of Contents**

<b>Signature</b>	<b>Title</b>	<b>Date</b>
<i>/s/</i> ARMAND P. NEUKERMANS Armand P. Neukermans	Director	March 10, 2009
<i>/s/</i> JON S. SAXE Jon S. Saxe	Director	March 10, 2009