DURECT CORP
Form 10-K
March 04, 2010
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2009

OR

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from _____ to _____

Commission file number: 000-31615

DURECT CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**94-3297098**

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

2 Results Way

Cupertino, CA 95014

(Address of principal executive offices, including zip code)

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

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

None

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

Common Stock, $0.0001 par value

Preferred Share Purchase Rights

(Title of Class)

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). 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. x

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 x 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 x

The aggregate market value of the voting stock held by non-affiliates of the registrant was approximately $184,167,623 as of June 30, 2009 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 86,754,768 shares of the registrant s Common Stock issued and outstanding as of February 26, 2010.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference from the definitive Proxy Statement for the 2010 annual meeting of stockholders, which is expected to be filed not later than 120 days after the Registrant s fiscal year ended December 31, 2009.

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DURECT CORPORATION

ANNUAL REPORT ON FORM 10-K

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2009

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PART I

Item 1. Business.

Overview

We are an emerging specialty pharmaceutical company focused on the development of pharmaceutical products based on our proprietary drug delivery technology platforms. Our product pipeline currently consists of six investigational drug candidates in clinical development, with one program the subject of a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA), one program in Phase III, two programs in Phase II and two programs in Phase I. These more advanced programs are all in the field of pain management and we believe that each of these targets large market opportunities with product features that are differentiated from existing therapeutics. We have other earlier stage research programs underway in fields outside of pain management, including several efforts underway which seek to improve the administration of biotechnology agents such as proteins and peptides.

A central aspect of our business strategy involves advancing multiple product candidates at one time, which is enabled by leveraging our resources with those of corporate collaborators. Thus, certain of our programs are currently licensed to corporate collaborators on terms which typically call for our collaborator to fund all or a substantial portion of future development costs and then pay us milestone payments based on specific development or commercial achievements plus a royalty on product sales. At the same time, we have retained the rights to other programs, which are the basis of future collaborations and over time may provide a pathway for us to develop our own commercial, sales and marketing organization.

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

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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 (CNS) disorders, cardiovascular disease and other chronic diseases. Our more advanced product research and development efforts in these areas are set forth in the following table:

Product Candidate	Disease/Indication	Collaborator	Technology Platform	Stage
Remoxy (Oral controlled release oxycodone)	Chronic Pain	King/Pain Therapeutics (worldwide)	ORADUR	NDA accepted but not approved/ Complete Response Letter received
POSIDUR (Controlled release injection of bupivacaine)	Post Operative Pain	Nycomed (Europe and other defined territories); DURECT retains rights in U.S., Canada, Japan and other countries	SABER	Phase III (U.S.) Phase II (E.U.)
ELADUR (Transdermal bupivacaine)	Pain	King (worldwide)	TRANSDUR	Phase II
TRANSDUR-Sufentanil (Transdermal sufentanil)	Chronic Pain	DURECT retains worldwide rights	TRANSDUR	Phase II
Oral controlled release opioid (active agent undisclosed)	Pain	King/Pain Therapeutics (worldwide)	ORADUR	Phase I
Oral controlled release opioid (active agent undisclosed)	Pain	King/Pain Therapeutics (worldwide)	ORADUR	Phase I
ORADUR-ADHD	Attention Deficit Hyperactivity Disorder (ADHD)	Orient Pharma (Defined Asian and South Pacific countries); DURECT retains rights in North American, Europe, Japan and all other countries	ORADUR	Preclinical/ Research Stage
Various	Biologics Programs/Research Programs in other Therapeutic Categories	DURECT retains worldwide rights, except for certain feasibility projects whereby our collaborator generally has an option on rights	SABER/ DUROS/ DURIN	Preclinical/ Research Stage

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Remoxy (ORADUR-Oxycodone)

Market Opportunity. Chronic pain 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 $2.8 billion in worldwide sales in 2009.

Development Strategy. Remoxy is an oral, long-acting oxycodone gelatin capsule under development with Pain Therapeutics, Inc. (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 Pharmaceuticals, Inc. (King) and, as of March 2009, we are working directly with King on further development of Remoxy. 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 $2.8 billion in 2009. Under the agreement with Pain Therapeutics, subject to and upon the achievement of predetermined development and regulatory milestones, we are entitled to receive milestone payments of up to $9.3 million in the aggregate. As of December 31, 2009, we had received $1.7 million in cumulative 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 commercialized, we will receive royalties for Remoxy and other licensed products which do not contain an opiod antagonist of between 6.0% to 11.5% of net sales depending on sales volumes.

Clinical Program. In December 2007, Pain Therapeutics and King 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 FDA accepted the NDA 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 would be required to support the approval of Remoxy, but the FDA has not requested or recommended additional clinical efficacy studies prior to approval. King assumed responsibility for further development of Remoxy from Pain Therapeutics in March 2009. On July 2, 2009, King met with the FDA to discuss the Complete Response Letter. According to King and Pain Therapeutics, the outcome of that meeting provided King with a clearer path forward to resubmit the Remoxy NDA and to address all FDA comments in the Complete Response Letter. King recently announced that it has undertaken a likeability study and a pharmacokinetic trial in volunteers and plans to resubmit the NDA in the fourth quarter of 2010.

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 which would address the chronic pain market. Phase I clinical trials have been completed for two of these ORADUR-based products. The active ingredients in these two drug candidates are opioids whose identities have not been publicly disclosed.

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 annually in the U.S.

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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 and 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 also 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 (Nycomed), which was subsequently amended in February 2010. Under the terms of the amended agreement, as amended, 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 $181.0 million upon achievement of defined development, regulatory and sales milestones. Prior to the February 2010 amendment, the agreement provided for us and Nycomed to jointly direct and equally fund a development program for POSIDUR intended to secure regulatory approval in both the U.S. and the E.U. After the amendment, we now have final decision-making authority over clinical trials intended for the U.S. registration of POSIDUR. Subject to our right to initiate dispute resolution procedures in specified circumstances, Nycomed will now have final decision-making authority over clinical trials for the E. U. and other countries licensed to it. We have funding responsibility for all current and future clinical trials intended for U.S. registration of POSIDUR and, commencing April 1, 2010, Nycomed will have sole funding responsibility for all clinical trials intended for E.U. registration of POSIDUR. The final decision making authority and financial responsibility for the remainder of the development activities, such as the non-clinical and CMC activities, will be jointly managed and funded by DURECT and Nycomed. 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, Japan 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. 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 trial 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

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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.

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 Phase II Clinical Trials

In addition to the Phase IIb clinical trial described above, we have also conducted 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. 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

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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 have applied our learnings in the design of our Phase III program.

In December 2009, we announced positive results from a 60 patient Phase IIb clinical trial of POSIDUR in patients undergoing arthroscopic shoulder surgery. Top line results showed a consistent reduction of pain scores (as measured by mean pain intensity on movement AUC, time normalized under the curve, during the period 0 to 72 hours post-surgery) in parallel with a reduction of opioid use (as measured by the amount of opioids taken in the three days post-surgery) in favor of POSIDUR versus placebo. These reductions were not statistically significant given the size of the study. In addition, there was a comparable safety profile between the two groups in this study and POSIDUR appeared well tolerated. Nycomed is currently conducting two Phase IIb clinical trials in hysterectomy patients and in shoulder surgery patients. These trials are being conducted in a different manner than U.S. clinical trials and are designed to be suitable for European regulatory approval purposes.

U.S. Phase III Program

In January 2010, we announced that we had commenced BESST (Bupivacaine Effectiveness and Safety in SABER Trial), which is intended to be the pivotal Phase III clinical trial in the U.S. BESST is an international, multi-center, randomized, double-blind, controlled trial evaluating the safety, efficacy, effectiveness, and pharmacokinetics of POSIDUR in approximately 300 patients undergoing a variety of general abdominal surgical procedures. Eligible patients will be randomly assigned to one of three cohorts:

Cohort 1: An active comparator cohort in which patients are randomized to receive either POSIDUR 5.0 mL or commercially available Bupivacaine HCl solution after laparotomy.

Cohort 2: An active comparator cohort in which patients are randomized to receive either POSIDUR 5.0 mL or commercially available Bupivacaine HCl solution after laparoscopic cholecystectomy.

Cohort 3: A double blind, placebo controlled cohort in which patients are randomized to receive either POSIDUR 5.0 mL or SABER-Placebo after laparoscopically-assisted colectomy.

Efficacy evaluation in the BESST trial will encompass a number of parameters. The two co-primary efficacy endpoints for Cohort 3 will be mean pain intensity on movement (normalized) Area Under the Curve (AUC) during the period 0-72 hours post-dose and mean total morphine equivalent opioid dose for supplemental analgesia during the period 0-72 hours post-dose. An adaptive feature of BESST allows for increasing the patient sample size in Cohort 3 based on pooled and blinded data. The purpose of Cohorts 1 and 2 is to give us additional experience with the use of POSIDUR in a broader group of surgeries and patients.

ELADUR

Market Opportunity. Pain can arise from a variety of diseases and conditions, and in many instances, pain originates from a localized point in the body and can benefit from treatments which are administered and act locally as opposed to in a systemic fashion. One such example is post-herpetic neuralgia (PHN or post-shingles pain), a debilitating complication of herpes zoster, which is usually defined as the presence of pain at the site of eruption that lasts more than a month after the onset of a zoster eruption. The prevalence of PHN (including PHN lasting more than one year) is estimated to be approximately 144,000 people in the U.S. In addition to PHN, there are a number of other widely prevalent chronic and acute local pain conditions (e.g., neuropathic pain, back pain, sprains, strains, and contusions) that could benefit from a locally acting pain product.

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

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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 PHN, such that if ELADUR is the first bupivacaine product approved for PHN, ELADUR would be eligible to receive seven years of data exclusivity following its approval 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 data exclusivity period for orphan drugs. Effective October 2008, we licensed the worldwide development and commercialization rights for ELADUR to Alpharma Ireland Limited (Alpharma), which was acquired by King in December 2008. Together with King, we are exploring the development of ELADUR for a variety of clinical indications.

Clinical Program. In 2007, we reported positive results from a completed 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 supplies for Phase II and Phase III clinical trials, and developed our clinical and regulatory strategy for further development of this program. King has stated that it intends to initiate further studies with ELADUR in the first half of 2010.

TRANSDUR-Sufentanil Patch

Market Opportunity. Chronic pain affects as many as 50 million Americans annually. One major class of drugs utilized to treat chronic pain is comprised of oral opioids, such as OxyContin, a branded extended-release oral oxycodone-based painkiller which accounted for approximately $2.8 billion in worldwide sales in 2009. Another major class of drugs utilized to treat chronic pain are transdermally delivered opioids such as Duragesic®, a leading transdermal fentanyl product which accounted for approximately $900 million in worldwide sales in 2009. It is our belief that a best-in-class sufentanil patch could compete effectively in both the transdermal fentanyl patch market and in the oral opioid market.

Development Strategy. 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.

In March 2005, we entered into an agreement with Endo Pharmaceuticals, Inc. (Endo) granting Endo exclusive rights to develop, market and commercialize TRANSDUR-Sufentanil in the U.S. and Canada. We 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. We are in active discussions with multiple potential collaborators regarding licensing development and commercialization rights to this program to which we hold worldwide rights.

Clinical Program. In 2008, Endo successfully completed a Phase II clinical trial for TRANSDUR- Sufentanil in which they evaluated the conversion of patients on oral and transdermal opioids to TRANSDUR-Sufentanil. This Phase II trial 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

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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.

ORADUR-ADHD Program

Market Opportunity. Attention Deficit Hyperactivity Disorder (ADHD) is a neurobehavioral condition that is estimated to affect approximately 8% of U.S. children ages 4-17, according to the U.S. Centers for Disease Control and Prevention (the CDC). The principal characteristics of ADHD are inattention, hyperactivity, and impulsivity. The condition presents itself in childhood and can be life long as 65% of children with ADHD continue to present symptoms as adults. Over 50% of children with ADHD are currently treated with stimulants such as amphetamine or methylphenidate and sales of ADHD treatments were approximately $4.0 billion in 2008. The National Survey on Drug Use & Health estimates that 1.4 million Americans over the age of 12 abuse stimulants for euphoric highs and increased performance or wakefulness.

Development Strategy. We are developing a drug candidate (ORADUR-ADHD) based on DURECT s ORADUR Technology for the treatment of ADHD. This drug candidate is intended to provide once-a-day dosing with added tamper resistant characteristics to address common methods of abuse and misuse of these types of drugs. In August 2009, we entered into a development and license agreement with Orient Pharma Co., Ltd., a diversified multinational pharmaceutical, healthcare and consumer products company with headquarters in Taiwan, under which we granted to Orient Pharma development and commercialization rights in certain defined Asian and South Pacific countries toORADUR-ADHD. DURECT retains rights to North America, Europe, Japan and all other countries not specifically licensed to Orient Pharma. Under our agreement with Orient Pharma, the parties will collaborate to perform a clinical development program through a Phase II study intended to produce a data package suitable for further development of the drug candidate by us as well as Orient Pharma in their respective territories. We will be responsible for formulation and study design of the Phase I and Phase II clinical program which Orient Pharma has agreed to fund and execute. Orient Pharma would be responsible for all remaining development and commercialization activities for ORADUR-ADHD in the licensed territory. If commercialized, we will be entitled to receive a royalty on sales of ORADUR-ADHD by Orient Pharma. Orient Pharma has committed to supply a portion of DURECT s commercial requirements for ORADUR-ADHD in all territories other than the U.S. We anticipate commencing Phase I studies in 2010.

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 including schizophrenia, and cancer. 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.

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Industry Background

Chronic Diseases and Conditions

Although the pharmaceutical, biotechnology and medical device industries have played key roles in increasing life expectancy and improving health, many chronic, debilitating diseases continue to be inadequately addressed with current drugs or medical devices. Cardiovascular disease, cancer, neurodegenerative diseases, diabetes, arthritis, epilepsy and other chronic diseases claim the lives of millions of Americans each year. These illnesses are prolonged, are rarely cured completely, and pose a significant societal burden in mortality, morbidity and cost. The CDC estimates that the major chronic diseases are responsible for approximately 1.7 million deaths annually, 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 the U.S. 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.

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

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

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The Drug Delivery Industry. In the last thirty-five years, a multibillion dollar drug delivery industry has developed on the basis that medicine can be improved by delivering drugs to patients in a precise, controlled fashion. Several commercially successful oral controlled release products, transdermal controlled release patches, and injectable controlled release formulations have been developed. These products demonstrate that the delivery system can be as important to the ultimate therapeutic value of a pharmaceutical product as the active molecule or compound 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 and peptides.

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 and at the right time to treat chronic and episodic diseases and conditions. 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 would otherwise 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 the 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 months, without the fluctuations in drug levels typically 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 to 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 engineering with proprietary small molecule pharmaceutical and biotechnology drug formulations 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

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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.

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 a 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.

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.

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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 III clinical trials in the U.S. and Phase II clinical trials in the E.U. 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, and for which we 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 (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. 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 clinical trial. 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. King Pharmaceuticals assumed responsibility for further development of Remoxy from Pain Therapeutics in March 2009. On July 2, 2009, King met with the FDA to discuss the Complete Response Letter. According to King and Pain Therapeutics, the outcome of that meeting provided King with a clearer path forward to resubmit the Remoxy NDA and to address all FDA comments in the Complete Response Letter. King has recently announced that it has undertaken a likeability study and a pharmacokinetic trial in volunteers and plans to resubmit the NDA in the fourth quarter of 2010.

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.

We also have an ORADUR-ADHD program in the preclinical / research stage and we expect to commence Phase I trials in 2010.

The DURIN Biodegradable Implant Technology

Our DURIN technology is a proprietary biodegradable implant that enables parenteral delivery of drugs from several weeks to six months or more using our LACTEL® brand polymers and co-polymers of lactic and glycolic acid. The DURIN technology can deliver a wide variety of drugs including small and large molecule

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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 Curaxis.

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 Corporation (ALZA), pursuant to a development and commercialization agreement entered into effective April 1998. 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 a 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 the manufacturing of the polymer raw material to process and product development, scale-up and cGMP manufacturing.

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, CNS disorders, cardiovascular disorders, cancer and degenerative neurological diseases. In addition, we have identified certain local and acute pain conditions that we believe can be addressed by 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;
- enhance drug performance by minimizing side effects; and
- expand uses of drugs by delivering them to the target site.

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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 where we have collaborated, 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 or collaborations from time to time consistent with our strategy to leverage the established sales organizations of third-party collaborators to achieve greater market penetration for some of our products than we could on our own. If we choose to enter into third-party collaborations to commercialize our pharmaceutical systems, we believe we have the flexibility to enter into these alliances under circumstances that allow us to retain greater economic participation because our pharmaceutical systems combine drugs for which medical data on efficacy and safety are available with proven technology platforms.

Third-Party Collaborations

We have entered into the following agreements in connection with our third party collaborations:

Alpharma Ireland Limited (acquired by King in December 2008). In September 2008, we and Alpharma entered into a development and license agreement granting Alpharma the exclusive worldwide rights to develop and commercialize ELADUR, our investigational transdermal bupivacaine patch. The agreement became

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effective in October 2008. 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. 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 each 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 will 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, King assumed Alpharma s rights and obligations under the agreement. As of December 31, 2009, the cumulative aggregate payments received by us under this agreement were $24.9 million.

Nycomed Danmark ApS. In November 2006, we entered into a collaboration agreement with Nycomed, and this agreement was amended in February 2010. Under the terms of the amended 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 $181.0 million upon achievement of defined development, regulatory and sales milestones. Prior to the February 2010 amendment, the agreement provided for us and Nycomed to jointly direct and equally fund a development program for POSIDUR intended to secure regulatory approval in both the U.S. and the E.U. After the amendment, we now have final decision-making authority over clinical trials intended for the U.S. registration of POSIDUR. Subject to our right to initiate dispute resolution procedures in specified circumstances, Nycomed will now have final decision-making authority over clinical trials for the E. U. and other countries licensed to it. We now have funding responsibility for all current and future clinical trials intended for U.S. registration of POSIDUR and, commencing April 1, 2010, Nycomed will have sole funding responsibility for all clinical trials intended for E.U. registration of POSIDUR. The final decision making authority and financial responsibility for the remainder of the development activities, such as the non-clinical and CMC activities, will be jointly managed and funded by us and Nycomed. 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, Japan and certain other countries. The agreement will 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 has the right to terminate the agreement after the expiration of patents covering POSIDUR in all major market countries in the E.U., for adverse product events, and within specified periods after certain clinical trials of POSIDUR. As of December 31, 2009, the cumulative aggregate payments received by us under this agreement were $34.8 million. In addition, the cumulative aggregate payments paid by us under this agreement to Nycomed were $6.8 million as of December 31, 2009.

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

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Therapeutics in order to specify our obligations with respect to the supply of key excipients for use in the licensed products. Under the amended agreement, 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, subject to and upon the achievement of predetermined development and regulatory milestones for the four drug candidates currently in development, we are entitled to receive milestone payments of up to $9.3 million in the aggregate. As of December 31, 2009, we had received $1.7 million in cumulative 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, 2009, the cumulative aggregate payments received by us from Pain Therapeutics under this agreement were $31.2 million.

In March 2009, King assumed the responsibility for further development of Remoxy from Pain Therapeutics. As a result of this change, we will continue to perform Remoxy related activities in accordance with the terms and conditions set forth in the license agreement between us and Pain Therapeutics, but with King substituted in lieu of Pain Therapeutics with respect to interactions with us in our performance of those activities including the obligation to pay us with respect to all Remoxy related costs incurred by us. The cumulative aggregate payments received by us from King as of December 31, 2009 were $811,000 under this agreement.

During 2008, we began to manufacture commercial lots of certain key excipients that are included in Remoxy to meet the anticipated requirements for these components. In addition, during the second, third and fourth quarters of 2008 and the first quarter of 2009, we made shipments of these materials to meet the production requirements of King, which has rights to commercialize Remoxy upon approval by the FDA. During these periods, all product revenue and associated cost of goods sold was deferred pending the establishment of definitive final terms and conditions even though cash receipts and expenditures occurred during these periods.

In August 2009, we entered into an exclusive long term excipient supply agreement with respect to REMOXY with King. This agreement stipulates the terms and conditions under which we will supply to King, based on our manufacturing cost plus a specified percentage mark-up, two key excipients used in the manufacture of REMOXY. The term of the agreement commenced on August 5, 2009 and will continue in effect until the earlier of the expiration of all licenses granted under the development and license agreement between the us and Pain Therapeutics or the termination or expiration of the 2005 development and license agreement between Pain Therapeutics and King, unless the agreement is terminated earlier in accordance with its terms. The agreement provides each party with specified termination rights, which include, but are not limited to, the right of King to terminate the agreement in the event that governmental action requires the withdrawal of REMOXY from all countries in the territory or results in the withdrawal of required manufacturing approvals, or upon a change of control of us, in which case termination will be effective one year after notice by King. We may terminate the agreement if we are unable to procure suitable and sufficient quantities of certain raw materials required to produce the excipient ingredients. Each party may terminate the agreement upon material breach of the agreement by, or the bankruptcy or insolvency of, the other party, in each case subject to a cure period. The agreement further specifies the rights and obligations of us and King with respect to plant allocation, adding additional production capacity and sourcing of raw materials, as well as other terms and conditions customary for this type of agreement, including those regarding forecasting, purchasing, invoicing, representations, warranties and indemnities.

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 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 returned their right to develop and commercialize TRANSDUR-Sufentanil in the

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U.S. and Canada to us effective August 26, 2009. As of December 31, 2009, the cumulative aggregate payments received by us under this agreement were $21.5 million.

Curaxis Pharmaceutical Corporation (formerly Voyager Pharmaceutical Corporation). In July 2002, we entered into a development and commercialization agreement with Voyager Pharmaceutical Corporation (now Curaxis). Under the terms of the agreement, as amended in January 2007, we have licensed Curaxis world-wide rights to develop a product using our DURIN technology to provide sustained release of leuprolide based on Curaxis s patented method of treatment of Alzheimer s disease. The amended agreement also provides Curaxis 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 amended agreement, subject to and upon the achievement of predetermined development and regulatory milestones, we are entitled to receive milestone payments from Curaxis of up to $3.0 million in the aggregate. As of December 31, 2009, we had received $500,000 in cumulative milestone payments. We are also entitled to receive reimbursement for any research and development work we perform. If Memryte is commercialized, we will receive royalties based on product sales of between ten to fourteen percent (10-14%) of the net sales of Memryte. In addition, we are entitled to receive ten percent (10%) of any upfront, milestone and other fees received by Curaxis in the event that Memryte is sublicensed to a third party. This agreement can be terminated by either party for material breach by the other party. As of December 31, 2009, the cumulative aggregate payments received by us under this agreement were $11.6 million. Development of Memryte has been halted pending raising of additional funds by Curaxis.

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. This agreement can be terminated by either party for material breach by the other party and by us without cause.

EpiCept Corporation. In December 2006, we entered into a license agreement with EpiCept Corporation (EpiCept) that provides us with the exclusive, worldwide license to certain of EpiCept s intellectual property for a transdermal patch containing bupivacaine for the treatment of back pain. In September 2008, the license was converted to an exclusive, worldwide, fully paid up, royalty-free, perpetual and irrevocable license for a transdermal patch containing bupivacaine under all fields of use covered by the EpiCept intellectual property. In consideration of the license, we paid EpiCept a cumulative amount of $3.25 million 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 Alfred E. 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 a minority equity ownership interest in NeuroSystec.

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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. The wide use and applications of the ALZET product line is evidenced by the more than 11,000 scientific references that now exist.

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- release and medical-device applications, including several FDA-approved commercial products.

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 and collaborators 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 through a direct sales force in the U.S. and through a network of distributors 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 purchase sufentanil for TRANSDUR-Sufentanil pursuant to a supply agreement with Mallinckrodt, Inc. We have entered

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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 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 initial term of the agreement expired 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.

Customers

Our product revenues are derived from sale of the ALZET and LACTEL product lines as well as from the sale of certain key excipients that are included in Remoxy to our customer (King). 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 2009, King accounted for 41% of our total revenues and no other customers accounted for more than 10% of total revenues. 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.

At December 31, 2009, Nycomed and King accounted for 39% and 11% of our net accounts receivable, 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.

Manufacturing

The process for manufacturing our pharmaceutical systems is technically complex, requires special skills, and must be performed in a qualified facility. We have contracted with Hospira Worldwide and Corium International to manufacture clinical and commercial supplies of POSIDUR and ELADUR respectively. In addition, we have a small multi-discipline manufacturing facility in Cupertino, CA 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

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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 26, 2010, we held 58 issued U.S. patents and 371 issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have 90 pending U.S. patent applications and have filed 107 patent applications under the Patent Cooperation Treaty, from which 532 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.

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 (USPTO) may be

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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 Investigational New Drug (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.

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

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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 clinical trials 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 clinical trials demonstrate that a dosage range of the product is effective and has an acceptable safety profile, Phase III clinical 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 clinical trials. We cannot be certain that we will successfully complete Phase I, Phase II or Phase III clinical trials of our pharmaceutical systems within any specific time period, if at all. Furthermore, the FDA or the Institutional Review Board or the sponsor may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. During the clinical development of products, sponsors frequently meet and consult with the FDA in order to ensure that the design of their studies will likely provide data both sufficient and relevant for later regulatory approval; however, no assurance of approvability can be given by the FDA.

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

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

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

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

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

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 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

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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. The FDA also held a public meeting on May 27 and 28, 2009 to allow for broader public input and participation. On December 4, 2009, FDA held a public meeting with the drug company sponsors to hear from them about the status of the development of a proposed REMS and their views regarding the specific features of the REMS. 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.

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, 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, Nektar, NeurogesX, Alexza, I-Flow (Kimberly-Clark), Javelin

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Pharmaceuticals, Cadence Pharmaceuticals, Cumberland Pharmaceuticals, Egalet, Acura 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.

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

We were incorporated in Delaware in February 1998. We completed our initial public offering on September 28, 2000. Our principal executive offices are located at 2 Results Way, Cupertino, California, 95014. Our telephone number is (408) 777-1417, and our web site address is www.durect.com. We make our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to these 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. Our Code of Ethics can be found on our website.

Employees

As of February 26, 2010 we had 127 employees, including 77 in research and development, 22 in manufacturing and 28 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

Our executive officers and their ages as of February 26, 2010 are as follows:

Name	Age	Position
Felix Theeuwes, D.Sc.	72	Chairman, Chief Scientific Officer and Director
James E. Brown, D.V.M.	53	President, Chief Executive Officer and Director
Matthew J. Hogan, M.B.A.	50	Chief Financial Officer
Joseph Stauffer, D.O., M.B.A.	43	Chief Medical Officer and Executive Vice President, Corporate Strategy
Jean I Liu, J.D., M.S.	41	Senior Vice President, General Counsel and Secretary
Paula Mendenhall, Pharm.D.	66	Executive Vice President, Operations and Administration
Su Il Yum, Ph.D.	70	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.

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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.

Joseph Stauffer, D.O., M.B.A. joined DURECT in June 2009 as Chief Medical Officer and Executive Vice President, Corporate Strategy. Prior to joining DURECT, Dr. Stauffer was at Alpharma Inc. from 2004 to 2009, where his latest position was as Chief Medical Officer and Senior Vice President of Clinical Research & Medical Affairs. Prior to joining Alpharma, Dr. Stauffer was employed at Abbott Laboratories from 2002 to 2004 as Global Medical Director. Prior to Abbott, he worked at the FDA from 2000 to 2002 as a Medical Review Officer in the Analgesic Division of the Center for Drug Evaluation and Research. Dr. Stauffer is a founding member of the Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT). This on-going collaboration between pharma, FDA, NIH, academia and patient advocacy groups helps to develop core domains and outcomes for chronic pain clinical trials. Dr. Stauffer graduated from the Philadelphia College of Osteopathic Medicine and completed residency training in Anesthesiology at the Johns Hopkins University Hospital, where he is currently an Adjunct Assistant Professor in the Department of Anesthesiology and Critical Care Medicine. Dr. Stauffer is a veteran of the U.S. Navy, honorably discharged as a Lieutenant Commander after serving eight years as a Naval Medical Officer. He completed his MBA in September 2009 as part of the TRIUM Global Executive MBA Program, a joint degree granted by NYU Stern School of Business, HEC School of Management (Paris) and the London School of Economics and Political Science.

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 USPTO.

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

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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®. 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;
- 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 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

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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, 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 most advanced 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 would be required to support the approval of Remoxy, but the FDA had not requested or recommended additional clinical efficacy studies prior to approval. In March 2009, King assumed the responsibility for further development of Remoxy from Pain Therapeutics. In July 2009, King met with the FDA to discuss the Complete Response Letter for Remoxy. According to King and Pain Therapeutics, the outcome of that meeting provided King with a clearer path forward to resubmit the REMOXY NDA and to address all FDA comments in the Complete Response Letter. King recently announced that it has undertaken a likeability study and a pharmacokinetic trial in volunteers and plans to resubmit the NDA in the fourth quarter of 2010. There can be no assurance that any resubmission of the NDA by King will be timely or sufficient to gain approval of 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. In 2009, we completed a successful Phase IIb clinical study in 60 shoulder surgery patients, and Nycomed is conducting Phase IIb studies in hysterectomy patients and shoulder surgery patients. These trials are being conducted by Nycomed in a different manner than U.S. studies and are designed to be suitable for European regulatory approval purposes. In January 2010, we announced that we had commenced BESST (Bupivacaine Effectiveness and Safety in SABER Trial), which is intended to be the pivotal Phase III clinical trial in the U.S. BESST is an international, multi-center, randomized, double-blind, controlled trial evaluating the safety, efficacy, effectiveness, and pharmacokinetics of POSIDUR in approximately 300 patients undergoing a variety of general abdominal surgical procedures. There can be no assurance that these trials will be successful. Furthermore, there can be no assurance that our planned development program for POSIDUR will generate data and information that will be deemed sufficient for marketing approval by the FDA or other regulatory agencies.

TRANSDUR-Sufentanil Patch Our license agreement with Endo to develop and commercialize TRANSDUR-Sufentanil in the U.S. and Canada was terminated effective August 26, 2009. Prior to the termination of the license agreement, Endo successfully completed a Phase II program for TRANSDUR-Sufentanil in which they evaluated the conversion of patients on oral and transdermal

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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. There can be no assurance that our planned development program for TRANSDUR-Sufentanil will generate data and information that will be deemed sufficient for marketing approval by the FDA or other regulatory agencies or that we will be able to find a collaborator with respect to the development and commercialization of this drug candidate.

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 supplies for Phase II and Phase III clinical trials, and developed our clinical and regulatory strategy for further development of this program. Effective October 2008, we entered into a development and license agreement with Alpharma, granting it the exclusive worldwide rights to develop and commercialize ELADUR. Alpharma was acquired by King in December 2008 and, as a result, Alpharma s rights and obligations under the agreement have now been assumed by King. Our main activities since December 2008 have involved interacting with the King team on details associated with next steps in the clinical program, which King expects to initiate in the first half of 2010. There can be no assurance that King will be able to successfully develop ELADUR to obtain marketing approval by the FDA or other regulatory agencies.

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 Remoxy 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 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 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

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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 products in development 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.

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.

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

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

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 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. The FDA also held a public meeting on May 27 and 28, 2009 to allow for broader public input and participation. On December 4, 2009, FDA held a public meeting with the drug company sponsors to hear from them about the status of the development of a proposed REMS and their views regarding the specific features of the REMS. Through this process, the 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.

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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 agreements with Pain Therapeutics, Nycomed, Alpharma (acquired by King), Orient Pharma and others 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, POSIDUR, ELADUR and other product candidates, 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 these 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 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 Orient Pharma with respect to ORADUR-ADHD, 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 products in development related to those agreements may not be commercialized.

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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;

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

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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, 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 other ORADUR-based drug candidates. 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.

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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 are unable to 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 affect our operations, development timeline and financial results.

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 by the FDA relating to our pharmaceutical systems. If we, our third-party collaborators or our respective

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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, 2009, had an accumulated deficit of approximately $313.9 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. We have 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

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.

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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 other ORADUR-based drug candidates) are currently purchased from a single or a limited number of outside sources. In particular, Eastman Chemical 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 other 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.

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If we are unable to adequately protect, maintain 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 and maintain patents, maintain trade secret protection and operate without infringing the proprietary rights of others. As of February 26, 2010, we held 58 issued U.S. patents and 371 issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have 90 pending U.S. patent applications and have filed 107 patent applications under the Patent Cooperation Treaty, from which 532 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. Telefex, 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 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

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provide that all materials and confidential information developed or made known to the individual during the course of the individual s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances, and that all inventions arising out of the individual s relationship with us will 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 USPTO 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.

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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 other 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. In particular, among other things, there is a risk that these 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.

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

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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. 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 2009 and determined that goodwill was not impaired as of December 31, 2009. 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.

Global credit and financial market conditions could negatively impact the value of our current portfolio of cash equivalents, short-term investments or long-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 original maturities of greater than 90 days from the date of purchase but less than one year from the balance sheet date. Our long-term investments consist primarily of readily marketable debt securities with maturities in one year or beyond from the balance sheet date. 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, short-term investments or long-term investments since December 31, 2009, 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, short-term investments or long-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 may 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.

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,

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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 drug candidates, if approved, will compete with currently marketed oral opioids, transdermal opioids, local anesthetic patches, stimulants, 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, AstraZeneca, Arrow International, Tricumed, I-Flow, Cumberland Pharmaceuticals, Covidien, Shire, Johnson & Johnson, Eli Lilly and Novartis. 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, Nektar, I-Flow (Kimberly-Clark), NeurogesX, Alexza, Cadence Pharmaceuticals, Javelin Pharmaceuticals, Cumberland Pharmaceuticals, Egalet, Acura 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 capabilities than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. Acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors financial, marketing, manufacturing and other resources.

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We are engaged in the development of novel therapeutic technologies. Our resources are limited and we may experience technical challenges inherent in such novel technologies. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these products may have an entirely different approach or means of accomplishing similar therapeutic effects than our 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. Even if approved for marketing, our pharmaceutical systems may not achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including:

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

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

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

The continuing efforts of government and insurance companies, health maintenance organizations and other payors of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and 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 rules, are creating uncertainty for companies such as ours and insurance, accounting and auditing costs are increasing as a result of this uncertainty and other factors. We are committed to maintaining high standards of corporate governance and public disclosure. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities.

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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 Pain Therapeutics or its commercialization sub-licensee King, Nycomed, Alpharma (now owned by King) and Orient Pharma) 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 other ORADUR-based drug candidates 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 or law enforcement 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;
- 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;

developments concerning our strategic alliances or acquisitions;

actual or anticipated variations in our operating results;

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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; or

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

the defeat of any non-negotiated takeover attempt that might otherwise benefit the public stockholders.

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

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

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

providing for a dividend on our common stock, commonly referred to as a poison pill, which can be triggered after a person or group acquires 17.5% or more of common stock;

providing for a classified board of directors with staggered terms;

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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.

Location	Approximate Square Feet	Operation	Expiration
Cupertino, CA	30,000 sq. ft.	Office, Laboratory and Manufacturing	Lease expires February 2011
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. Reserved.

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PART II

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

Price Range of Common Stock

Our common stock has been 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	
Year ended December 31, 2008	**Low**	**High**
First Quarter	$ 4.07	$ 6.43
Second Quarter	3.67	5.41
Third Quarter	3.66	5.96
Fourth Quarter	2.87	5.38

Year ended December 31, 2009	**Low**	**High**
First Quarter	$ 1.44	$ 3.39
Second Quarter	2.03	2.82
Third Quarter	2.25	2.92
Fourth Quarter	2.09	2.54

The closing sale price of our common stock as reported on the NASDAQ Global Market on February 26, 2010 was $2.39 per share. As of that date there were approximately 139 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.

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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, 2004. The graph assumes that $100 was invested on December 31, 2004. The stock price performance on the following graph is not necessarily indicative of future stock price performance.

* $100 Invested on 12/31/04 in stock or index including reinvestment of dividends. Fiscal year ending December 31.

DURECT CORPORATION

	Cumulative Total Return					
	12/31/04	**12/31/05**	**12/31/06**	**12/31/07**	**12/31/08**	**12/31/09**
DURECT CORPORATION	100.00	154.57	135.37	196.04	103.35	75.30
NASDAQ STOCK MARKET (U.S.)	100.00	101.37	111.03	121.92	72.49	104.31
NASDAQ BIOTECHNOLOGY	100.00	102.84	103.89	108.65	94.93	109.77

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

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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, 2009, 2008 and 2007 and the balance sheet data at December 31, 2009 and 2008 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, 2006 and 2005, and the balance sheet data at December 31, 2007, 2006 and 2005 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.

	Year Ended December 31,				
	2009	2008	2007	2006	2005
	(in thousands, except per share data)				
Statement of Operations Data:					
Collaborative research and development and other revenue	$ 12,180	$ 18,336	$ 22,417	$ 13,786	$ 20,032
Product revenue, net	12,113	8,765	8,258	8,108	6,939
Revenue from sale of intellectual property rights					1,600
Total revenue	24,293	27,101	30,675	21,894	28,571
Operating expenses:					
Cost of revenue	5,311	3,365	3,225	3,248	2,815
Research and development	34,634	39,411	38,342	37,241	29,141
Selling, general and administrative	15,020	15,510	13,649	12,841	12,243
Write down of deferred royalties and commercial rights		13,480			
Total operating expenses	54,965	71,766	55,216	53,330	44,199
Loss from operations	(30,672)	(44,665)	(24,541)	(31,436)	(15,628)
Other income (expense):					
Interest income and other	420	1,547	3,545	3,832	2,270
Interest expense	(36)	(789)	(2,625)	(3,436)	(4,363)
Debt conversion expense			(718)	(2,287)	(403)
Net other income (expense)	384	758	202	(1,891)	(2,496)
Loss before income taxes	(30,288)	(43,907)	(24,339)	(33,327)	(18,124)
Income tax provision					4
Net loss	$ (30,288)	$ (43,907)	$ (24,339)	$ (33,327)	$ (18,128)
Basic and diluted net loss per share	$ (0.36)	$ (0.56)	$ (0.35)	$ (0.51)	$ (0.34)
Shares used in computing basic and diluted net loss per share	83,427	78,332	70,483	65,961	53,719

	As of December 31,				
	2009	2008	2007	2006	2005
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and investments	$ 41,552	$ 52,692	$ 62,016	$ 81,607	$ 90,997
Working capital	34,796	43,401	25,700	63,100	84,202
Total assets	58,151	74,874	84,020	102,485	117,414
Convertible subordinated notes			23,559	37,337	57,337
Other long-term liabilities	508	656	1,083	910	832
Stockholders equity	27,843	37,564	34,581	37,032	43,352

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

This Management s Discussion and Analysis of Financial Condition and Results of Operations as of December 31, 2009, 2008 and 2007 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;

our intention to seek, and ability to enter into strategic alliances and collaborations;

responsibilities of our collaborators, including the responsibility to make cost reimbursement, milestone, royalty and other payments to us;

our responsibilities to our collaborators, including our responsibilities to conduct research and development, clinical trials, protect intellectual property and manufacture product;

market opportunities for products in our product pipeline;

the number of patients enrolled and the timing of patient enrollment in clinical trials;

the progress and results of our research and development programs;

requirements for us to purchase supplies and raw materials from third parties, and the ability of third parties to provide us with required supplies and raw materials;

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

conditions for obtaining regulatory approval of our product candidates;

submission and timing of applications for regulatory approval;

the impact of FDA, DEA, E.U. and other government regulation on our business;

the impact of potential Risk Evaluation and Mitigation Strategies 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;

the possibility we may commercialize our own products and build up our commercial, sales and marketing capabilities and other required infrastructure in focused specialty areas;

the continued services of key management, technical and scientific personnel;

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

the composition of future revenues;

tax benefits, including net operating loss carryforwards and research and development tax credits; and

accounting policies and estimates, including revenue recognition policies;

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

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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.

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 clinical development.

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 with Endo, Pain Therapeutics, Nycomed, King and others. 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 pursuant to ASC 808-10, *Accounting for Collaborative Arrangements*. 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 three product lines:

- ALZET® osmotic pumps for animal research use;
- LACTEL® biodegradable polymers which are used by our customers as raw materials in their pharmaceutical and medical products; and
- certain key excipients that are included in Remoxy.

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

Reduction In Force

In March 2009, we reduced the size of our California workforce by 41 employees or approximately 24% of our headcount. The goal of this action was to better align our cost structure with anticipated revenues and operating expenses, while not compromising our key corporate objectives for the year. We substantially completed this headcount reduction during the first quarter of 2009, and incurred approximately $443,000 in severance costs for the impacted employees in 2009.

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Operating Results

Since our inception in 1998, we have had a history of operating losses. At December 31, 2009, we had an accumulated deficit of $313.9 million and our net losses were $30.3 million, $43.9 million and $24.3 million for the years ended December 31, 2009, 2008 and 2007, 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 clinical trials, nonclinical studies and other research and development activities as well as to incur additional stock-based compensation costs related to research and development personnel. We expect selling, general and administrative expenses to remain comparable in the near future. 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.

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 Accounting Standards Codification (ASC) 605, *Revenue Recognition*. Multiple element agreements entered into are evaluated under the provision of ASC 605-25, *Multiple-Element Arrangements*. We evaluate whether there is stand-alone value for the delivered elements and objective and reliable evidence of fair value for the undelivered element(s) 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

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effort during a specific period in comparison to funds received under the respective agreement. Pursuant to ASC 808-10, *Collaborative Arrangements*, for joint control and funding development activities, we will not recognize revenue from the reimbursement of the research and development expenses but instead those reimbursements receivable from the joint venture party 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.

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 in the period incurred.

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.

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.

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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.

We perform a review for impairment of goodwill at least annually in accordance with ASC350, *Intangibles Goodwill and Other*. No impairment of goodwill has been recorded through December 31, 2009. 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 ASC 718, *Compensation Stock Compensation* , 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 ASC 718, *Compensation Stock Compensation.* 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. ASC 718 equires 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

See Note 1 under *Summary of Significant Accounting Policies* of the Notes to Financial Statements in Item 8. Financial Statements and Supplementary Data for a full description of recent accounting pronouncements including the respective expected dates of adoption and effects on Balance Sheets and Statements of Operations.

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Results of Operations

Comparison of years ended December 31, 2009, 2008 and 2007

Revenues. Net revenues were $24.3 million in 2009 compared to $27.1 million in 2008. The decrease in total revenues in 2009 was primarily attributable to lower collaborative research and development revenue recognized from our agreements with Pain Therapeutics, Endo and Nycomed, partially offset by higher collaborative research and development revenue from King, higher product revenue from the sale of our LACTEL biodegradable polymer product line and revenue from the sale of certain excipients included in Remoxy to King. Revenue in 2009 also included $3.0 million related to shipments to King that occurred in 2008 and the first quarter of 2009 but that had been deferred until a long term supply agreement was signed such that final terms and conditions of the sales were established. This agreement was executed in the quarter ended September 30, 2009, and all of the deferred revenue was recognized as product revenue in that period.

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. 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 Alpharma (acquired by King) 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.

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 $12.2 million of collaborative research and development and other revenue in 2009 compared to $18.3 million in 2008. The decrease in collaborative research and development revenue in 2009 was primarily attributable to lower revenue recognized in connection with our agreements with Pain Therapeutics and Endo as well as lower amortization of the upfront payment under our agreement with Nycomed, partially offset by higher collaborative research and development revenue recognized in connection with our agreements with King and other feasibility agreements compared with 2008.

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 with Alpharma (acquired by King) and Pain Therapeutics, partially offset by lower collaborative research and development revenue recognized in connection with our agreement with Endo and from feasibility agreements compared with 2007.

We received a $20.0 million upfront fee in connection with the development and license agreement signed with Alpharma 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 Alpharma with respect to ELADUR. Our estimate of the remaining term of our continuing involvement was modified in the second quarter of 2009 as a result of an updated development plan for ELADUR.

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

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collaborative research and development revenue ratably over the term of our continuing involvement with Nycomed with respect to POSIDUR. Our estimate of the remaining term of our continuing involvement was modified in the first quarter and the fourth quarter of 2009 as a result of updated development plans for POSIDUR in Europe.

We also 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. The term of the continuing involvement had been estimated based on the product development plan pursuant to the agreement. Our estimate of the remaining term of our continuing involvement was modified in the fourth quarter of 2008 as a result of Endo s termination notice that we received in February 2009.

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):

	Year ended December 31,		
	2009	2008	2007
Collaborator			
King Pharmaceuticals, Inc. (King)(1)	$ 7,024	$ 3,412	$
Nycomed Danmark ApS (Nycomed)(2)	1,453	3,051	11,051
Endo Pharmaceuticals, Inc. (Endo)(3)	985	3,934	4,818
Pain Therapeutics, Inc. (Pain Therapeutics)(4)	317	6,410	4,864
Others	2,401	1,529	1,684
Total collaborative research and development and other revenue	$ 12,180	$ 18,336	$ 22,417

(1) Amounts related to the amortization of upfront fees were $3.4 million in 2009, $752,000 in 2008 and zero in 2007. Alpharma is now owned by King.

(2) Amounts related to the amortization of upfront fees were $1.5 million in 2009, and $3.1 million in both 2008 and 2007. 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.

(3) Amounts related to the amortization of upfront fees were $875,000 in 2009, $3.0 million in 2008 and $2.2 million in 2007. Our agreement with Endo was terminated effective August 26, 2009.

(4) Amounts related to milestone revenue recognized in connection with the Pain Therapeutics collaboration were zero in 2009, $850,000 in 2008 and zero in 2007.

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. We recorded $850,000 of milestone revenue from our Pain Therapeutics collaboration related to the achievement of clinical and regulatory milestones in 2008 and $8.0 million of milestone revenue from our Nycomed collaboration due to the achievement of a clinical development milestone for POSIDUR in 2007.

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Product revenue

A portion of our revenues is derived from our product sales, which include our ALZET mini pump product line, our LACTEL biodegradable polymer product line and certain excipients that are included in Remoxy. Net product revenues were $12.1 million, $8.8 million and $8.3 million in 2009, 2008 and 2007, respectively. The increase in product revenue in 2009 compared with 2008 was primarily attributable to higher product revenue from the sale of certain excipients included in Remoxy to King. Product revenue in 2009 also included $3.0 million related to shipments to King that occurred in 2008 and the first quarter of 2009 but that had been deferred until a long term supply agreement was signed such that final terms and conditions of the sales were established. This agreement was executed in the quarter ended September 30, 2009, and all of the deferred revenue was recognized as revenue in that period. In addition, we experienced higher product revenue from our LACTEL polymer product line as a result of higher units sold, partially offset by lower revenue from our ALZET mini pump product line as a result of lower units sold in 2009.

The increase in product revenue in 2008 compared with 2007 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 certain excipients that are included REMOXY in 2008 aggregating $1.3 million in 2008 had been deferred until a final supply agreement with King was signed in the third quarter of 2009.

Cost of revenues. Cost of revenues was $5.3 million, $3.4 million and $3.2 million in 2009, 2008 and 2007, respectively. Cost of revenues includes the cost of product revenue from our ALZET mini pump product line, our LACTEL polymer products and certain excipients that are included in Remoxy. The increase in the cost of product revenue in 2009 compared with 2008 was primarily the result of recognizing $2.0 million of cost of certain excipients for Remoxy sold to King, partially offset by lower units sold from our ALZET mini pump product line and improved manufacturing efficiency from our LACTEL polymer product line. Cost of product revenue and gross profit margin will fluctuate from period to period depending upon the product mix in a particular period. The increase in the cost of product revenue in 2008 compared with 2007 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 had been deferred until the execution of a final supply agreement with King in the third quarter of 2009. Stock based compensation expense recognized related to cost of revenues was $433,000, $135,000 and $130,000 in 2009, 2008 and 2007, respectively.

As of December 31, 2009, 2008 and 2007, we had 22, 31 and 23 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 $34.6 million, $39.4 million and $38.3 million in 2009, 2008 and 2007. The decrease in 2009 was primarily attributable to lower development costs associated with ELADUR, Remoxy and other select ORADUR-based opioid drug candidates and our biologics programs, partially offset by higher development costs associated with POSIDUR and other research programs compared to 2008 as more fully discussed below. In addition, we paid $2.25 million to EpiCept in the third quarter of 2008 under our amended agreement with EpiCept and recorded this amount as a research and development expense in 2008. Stock-based compensation expense recognized related to research and development personnel was $7.2 million, $5.6 million and $4.3 million in 2009, 2008 and 2007, respectively.

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 in 2008.

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

	Year Ended December 31,		
	2009	2008	2007
POSIDUR(1)	$ 14,083	$ 8,081	$ 10,924
ELADUR(2)	3,823	11,852	5,132
ORADUR-ADHD	2,155	1,091	
Remoxy and other ORADUR-based opioid products licensed to Pain Therapeutics	1,688	5,274	4,372
Biologics Programs	1,638	4,614	3,193
TRANSDUR-Sufentanil	1,387	1,365	2,843
CHRONOGESIC	36	89	1,719
Memryte(3)			1,271
Others	9,824	7,045	8,888
Total research and development expenses(4)	$ 34,634	$ 39,411	$ 38,342

(1) Research and development expenses for POSIDUR incurred by us but reimbursable by Nycomed under the terms of our agreement with Nycomed were $3.5 million, $3.6 million and $6.2 million in 2009, 2008 and 2007, 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 $4.7 million, $2.2 million and $1.2 million in 2009, 2008 and 2007, respectively, which were accounted for as additional research and development expenses. The agreement with Nycomed was signed in November 2006.

(2) Reported research and development expenses in 2008 includes a one-time cash payment of $2.25 million which we made in September 2008 as part of the amendment of its license agreement with EpiCept.

(3) Reported research and development expenses in 2007 includes a one-time cash payment of $1.0 million which we made in January 2007 as part of the amendment of its license agreement with Curaxis.

(4) Includes stock-based compensation expenses of $7.2 million, $5.6 million, and $4.3 million in 2009, 2008 and 2007, respectively.

POSIDUR

Our research and development expenses for POSIDUR increased to $14.1 million in 2009 from $8.1 million in 2008. The increase was primarily due to higher costs associated with clinical trials conducted by Nycomed and us. Research and development expenses for POSIDUR incurred by us but reimbursable by Nycomed under the terms of our agreement with Nycomed were $3.5 million in 2009 compared to $3.6 million in 2008, 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 $4.7 million in 2009 compared to $2.2 million in 2008, 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 increased by $1.2 million in 2009 compared with a reduction of $1.4 million in 2008. The net increase or reduction in research and development expenses represents a net payment to or 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 $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

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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.

ELADUR

Our research and development expenses for ELADUR decreased to $3.8 million in 2009 from $11.9 million in 2008. The decreases in 2009 were primarily due to lower employee costs, non-clinical studies and contract manufacturing expenses related to this product candidate. In addition, we paid $2.25 million to EpiCept in 2008 related to certain intellectual property relevant to ELADUR under the amended agreement with EpiCept.

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 supplies for Phase II and Phase III clinical trials for this drug candidate in 2008 as well as the $2.25 million to EpiCept in 2008 related to certain intellectual property relevant to ELADUR.

ORADUR-ADHD

Our research and development expenses for ORADUR-ADHD increased to $2.2 million in 2009 from $1.1 million in 2008. The increase was primarily due to increased formulation and other development activities for this program in 2009.

Our research and development expenses for ORADUR-ADHD increased to $1.1 million in 2008 from zero in 2007. The increase was primarily due to the initial formulation and other development activities for this program in 2008.

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

Our research and development expenses for Remoxy and other opioids licensed to Pain Therapeutics decreased to $1.7 million in 2009 from $5.3 million in 2008. The decrease was primarily due to decreased support activities for Remoxy after the filing of the Remoxy NDA as well as decreased formulation and clinical manufacturing activities for other select ORADUR-based opioid drug candidates in 2009.

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.

Biologics Programs

Our research and development expenses for biologics programs decreased to $1.6 million in 2009 from $4.6 million in 2008. The decrease was primarily due to lower external costs and employee related costs in support of these programs in 2009.

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.

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TRANSDUR-Sufentanil

Our research and development expenses for TRANSDUR-Sufentanil were $1.4 million in both 2009 and 2008. We incurred higher employee related cost for this product candidate in 2009 than in 2008, offset by decreased external costs after Endo returned the program to us in 2009.

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.

CHRONOGESIC® (sufentanil) Pain Therapy System

Our research and development expenses for CHRONOGESIC decreased to $36,000 in 2009 from $89,000 in 2008. The decrease was primarily due to minimal costs incurred for this program in 2009.

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.

Memryte

Our research and development expenses for Memryte decreased to zero in both 2009 and 2008 from $1.3 million in 2007 as we did not undertake any research and development activities for this product candidate in 2009 and 2008. 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 Curaxis.

Other DURECT Research Programs

Our research and development expenses for all other activities increased to $9.8 million from $7.0 million in 2008. The increase was primarily due to higher employee related costs and increased formulation and clinical development activities for these programs.

Our research and development expenses for all other activities decreased to $7.0 million in 2008 from $8.9 million in 2007. The decrease was primarily due to lower employee related costs, partially offset by increased formulation and clinical development activities for these programs.

As of December 31, 2009, 2008 and 2007, we had 77, 104 and 117 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.

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.

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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 $15.0 million in 2009 compared with $15.5 million in 2008. The decrease in selling, general and administrative expenses was primarily attributable to lower employee, patent and consulting expenses incurred in 2009 compared with 2008. Stock-based compensation expense recognized related to selling, general and administrative personnel was $3.8 million, $2.8 million and $2.3 million in 2009, 2008 and 2007, respectively.

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 as well as increased patent related expenses in 2008 compared with 2007.

As of December 31, 2009, 2008 and 2007, we had 28, 38 and 36 selling, general and administrative personnel, respectively. We expect selling, general and administrative expenses to remain comparable in the near future to support our business activities.

Write down of deferred royalties and commercial rights. Write down of deferred royalties and commercial rights was zero, $13.5 million and zero in 2009, 2008 and 2007, respectively. 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.

Other Income (Expense). Interest and other income was $420,000, $1.5 million and $3.5 million in 2009, 2008 and 2007, respectively. The decreases in interest income were primarily the result of lower yields on our investments as well as lower average cash and investment balances in 2009 and 2008 compared with 2007.

Interest expense was $36,000, $789,000 and $2.6 million in 2009, 2008 and 2007, respectively. The decrease in interest expense in 2009 and 2008 was primarily due to lower outstanding balances on our convertible notes in 2009 and 2008 compared with 2007 due to the conversion of the remaining $23.6 million in aggregate principal amount of convertible notes in June 2008.

Debt conversion expense was zero, zero and $718,000 in 2009, 2008 and 2007, respectively. 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.

Income taxes. As of December 31, 2009, we had net operating loss (NOL) carryforwards for federal income tax purposes of approximately $212.5 million, which expire in the years 2018 through 2029, and federal research and development tax credits of approximately $4.2 million, which expire at various dates beginning in 2018 through 2029, if not utilized. As of December 31, 2009, we had NOL carryforwards for state income tax purpose of approximately $131.8 million, which expire in the years 2012 through 2029, and state research and development tax credits of approximately $4.6 million, which do not expire. Utilization of the net operating losses may be subject to a substantial annual limitation due to federal and state ownership change limitations. The annual limitation may result in the expiration of net operating losses and credits before utilization.

As of December 31, 2009 and 2008, we had net deferred tax assets of $107.3 million and $96.4 million, respectively. 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

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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, 2009 and December 31, 2008. 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 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. We also issued approximately 4.4 million shares of our common stock to Venrock in connection with an equity financing in September 2009. 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 our 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 ASC 740, *Income Taxes*. Interest and penalties related to uncertain tax positions will be reflected in income tax expense. Tax years 1998 to 2009 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 $41.6 million and $52.7 million at December 31, 2009 and 2008, respectively. This includes $431,000 and $1.0 million of interest-bearing marketable securities classified as restricted investments on our balance sheet as of December 31, 2009 and 2008, respectively, which primarily serve as collateral for letters of credit securing our leased facilities and Alabama State Industrial Development Bonds payments which were assumed by us as part of our acquisition of SBS (SBS Bonds). The letter of credit related to the SBS bonds expired in November 2009. The letter of credit related to the security deposit of the leased facilities will expire in December 2012.

The decrease in cash, cash equivalents and investments from 2008 to 2009 was primarily the result of ongoing operating expenses, partially offset by approximately $9.9 million received from our equity financing in 2009 as well as other payments received from our customers and third-party collaborators. 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.

Working capital was $34.8 million, $43.4 million and $25.7 million at December 31, 2009, 2008 and 2007, respectively. The decrease in working capital from 2008 to 2009 was primarily attributable to cash used for operations in 2009, partially offset by the receipt of net proceeds from our equity financing in 2009. The increase

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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.

We used $20.9 million, $9.4 million and $18.3 million of cash in operating activities in the years ended December 31, 2009, 2008 and 2007, respectively. The increase in cash used in operating activities in 2009 was primarily due to decreases in accounts receivable and inventory balances in 2009 compared with 2008. 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.

We used $10.4 million of cash from investing activities in the year ended December 31, 2009 but generated $289,000 and $13.1 million of cash from investing activities in the years ended December 31, 2008 and 2007, respectively. The increase in cash used in investing activities in 2009 was primarily due to higher net purchases of investments, offset by reduced purchases of property and equipment compared with 2008. 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.

We generated $10.1 million, $1.0 million and $1.3 million of cash from financing activities in the years ended December 31, 2009, 2008 and 2007, respectively. The increase in cash provided by financing activities in 2009 was primarily due to approximately $9.9 million of cash received from an equity financing, partially offset by lower proceeds from exercises of stock options and purchases of our employee stock purchase plan in 2009. 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.

In November 2008, we filed a new shelf registration statement on Form S-3 with the SEC, which upon being declared effective in May 2009, allowed us to offer up to $75 million of securities from time to time in one or more public offerings of our common stock.

On September 10, 2009, we entered into a privately negotiated transaction to sell 4,444,444 shares of our common stock to affiliates of Venrock at a price of $2.25 per share, raising total gross proceeds of approximately $10.0 million. This transaction was completed on September 18, 2009. Total stock issuance costs related to this financing were approximately $126,000.

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	2010	2011	2012	2013	2014	2015 and thereafter	Total
Capital lease(1)	$ 52	$ 12	$	$	$	$	$ 64
Purchase commitments	500	500	500	500	500	2,000	4,500
Operating lease obligations	2,031	1,496	1,436	494	83		5,540
Total contractual cash obligations	$ 2,583	$ 2,008	$ 1,936	$ 994	$ 583	$ 2,000	$ 10,104

(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.

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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.

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. 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, 2009, approximately 100% of our investment portfolio is composed of investments with original maturities of one year or less and approximately 16% of our investment portfolio matures less than 90 days from the date of purchase.

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The following table presents the amounts of our cash equivalents and investments that may be subject to interest rate risk and the average interest rates as of December 31, 2009 by year of maturity (dollars in thousands):

	2010	2011	Total
Cash equivalents:			
Fixed rate	$ 2,350	$	$ 2,350
Average fixed rate	0.16%		0.16%
Variable rate	$ 4,157		$ 4,157
Average variable rate	0.08%		0.08%
Short-term investments:			
Fixed rate	$ 32,834	$	$ 32,834
Average fixed rate	0.53%		0.53%
Long-term investments:			
Fixed rate	$	$	$
Average fixed rate			
Restricted investments:			
Fixed rate	$ 431	$	$ 431
Average fixed rate	0.30%		0.30%
Total investment securities	$ 39,772	$	$ 39,772
Average rate	0.47%		0.47%

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%

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Item 8. Financial Statements and Supplementary Data.

DURECT CORPORATION

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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, 2009 and 2008, and the related statements of operations, stockholders equity, and cash flows for each of the three years in the period ended December 31, 2009. Our audits also included the financial statement schedule listed in the Index at Item 15(a)(2). 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, 2009 and 2008, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2009, 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, 2009, 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 4, 2010 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Palo Alto, California

March 4, 2010

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DURECT CORPORATION

BALANCE SHEETS

(in thousands, except per share amounts)

	December 31, 2009	December 31, 2008
ASSETS		
Current assets:		
Cash and cash equivalents	$ 8,287	$ 29,445
Short-term investments	32,834	20,836
Short-term restricted investments		624
Accounts receivable (net of allowances of $103 at December 31, 2009 and $113 at December 31, 2008)	1,700	4,055
Inventories	2,799	3,474
Prepaid expenses and other current assets	1,433	1,850
Total current assets	47,053	60,284
Property and equipment, net	3,808	5,971
Goodwill	6,399	6,399
Intangible assets, net	108	157
Long-term investments		1,362
Long-term restricted investments	431	425
Other long-term assets	352	276
Total assets	$ 58,151	$ 74,874
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 1,019	$ 1,018
Accrued liabilities	5,337	5,204
Contract research liabilities	990	995
Deferred revenue, current portion	4,703	9,235
Other short-term liabilities	208	431
Total current liabilities	12,257	16,883
Deferred revenue, non-current portion	17,543	19,771
Other long-term liabilities	508	656
Commitments (Note 7)		
Stockholders equity:		
Common stock, $0.0001 par value: 110,000 shares authorized; 86,755 and 82,018 shares issued and outstanding at December 31, 2009 and 2008, respectively	8	8
Additional paid-in capital	341,705	321,067
Accumulated other comprehensive income	10	81
Accumulated deficit	(313,880)	(283,592)
Stockholders equity	27,843	37,564
Total liabilities and stockholders equity	$ 58,151	$ 74,874

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

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DURECT CORPORATION

STATEMENTS OF OPERATIONS

(in thousands, except per share amounts)

	Year ended December 31,		
	2009	**2008**	**2007**
Collaborative research and development and other revenue	$ 12,180	$ 18,336	$ 22,417
Product revenue, net	12,113	8,765	8,258
Total revenues	24,293	27,101	30,675
Operating expenses:			
Cost of revenues(1)	5,311	3,365	3,225
Research and development(1)	34,634	39,411	38,342
Selling, general and administrative(1)	15,020	15,510	13,649
Write down of deferred royalties and commercial rights		13,480	
Total operating expenses	54,965	71,766	55,216
Loss from operations	(30,672)	(44,665)	(24,541)
Other income (expense):			
Interest and other income	420	1,547	3,545
Interest expense	(36)	(789)	(2,625)
Debt conversion expense			(718)
Net other income (expense)	384	758	202
Net loss	$ (30,288)	$ (43,907)	$ (24,339)
Net loss per share, basic and diluted	$ (0.36)	$ (0.56)	$ (0.35)
Shares used in computing basic and diluted net loss per share	83,427	78,332	70,483

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

Cost of revenues	$ 433	$ 135	$ 130
Research and development	7,159	5,575	4,286
Selling, general and administrative	3,838	2,790	2,273
	$ 11,430	$ 8,500	$ 6,689

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

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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, 2006	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)
Total comprehensive net loss							(24,244)
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)
Total comprehensive net loss							(43,876)
Balance at December 31, 2008 (carried forward)	82,018	$ 8	$ 321,067	$	$ 81	$ (283,592)	$ 37,564

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

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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, 2008 (carried forward)	82,018	$ 8	$ 321,067	$	$ 81	$ (283,592)	$ 37,564
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	293		528				528
Stock-based compensation expense from stock options and ESPP shares			10,236				10,236
Issuance of common stock upon equity financing	4,444		9,874				9,874
Net change in unrealized gain on available-for-sale securities					(71)		(71)
Net loss						(30,288)	(30,288)
Total comprehensive net loss							(30,359)
Balance at December 31, 2009	86,755	$ 8	$ 341,705	$	$ 10	$ (313,880)	$ 27,843

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

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DURECT CORPORATION

STATEMENTS OF CASH FLOWS

(in thousands)

	Year ended December 31,		
	2009	**2008**	**2007**
Cash flows from operating activities			
Net loss	$ (30,288)	$ (43,907)	$ (24,339)
Adjustments to reconcile net loss to net cash used in operating activities:			
Write down of deferred royalties and commercial rights		13,480	
Depreciation	2,457	2,580	2,287
Amortization	49	48	31
Stock-based compensation	11,430	8,500	6,689
Asset retirement obligation	383		
Loss on impairment and disposal of fixed assets		4	31
Inventory write-off	487	529	167
Changes in assets and liabilities:			
Accounts receivable	2,355	(433)	(1,470)
Inventories	190	(2,024)	(82)
Prepaid expenses and other assets	341	56	402
Accounts payable			