UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2013

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.)**

10260 Bubb Road
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:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock $0.0001 par value per share	**The NASDAQ Stock Market LLC**
Preferred Share Purchase Rights	**(NASDAQ Global Market)**

Securities registered pursuant to Section 12(g) of the Act:
None

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

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

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

Indicate by check mark 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. ☒

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

Large accelerated filer ☐ Accelerated filer ☒ Non-accelerated filer ☐ Smaller reporting company ☐

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

The aggregate market value of the voting stock held by non-affiliates of the registrant was approximately $102,590,039 as of June 30, 2013 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 110,483,636 shares of the registrant's Common Stock issued and outstanding as of February 14, 2014.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference from the definitive Proxy Statement for the 2013 annual meeting of stockholders, which is expected to be filed not later than 120 days after the Registrant's fiscal year ended December 31, 2013.

DURECT CORPORATION

ANNUAL REPORT ON FORM 10-K

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2013

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PART I

Item 1. Business.

Overview

We are a specialty pharmaceutical company focused on the development of pharmaceutical products based on our proprietary drug delivery technology platforms. Our product pipeline currently consists of eight 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) for which a Complete Response Letter was received in June 2011, another program the subject of an NDA with the FDA for which a Complete Response Letter was received in February 2014, two programs in Phase II and four programs in Phase I. The more advanced programs are 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 programs underway in fields outside of pain management, including central nervous system disorders, metabolic disorders, cardiovascular disease and other chronic diseases.

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 potential future collaborations and over time may provide a pathway for us to develop our own commercial, sales and marketing organization.

Product Research and Development Programs

Our development efforts are focused on the application of our drug delivery technologies to potential products in a variety of chronic and episodic disease areas including pain, central nervous system (CNS) disorders, metabolic 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	• Pfizer/Pain Therapeutics (worldwide)	• ORADUR	• NDA resubmitted in December 2010 but not approved / Complete Response Letter received in June 2011
• POSIDUR (controlled release injection of bupivacaine)	• Post-Operative Pain	• DURECT retains worldwide rights	• SABER	• NDA accepted in June 2013 / Complete Response Letter received in February 2014
• ELADUR (transdermal bupivacaine)	• Pain	• Impax Laboratories (worldwide)	• TRANSDUR	• Phase II
• TRANSDUR-Sufentanil (transdermal sufentanil)	• Chronic Pain	• DURECT retains worldwide rights	• TRANSDUR	• Phase II

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

Product Candidate	Disease/Indication	Collaborator	Technology Platform	Stage
• Relday (risperidone)	• Schizophrenia/ bipolar disorder	• Zogenix (worldwide)	• SABER	• Phase I
• ORADUR-based opioid (hydrocodone)	• Chronic Pain	• Pain Therapeutics (worldwide)	• ORADUR	• Phase I
• ORADUR-based opioid (hydromorphone)	• Chronic Pain	• Pain Therapeutics (worldwide)	• ORADUR	• Phase I
• ORADUR- ADHD	• Attention Deficit Hyperactivity Disorder (ADHD)	• Orient Pharma (defined Asian and South Pacific countries); DURECT retains development and commercialization rights in North America, Europe, Japan and all other countries	• ORADUR	• Phase I
• ORADUR-based opioid (oxymorphone)	• Chronic Pain	• Pain Therapeutics (worldwide)	• ORADUR	• IND accepted by the FDA
• Various	• Research Programs in various Therapeutic Categories	• DURECT retains worldwide rights, except for certain feasibility projects whereby our collaborator generally has an option on rights	• SABER/ DURIN	• Preclinical/ Research Stage

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 100 million Americans annually. OxyContin®, a brand name extended-release oral oxycodone-based painkiller, accounted for over $3.0 billion in worldwide sales in 2012.

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 sublicensed the worldwide commercialization rights of REMOXY (except for Australia and New Zealand) to King Pharmaceuticals, Inc. (King) and, as of March 2009, we began working directly with King on further development of REMOXY. In February 2011, Pfizer Inc (Pfizer) acquired King and thereby assumed the rights and obligations of King with respect to 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 greater than $3.0 billion in 2012. 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 for REMOXY and other licensed ORADUR-based opioids. As of December 31, 2013, 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 opioid 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 had 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. In July 2009, King met with the FDA to discuss the Complete Response Letter. King took over the NDA from Pain Therapeutics and resubmitted the NDA in December of 2010. In February 2011, King was acquired by Pfizer. On June 23, 2011, a Complete Response Letter from the FDA was received by Pfizer on the resubmission to the NDA for REMOXY. The FDA's June 2011 Complete Response Letter raised concerns related to, among other matters, the Chemistry, Manufacturing, and Controls section of the NDA for REMOXY. Pfizer has efforts underway to resolve these issues. In October 2013, Pfizer stated that, having achieved technical milestones related to manufacturing, they will continue the development program for REMOXY®. Following guidance received from the FDA earlier in 2013, Pfizer announced that they will proceed with the additional clinical studies and other actions required to address the Complete Response Letter. These new clinical studies will include, in part, a pivotal bioequivalence study with the modified REMOXY formulation to bridge to the clinical data related to the original REMOXY formulation, and an abuse-potential study with the modified formulation. As previously disclosed, the complete response submission is not expected to occur prior to mid-2015.

Additional ORADUR-Opioid Products in Development

Since 2006, we also worked with Pain Therapeutics on the development of three additional ORADUR abuse-resistant opioid drug candidates which would address the chronic pain market. Phase I clinical trials have been conducted for two of these ORADUR-based products (hydrocodone and hydromorphone), and an IND has been accepted by the FDA for the fourth ORADUR-based opioid (oxymorphone). In October 2013, Pain Therapeutics stated that it had regained all rights from Pfizer with respect to the three other ORADUR-based opioid drug candidates (hydrocodone, hydromorphone and oxymorphone). Pain Therapeutics is now free to develop and commercialize these product candidates on its own or with a licensee. Pain Therapeutics has stated that they have not yet made a decision to develop or out-license the three product candidates.

POSIDUR (SABER-Bupivacaine)

Market Opportunity. According to data published by the Center for Disease Control and Prevention, there are approximately 72 million ambulatory and inpatient surgical procedures performed annually in the U.S. Epidemiological studies indicate that up to 100% of surgical patients experience post-operative pain, with 50-75% reporting inadequate pain relief. The current standard of care for post-surgical pain includes oral opiate and non-opiate analgesics and muscle relaxants. While systemic opioids can effectively control post-surgical pain, they commonly cause side effects including drowsiness, constipation, nausea and vomiting, and cognitive impairment. Effective pain management can be compromised if patients fail to adhere to recommended dosing regimens because they are suffering from these side effects. Post-surgical pain also can be treated effectively with local anesthetics; however, their usefulness often is limited by their short duration of action.

Development Strategy. We are developing POSIDUR, an extended-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 extended analgesia from a single dose. We believe that by delivering effective amounts of a potent analgesic to the location from which the pain originates, improved pain control can be achieved with minimal exposure to the remainder of the body and reduced need for systemic analgesics, thus minimizing systemic side effects. POSIDUR is intended to provide local analgesia for up to 3 days, which we believe generally coincides with the time period of greatest need for post-surgical pain control in most patients.

POSIDUR was the subject of a collaboration agreement with Hospira, Inc. (Hospira) to develop and commercialize POSIDUR in the U.S. and Canada. POSIDUR was also the subject of a collaboration agreement with Nycomed Danmark ApS (Nycomed) to develop and commercialize POSIDUR in the European Union (E.U.) and certain other countries. In January 2012, Nycomed (now owned by Takeda) gave notice that its rights with respect to POSIDUR were being returned to us. In March 2012, Hospira gave notice that its rights with respect to POSIDUR were being returned to us. Please see "Third Party Collaborations" for additional information. We have initiated discussions with other potential partners regarding licensing development and commercialization rights to this program, for which we now hold worldwide rights.

Clinical Program. Our POSIDUR clinical development program has been devised to establish the safety and efficacy of POSIDUR for the treatment of post-surgical pain for up to 3 days. Toward that end, 15 clinical studies have been conducted, of which 13 clinical studies were with the final formulation of POSIDUR in either blinded, randomized controlled trials or open-label trials. These 15 trials are included in the Integrated Summary of Safety (ISS) which was included in the POSIDUR NDA. Seven randomized, controlled, parallel design clinical trials of POSIDUR using the instillation method of administration and dose proposed for marketing are included in the Integrated Summary of Efficacy (ISE) which was included in the NDA. Seven different surgical procedures have been investigated, including inguinal hernia repair, shoulder surgery (primarily subacromial decompression), appendectomy, abdominal hysterectomy, open laparotomy, laparoscopic cholecystectomy, and laparoscopic colectomy. The incision lengths treated ranged from a few centimeters for laparoscopic portals, to open laparotomy incisions of up to 35 cm. The seriousness of the surgery ranged from day surgery hernia repair in relatively healthy patients to major abdominal surgery for colon cancer in elderly patients with substantial co-morbidity who were often hospitalized for a week or more. The safety experience from this variety of procedures and patients was designed to allow a more confident extrapolation of the safety and efficacy data to a broad general surgical population.

Safety

As bupivacaine is a well known drug with an extensive understanding of its risks and benefits, the safety database in the Integrated Summary of Safety (ISS) is not as large as required for a new chemical entity. A total of 1075 patients are included in the ISS database, 951 of whom have been exposed to POSIDUR or SABER-Placebo in volumes ranging from 2.5 to 10 mL. A total of 683 patients have been exposed to POSIDUR with the dose of bupivacaine ranging from 330 to 990 mg. In addition, a total of 124 patients have been treated with bupivacaine HCl in control groups and 268 patients received SABER-Placebo in control groups.

Overall, the POSIDUR patient groups showed a similar systemic safety profile as the patient groups treated with SABER-Placebo and bupivacaine HCl. Local site reactions were observed more frequently in the POSIDUR and SABER-Placebo groups than in the active comparator groups, most frequently in abdominal surgeries; most of these observations were discolorations (e.g., surgical bruising), the majority of which resolved without treatment during the observation period. There was little difference in the incidence of severe or serious adverse events between the POSIDUR, SABER-Placebo and bupivacaine HCl treatment groups. Most of the serious adverse events seen in these trials appear to be due to complications of surgery, anesthesia, analgesics, or co-morbidity and not POSIDUR-related. The clinical history for serious adverse events has been reviewed and no evidence of bupivacaine toxicity was apparent. The adverse event data have been analyzed in a variety of ways to detect any evidence of bupivacaine central nervous system or cardiac toxicity or other unexpected effects. No patients treated with POSIDUR had an instance of a severe central nervous system or cardiac adverse event traditionally associated with bupivacaine toxicity.

Efficacy

In the NDA, we have presented the results from two efficacy trials that we positioned as pivotal (inguinal hernia repair and shoulder surgery, primarily subacromial decompression) and an Integrated Summary of Efficacy (ISE) based on 7 randomized, controlled, parallel design surgical trials of POSIDUR using the administration technique and 5 mL (660 mg) dose proposed for marketing.

Hernia pivotal efficacy trial

The hernia pivotal efficacy 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 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 (defined as 0-15 days).

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 and was statistically significant (p=0.0031). 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. The median decrease in supplemental opioid analgesics taken over the first three days after surgery was 80% (p=0.0085) for the POSIDUR 5 mL group as compared to the placebo group.

Shoulder pivotal efficacy trial

The shoulder pivotal efficacy trial was a multicenter, randomized, double-blind, active- and placebo-controlled, parallel-group, dose-response trial conducted at 9 investigational centers in Europe. Nycomed, DURECT's collaborator at the time, was responsible for the conduct of the clinical trial. In this study, 107 patients were randomly assigned to one of three treatment groups prior to undergoing elective arthroscopic shoulder surgery: POSIDUR 5 mL (n=53), SABER-Placebo (n=25) or bupivacaine HCl solution (n=29). All patients were given a background pain treatment consisting of a daily dose of two or four grams (depending on the patient's weight) of paracetamol (acetaminophen). In addition, each patient was provided supplemental opioid rescue medication, if needed. With respect to efficacy, the primary endpoints of the study were to demonstrate: (1) an improvement in terms of pain intensity on movement area under the curve (AUC) during the period 1–72 hours post-surgery, and (2) a decrease in the total use of opioid rescue analgesia 0–72 hours post-surgery.

Results from this study demonstrate that the POSIDUR group experienced a statistically significant reduction in pain intensity of approximately 21% (p=0.0122) versus SABER-Placebo. Applying the appropriate statistical test given the data distribution, the POSIDUR group showed a statistically significant reduction of approximately 67% (p=0.013) in median opioid use in favor of POSIDUR. No statistical differences were found when POSIDUR was compared to bupivacaine HCl.

Phase III trial in abdominal surgical procedures

We also conducted a Phase III U.S. and international, multi-center, randomized, double-blind, controlled trial evaluating the safety, efficacy, effectiveness, and pharmacokinetics of POSIDUR in 305 patients undergoing a variety of general abdominal surgical procedures. The trial included the following three cohorts:

Cohort 1: An active comparator cohort in which patients were randomized to receive either POSIDUR 5 mL or commercially available Bupivacaine HCl solution after laparotomy.

Cohort 2: An active comparator cohort in which patients were randomized to receive either POSIDUR 5 mL or commercially available Bupivacaine HCl solution after laparoscopic cholecystectomy.

Cohort 3: A double blind, placebo controlled cohort in which patients were randomized to receive either POSIDUR 5 mL or SABER-Placebo after laparoscopically-assisted colectomy.

Efficacy evaluation in the Phase III trial encompassed a number of parameters. The two co-primary efficacy endpoints for Cohort 3 were 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. The purpose of Cohorts 1 and 2 was to give us additional experience with the use of POSIDUR in a broader group of surgeries and patients.

Cohort 3. With respect to the co-primary efficacy endpoint of pain reduction as measured by mean pain intensity on movement (normalized) Area Under the Curve (AUC) during the period 0-72 hours post-dose, the patient group treated with POSIDUR reported a mean pain reduction in pain scores of approximately 7%, although this was not statistically significant (p=0.1466). The statistical analysis plan included pain on movement as recorded at scheduled times through an electronic diary plus pain scores reported whenever supplemental opioids were administered with such scores attributed as if they were pain on movement. In the prespecified sensitivity analysis (which includes only scheduled pain assessment on movement scores as collected on the electronic diary), the patient group treated with POSIDUR reported approximately 10% less pain versus placebo (p=0.0410). In relation to the co-primary efficacy endpoint of median total morphine-equivalent opioid dose for supplemental analgesia during the period 0-72 hours post-dose, the patient group treated with POSIDUR reported approximately 16% less opioids consumed versus the placebo group, although this was not statistically significant (p=0.5897).

Cohorts 1 and 2. Cohorts 1 and 2 were prespecified to be pooled due to their small sample size. For Cohorts 1 and 2 (pooled), the mean reduction in pain on movement was approximately 20% and statistically significant (p=0.0111) for the POSIDUR group compared to the patient group treated with bupivacaine HCl. With respect to the median total morphine-equivalent opioid dose for supplemental analgesia during the period 0-72 hours post-dose for Cohorts 1 and 2 (pooled), the patient group treated with POSIDUR reported approximately 18% less opioids consumed compared to the bupivacaine HCl group, although this was not statistically significant (p=0.5455).

Integrated Summary of Efficacy

The seven controlled trials in the ISE can be separated into two basically different surgical types. The four soft tissue trials involved incisions or laparoscopic portals either in the abdomen or in the inguinal area for hernia repair. In these surgeries, the pain producing tissue was primarily soft tissue such as viscera, fascia, muscle, or skin. However, in the three orthopedic surgeries involving shoulder surgery, a major pain producing tissue is bone that has been resected during the procedure. Given that the responsiveness to treatment of these different surgical types may be different, a pooled analysis has been conducted separately by tissue type.

In the soft tissue pooled analysis group comprised of 410 patients, 253 were treated with POSIDUR and 157 were treated with SABER-Placebo. The mean pain intensity was lower during the period 0-72 hours post-dose in the POSIDUR group than in the SABER-Placebo group and the difference was statistically significant (p=0.0099). The median total morphine-equivalent dose during the period 0-72 hours post-dose was lower in the POSIDUR group than in the SABER-Placebo group, however the difference was not statistically significant.

In the orthopedic pooled analysis group comprised of 187 patients, 114 were treated with POSIDUR and 73 were treated with SABER-Placebo. The mean pain intensity during the period 0-72 hours post-dose was lower in the POSIDUR group than in the SABER-Placebo group and the difference was statistically significant (p=0.0205). The median total morphine-equivalent dose during the period 0-72 hours post-dose was lower in the POSIDUR group than in the SABER-Placebo group and the difference was statistically significant (p=0.0025).

Current Status. In July 2012, we completed pre-NDA communications with the FDA regarding POSIDUR. Through this process, we received guidance and thoughtful comments from the FDA covering various chemistry, manufacturing, non-clinical, clinical pharmacology, clinical, statistical and product labeling topics. In April 2013, with the input we have received from the FDA and leveraging off the well established history of bupivacaine use, we submitted an NDA as a 505(b)(2) application, which relies in part on the FDA's findings of safety and effectiveness of a reference drug. In June 2013, we announced that our NDA submission had been accepted by the FDA indicating that the application is sufficiently complete to permit a substantive review. In February 2014 we received a Complete Response Letter from the FDA. Based on its review, the FDA has determined that they cannot approve the NDA in its present form, stating the NDA does not contain sufficient information to demonstrate that POSIDUR is safe when used in the manner described in the proposed label, and the FDA has indicated that additional clinical safety studies need to be conducted. We are evaluating the issues and recommendations described in the Complete Response Letter and plan to have further discussions with the FDA around them.

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, sprains, strains, and contusions) that could benefit from a locally acting pain product.

Development Strategy. Our transdermal bupivacaine patch (ELADUR) under development is intended to provide continuous delivery of bupivacaine for up to three days from a single application, as compared to a wearing time limited to 12 hours with currently available lidocaine patches. We anticipate that ELADUR will have several potential differentiating attributes compared with currently marketed lidocaine patches, including extended duration of action and better wearability. During 2008, we received Orphan Drug Designation for bupivacaine for relief of persistent pain associated with PHN, such that if ELADUR is the first bupivacaine product approved for PHN, ELADUR should 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. In February 2011, Pfizer acquired King and thereby assumed the rights and obligations of King with respect to ELADUR. In February 2012, Pfizer gave notice that its rights with respect to ELADUR were being returned to us. In January 2014, we and Impax Laboratories, Inc. (Impax) entered into a definitive agreement (the Impax Agreement) pursuant to which we have granted Impax an exclusive worldwide license to our proprietary TRANSDUR transdermal delivery technology and other intellectual property to develop and commercialize ELADUR, in addition to selling certain assets and rights in and related to the product. Impax will control and fund the development and commercialization programs, and the parties will establish a joint management committee to oversee, review and coordinate the development and commercialization activities of the parties under the Impax Agreement. Please see "Third Party Collaborations" for additional information.

Clinical Program. In 2007, we reported positive results from a 60 patient Phase IIa clinical trial for ELADUR. In this study of patients suffering from PHN, ELADUR showed improved pain control versus placebo during the 3-day continuous treatment period. In addition, ELADUR appeared well tolerated overall, and patients treated with ELADUR and placebo exhibited similar safety profiles. After acquiring Alpharma, King altered the clinical and regulatory strategy for further development of this program to prioritize chronic low back pain. We reported top line data from a Phase II clinical trial conducted by King for ELADUR in April 2011. In this study of 263 patients suffering from chronic low back pain, the primary efficacy endpoint of demonstrating a positive treatment difference for the mean change in pain intensity scores from baseline to the mean of weeks 11 and 12 between ELADUR as compared to placebo was not met. Commencing in January 2014, Impax is now in charge of the future development program for ELADUR which will initially focus on developing the product for patients suffering from PHN.

TRANSDUR-Sufentanil Patch

Market Opportunity. Chronic pain affects as many as 100 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 over $3.0 billion in worldwide sales in 2012. Another major class of drugs utilized to treat chronic pain is transdermally delivered opioids such as Duragesic®, a leading transdermal fentanyl product, which with generic fentanyl patches accounted for approximately $900 million in worldwide sales in 2011. 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 fentanyl 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.

Clinical Program. In 2008, Endo, our former licensee, 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 a potential regulatory pathway for the Phase III program were reviewed with the FDA at an end-of-Phase II meeting on February 19, 2009. It is our expectation that future development of this product candidate may follow a 505(b)2 pathway as discussed with FDA, which would allow us to reference third-party data, potentially reducing time and expense. We are in discussions with potential collaborators regarding licensing development and commercialization rights to this program to which we hold worldwide rights.

ORADUR-ADHD Program

Market Opportunity. Attention Deficit Hyperactivity Disorder (ADHD) is a neurobehavioral condition that is estimated to affect over 5 million (approximately 9%) of U.S. children ages 3-17, according to the U.S. Department of Health and Human Services. The principal characteristics of ADHD are inattention, hyperactivity, and impulsivity. The condition presents itself in childhood and can be life long as a significant number of children with ADHD continue to present symptoms as adults. Over 50% of children with ADHD are estimated to being treated by medication, with stimulants such as amphetamine or methylphenidate as first-line treatments. U.S. sales of ADHD treatments were approximately $8.4 billion in 2012. The 2010 National Survey on Drug Use & Health estimates that 1.1 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. (Orient Pharma), 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 to ORADUR-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 in all territories other than the U.S. for ORADUR-ADHD. Since 2010, we and Orient Pharma have conducted several Phase I clinical trials in this program with multiple formulations. In 2013, we and Orient Pharma selected a lead formulation based on its potential for rapid onset of action, long duration for once-a-day dosing and target pharmacokinetic profile as demonstrated in a Phase 1 trial. In addition, this product candidate is expected to utilize a small capsule size relative to the leading existing long-acting products on the market. Orient Pharma has met with the Taiwan Food and Drug Administration (TFDA) to discuss the Phase 3 program in that market and is developing its plans for further development in the defined Asian and South Pacific countries to which it has rights from us. We retain rights to all other territories in the world and are initiating licensing discussions with other companies now that the lead formulation has been selected.

Relday

Market Opportunity. Risperidone is one of the most widely prescribed medications used to treat the symptoms of schizophrenia and bipolar I disorder in adults and teenagers 13 years of age and older. Relday is being developed to address unmet clinical needs in this large patient population. An existing long-acting injectable risperidone product, which achieved global net sales of $1.3 billion in 2013, requires twice monthly, intramuscular injections and drug reconstitution prior to use. We and Zogenix expect that, if approved, Relday will be the first once-monthly, subcutaneous antipsychotic product that may offer an improved pharmacokinetic profile, significant reduction in injection volume and a simplified dosing regimen. We and Zogenix also expect that, if approved, Relday will provide a new long-acting treatment option for patients that currently use daily oral antipsychotic products. The combined market for oral and injectable antipsychotic products is estimated at more than $17 billion in 2011.

Development Strategy. Under the development and license agreement entered into in July 2011 after working together since October 2007 under a feasibility agreement, Zogenix will be responsible for the clinical development and commercialization of a proprietary, long-acting injectable formulation of risperidone using our SABER controlled-release formulation technology. We will share non-clinical development responsibilities. On January 3, 2013, Zogenix reported positive single-dose pharmacokinetic (PK) results from the Phase 1 clinical trial of Relday. According to Zogenix, adverse events in the Phase 1 trial in patients diagnosed with schizophrenia were generally mild to moderate and consistent with other risperidone products. The Phase 1 clinical trial for Relday was conducted as a single-center, open-label, safety and PK trial of 30 patients with chronic, stable schizophrenia or schizoaffective disorder. Per Zogenix, based on the favorable safety and PK profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, Zogenix extended the study to include a 100 mg dose of the same formulation. In May 2013, Zogenix announced positive results with the 100 mg arm, demonstrating dose proportionality across the full dose range that would be anticipated to be used in clinical practice. According to Zogenix, the positive results from this study extension positions Zogenix to begin a multi-dose clinical trial, which would provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies, and Zogenix plans to commence this multi-dose clinical trial in the second half of 2014.

Depot Injectable Programs

In addition to biologic drugs, many traditional small molecule drugs have to be given by frequent injections, which is costly, inconvenient and may result in either unwanted side effects or suboptimal efficacy. We have active programs underway to improve our depot injectable systems and to apply those systems to various drugs and drug candidates, and have entered into a number of feasibility studies with biotechnology and pharmaceutical companies to test their products in our systems.

Research Programs in other Therapeutic Categories

We have underway a number of research programs covering medical diseases and conditions other than pain. Such programs include various diseases and disorders of the central nervous system, cardiovascular disease and metabolic disorders. In conducting our research programs and determining which particular efforts to prioritize for formal development, we employ a rigorous opportunity assessment process that takes into account the unmet medical need, commercial opportunity, technical feasibility, clinical viability, intellectual property considerations, and the development path including costs to achieve various critical milestones.

Industry Background

Chronic Diseases and Conditions

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

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. The proteins, peptides 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 destroyed before they can have an effect; if given by injection, they may be destroyed by the body's natural processes before they can reach their intended sites of action. The body's natural elimination processes require frequent, high dose injections that may result in unwanted side effects. As a result, the development of biotechnology molecules for the treatment of human diseases has been limited.

The Drug Delivery Industry. In the last forty 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 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 for weeks or months 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 immediate release 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 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 several major active technology platforms:

Bioerodible Injectable Depot Systems

Our bioerodible injectable depot systems include our SABER and CLOUD™ platform technologies. SABER 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 easily injectable with standard syringes and needles. After injection of a SABER formulation, the excipients diffuse away, leaving a viscous depot which provides controlled sustained release of drug. CLOUD is a new class of bioerodible injectable depot technology which generally does not contain SAIB but does include various other release rate modifying excipients and/or bioerodible polymers to achieve the delivery of drugs for periods of days to months from a single injection. We are researching and developing a variety of controlled-release products based on the SABER and CLOUD technologies. Based on research and development work to date, our bioerodible injectable depot technologies have shown the following advantages:

- *Peptide/Protein/Small Molecule Delivery*—The chemical nature of our bioerodible injectable depot systems tend to repel water and body enzymes from its interior and thereby stabilizes proteins and peptides. For this reason, we believe that bioerodible injectable depot systems are well suited as a platform for biotechnology therapeutics based on proteins and peptides.
- *Controlled Release and Onset*—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 our bioerodible injectable depots can be associated with less post-injection burst than is typically associated with other commercially available injectable controlled release technologies, while still achieving controlled rapid onset of drug concentration.
- *High Drug Loading*—Drug loading in our bioerodible injectable depot formulations 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, our bioerodible injectable depot formulations are fairly liquid and therefore can be injected through small needles. Additionally, because of the higher drug concentration of our bioerodible injectable depot 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*—Our bioerodible injectable depot technology is covered by United States and foreign patents. See "Patents, Licenses and Proprietary Rights" below.

- *Ease of Manufacture*—Compared to microspheres and other polymer-based controlled release injectable systems, our bioerodible injectable depot formulations are readily manufacturable at low cost.

The SABER Technology is the basis of POSIDUR, for which the FDA accepted our NDA submission in June 2013. The SABER Technology is also the basis for Relday, which has completed a single dose Phase I clinical trial in the U.S. In our clinical studies thus far, our bioerodible injectable depot formulations have been observed to be safe and well-tolerated, and no significant side effects or adverse events have been reported.

The SABER Technology is also the basis for SucroMate™ Equine, an injectable animal health drug utilizing our SABER technology to deliver the peptide deslorelin. This is the first FDA approved SABER injectable product and it was launched in 2011 by our collaborator, CreoSalus, Inc.

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 Phase II clinical trials have been conducted and for which we hold worldwide development and commercialization rights. The TRANSDUR technology is also the basis for ELADUR, for which two Phase II clinical trials have been conducted and for which we licensed worldwide development and commercialization rights to Impax in January 2014.

The ORADUR Sustained Release Gel Cap Technology

We believe that our ORADUR sustained release technology 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 and then snorting, smoking, injecting or extracting by mixing with alcohol or water) 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. Since 2006, we also worked with Pain Therapeutics and King on the development of three additional ORADUR abuse-resistant opioid drug candidates which would address the chronic pain market. Phase I clinical trials have been conducted for two of these ORADUR-based products (hydrocodone and hydromorphone), and an IND has been accepted by the FDA for the fourth ORADUR-based opioid (oxymorphone). We also have an ORADUR-ADHD program for which we and Orient Pharma have conducted several Phase I clinical trials with multiple formulations since 2010. In 2013, we and Orient Pharma selected a lead formulation based on based on its potential for rapid onset of action, long duration for once-a-day dosing and target pharmacokinetic profile as demonstrated in a Phase 1 trial.

The DURIN Biodegradable Implant Technology

Our DURIN technology is a proprietary biodegradable implant that enables parenteral delivery of drugs from several weeks to six months or more using our LACTEL brand polymers and co-polymers of lactic and glycolic acid. The DURIN technology can deliver a wide variety of drugs including small and large molecule compounds. Our proprietary implant design allows for a variety of possible delivery profiles including constant rate delivery. Because DURIN implants are biodegradable, at the end of its delivery life, what remains of the DURIN implant is absorbed by the body.

DURECT Strategy

Our objective is to become a specialty pharmaceutical company by developing, and in the future, commercializing products based on our pharmaceutical systems that address significant unmet 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 and metabolic 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 current efforts focus on using our versatile drug delivery platform technologies to develop products that address these medical conditions.

Minimize Product Development Risk. Initially, we intend to minimize product development risk 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;
- deliver drugs by injection or transdermally to eliminate the first pass effect whereby the efficacy of the active agent is impacted by digestion and deactivation;
- enhance drug performance by minimizing side effects; and
- expand uses of drugs by delivering them to the target site.

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

Enable the Development of Pharmaceutical Systems Based on Biotechnology and Other New Compounds. We believe there is a significant opportunity for pharmaceutical systems to add value to therapeutic medicine by administering biologics, such as proteins and peptides. We believe our technologies will improve the specificity, potency, convenience and cost-effectiveness of proteins, peptides, 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, CLOUD and DURIN 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 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 two programs for which New Drug Applications have been filed and a Complete Response Letters have been received, and six different other disclosed programs in clinical development, including three 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 Commercial Organization. In the future, we may elect to build our own commercial, sales and marketing capability in order to capture more of the economic value of certain products that we may develop. If we choose to enter into third-party collaborations to commercialize our pharmaceutical systems, we may in the future enter into these alliances under circumstances that allow us to participate in the sales and marketing of these products.

Third-Party Collaborations

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

Impax Laboratories, Inc. On January 3, 2014, we and Impax Laboratories, Inc. (Impax) entered into a definitive agreement (the Impax Agreement). Pursuant to the Agreement, we have granted Impax an exclusive worldwide license to our proprietary TRANSDUR transdermal delivery technology and other intellectual property to develop and commercialize ELADUR, our investigational transdermal bupivacaine patch for the treatment of pain associated with PHN, in addition to selling certain assets and rights in and related to the product. Impax will control and fund the development and commercialization programs, and the parties will establish a joint management committee to oversee, review and coordinate the development and commercialization activities of the parties under the Impax Agreement. Impax will reimburse us for certain future research and development we may be requested to conduct on the product.

In connection with the Impax Agreement, Impax agreed to pay us an upfront fee of $2.0 million in cash and to make contingent cash payments to us of up to $61.0 million payable based upon the achievement of predefined milestones, of which $31.0 million are development-based milestones and $30.0 million are commercialization-based milestones. Upon the first commercialization of ELADUR by Impax, we would also receive a tiered mid single-digit to low double-digit royalty on annual net product sales determined on a country-by-country basis. Impax is also required to pay to us a percentage of fees received in connection with any sublicense of the licensed rights. Impax may terminate the Impax Agreement without cause at any time upon prior written notice, and either party may terminate the Impax Agreement upon certain circumstances including written notice of a material uncured breach.

Zogenix, Inc. On July 11, 2011, we and Zogenix, Inc., (Zogenix), entered into a Development and License Agreement (the Zogenix Agreement). We and Zogenix had previously been working together under a feasibility agreement pursuant to which our research and development costs were reimbursed by Zogenix. Under the Zogenix Agreement, Zogenix will be responsible for the clinical development and commercialization of a proprietary, long-acting injectable formulation of risperidone using our SABER and other controlled-release depot formulation technologies. We will be responsible for non-clinical, formulation and CMC development activities. We will be reimbursed by Zogenix for our research and development efforts on the product. Zogenix paid a non-refundable upfront fee to us of $2.25 million in July 2011. Zogenix is obligated to pay us up to $103 million in total future milestone payments with respect to the product subject to and upon the achievement of various development, regulatory and sales milestones. Of these potential milestones, $28 million are development-based milestones (none of which has been achieved as of December 31, 2013), and $75 million are sales-based milestones (none of which has been achieved as of December 31, 2013). Zogenix is also required to pay a mid single-digit to low double-digit percentage patent royalty on annual net sales of the product determined on a jurisdiction-by-jurisdiction basis. The patent royalty term is equal to the later of the expiration of all DURECT technology patents or joint patent rights in a particular jurisdiction, the expiration of marketing exclusivity rights in such jurisdiction, or 15 years from first commercial sale in such jurisdiction. After the patent royalty term, Zogenix will continue to pay royalties on annual net sales of the product at a reduced rate for so long as Zogenix continues to sell the product in the jurisdiction. Zogenix is also required to pay to us a tiered percentage of fees received in connection with any sublicense of the licensed rights.

We granted to Zogenix an exclusive worldwide license, with sub-license rights, to the intellectual property rights related to the proprietary polymeric and non-polymeric controlled-release formulation technology to make and have made, use, offer for sale, sell and import risperidone products, where risperidone is the sole active agent, for administration by injection in the treatment of schizophrenia, bipolar disorder or other psychiatric related disorders in humans. We retain the right to supply Zogenix's Phase 3 clinical trial and commercial product requirements on the terms set forth in the Zogenix Agreement. We retain the right to terminate the Zogenix Agreement with respect to specific countries if Zogenix fails to advance the development of the product in such country, either directly or through a sublicensee. In addition, either party may terminate the Zogenix Agreement upon insolvency or bankruptcy of the other party, upon written notice of a material uncured breach or if the other party takes any act impairing such other party's relevant intellectual property rights. Zogenix may terminate the Zogenix Agreement upon written notice if during the development or commercialization of the product, the product becomes subject to one or more serious adverse drug experiences or if either party receives notice from a regulatory authority, independent review committee, data safety monitoring board or other similar body alleging significant concern regarding a patient safety issue. Zogenix may also terminate the Zogenix Agreement with or without cause, at any time upon prior written notice. As of December 31, 2013, the cumulative aggregate payments received by us under this agreement and the prior feasibility agreement were $10.6 million.

Hospira, Inc. In June 2010, we entered into a license agreement with Hospira to develop and commercialize POSIDUR in the U.S. and Canada. Under terms of the agreement, Hospira made an upfront payment of $27.5 million. In March 2012, we were notified that Hospira was terminating the agreement effective September 28, 2012, or, as permitted under the agreement, at an earlier date elected by us. Hospira's termination returned to us the U.S. and Canadian rights to develop and commercialize POSIDUR and we now hold worldwide rights to POSIDUR. As a result of the termination of the Hospira agreement for POSIDUR, we recognized as revenue during the first quarter of 2012 the remaining $21.8 million of deferred revenue related to the upfront fee of the development and license agreement as we have no remaining performance obligations under the agreement; this recognition of revenue did not result in additional cash proceeds to us. As of December 31, 2013, the cumulative aggregate payments received by us under this agreement were $40.7 million. There will be no further payments under this agreement in the future.

Alpharma Ireland Limited (acquired in December 2008 by King which subsequently was acquired by Pfizer in February 2011). 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 effective in October 2008. Under the terms of the agreement, Alpharma paid us an upfront license fee of $20 million. As a result of the acquisition of Alpharma by King in December 2008, King assumed Alpharma's rights and obligations under the agreement. In February 2011, Pfizer acquired King and thereby assumed the rights and obligations of King with respect to ELADUR. In February 2012, Pfizer notified us that they were returning their worldwide development and commercialization rights to ELADUR. As a result of the termination of the agreement for ELADUR, we recognized as revenue during the first quarter of 2012 the remaining $9.9 million of deferred revenue related to the upfront fee of the development and license agreement as we have no remaining performance obligations under the agreement; this recognition of revenue did not result in additional cash proceeds to us. As of December 31, 2013, the cumulative aggregate payments received by us under this agreement were $29.2 million. There will be no further payments under this agreement in the future.

Nycomed Danmark ApS. In November 2006, we entered into a collaboration agreement with Nycomed, and this agreement was amended in February 2010 and February 2011. Under the terms of the 2010 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. Nycomed also paid a portion of development expenses. In January 2012, Nycomed (acquired by Takeda in October 2011) notified us that it was terminating the license agreement with us, and thereby returning their right to develop and commercialize POSIDUR (SABER™-Bupivacaine) in Europe and their other licensed territories to us effective April 26, 2012. As a result of the termination of the Nycomed agreement for POSIDUR, we recognized as revenue during the first quarter of 2012 the remaining $3.7 million of deferred revenue related to the upfront fee of the development and license agreement as we have no remaining performance obligations under the agreement; this recognition of revenue did not result in additional cash proceeds to us. As of December 31, 2013, the cumulative aggregate payments received by us under this agreement were $37.3 million. In addition, the cumulative aggregate payments paid by us under this agreement to Nycomed were $9.0 million as of December 31, 2013. There will be no further payments under this agreement in the future.

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 worldwide commercialization rights (except for Australia and New Zealand) to certain products developed under the agreement (including REMOXY) to King. In February 2011 Pfizer acquired King and thereby assumed the rights and obligations of King with respect to the sublicense agreement. In December 2005, we amended our agreement with Pain Therapeutics in order to specify our obligations with respect to the supply of key excipients for use in the licensed products. Under the 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, 2013, 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, 2013, the cumulative aggregate payments received by us from Pain Therapeutics under this agreement were $34.2 million.

In March 2009, King assumed the responsibility for further development of REMOXY from Pain Therapeutics. As a result of this change, we 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 (now Pfizer) as of December 31, 2013 were $7.1 million under this agreement.

Starting in 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 2008 and 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.

Long Term Supply Agreement with King (now Pfizer). In August 2009, we entered into an exclusive long term excipient supply agreement with respect to REMOXY with King. In February 2011, Pfizer acquired King and thereby assumed the rights and obligations of King with respect to the long term excipient supply agreement. 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 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.

In 2011, 2012 and 2013, the Company recognized $490,000, $48,000 and $273,000 of product revenue, respectively, related to key excipients for REMOXY and the associated cost of goods sold was $302,000, $33,000 and $165,000, respectively.

Commercial Product Lines

ALZET

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 six 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 13,000 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 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 products based on our pharmaceutical systems to leverage the established sales organizations that certain pharmaceutical companies have in markets we are targeting. In the future, we may elect to build our own commercial, sales and marketing capability in order to capture more of the economic value of certain products that we may develop. If we choose to enter into third-party collaborations to commercialize our pharmaceutical systems, we may in the future enter into these alliances under circumstances that allow us to participate in the sales and marketing of these products. 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 and LACTEL product lines through a direct sales force in the U.S. and through a network of distributors outside of the U.S.

Suppliers

We purchase sucrose acetate isobutyrate, a raw material for our ORADUR and SABER-based pharmaceutical systems, including POSIDUR, REMOXY and other ORADUR-based drug candidates, pursuant to a supply agreement with Eastman Chemical Company. We have entered into a supply agreement with Corium International, Inc. for clinical and commercial supplies of ELADUR and a supply agreement with Hospira Worldwide, Inc. for clinical and commercial supplies of POSIDUR.

Our supply agreement with Eastman Chemical Company requires us to purchase a certain portion of our requirements for sucrose acetate isobutyrate from Eastman Chemical and obligates us to pay a 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.

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 principally are derived from sale of the ALZET product line to academic and pharmaceutical industry researchers, the LACTEL product lines to pharmaceutical and medical device customers, and from the sale of certain key excipients that are included in REMOXY to our customer (Pfizer). Until such time that we are able to bring our pharmaceutical systems to market, if at all, we expect these to be our principal sources of product revenue. We also receive revenue from collaborative research and development arrangements with our third-party collaborators. In 2013, Tolmar Inc. accounted for 15% of our total revenues. In 2012, Hospira and Pfizer accounted for 45% and 22% of our total revenues, respectively. In 2011, Hospira and Pfizer accounted for 34% and 16% of our total revenues, 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 California that we have used to manufacture research and clinical supplies of several of our pharmaceutical systems under GMP, including POSIDUR, REMOXY, TRANSDUR-Sufentanil, and ELADUR. 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 potentially constructing additional manufacturing space at our current facilities in California and Alabama. We manufacture our ALZET product line and certain key components for REMOXY at one of our California facilities and our LACTEL product line at our Alabama facility.

Patents, Licenses and Proprietary Rights

Our success depends in part on our ability to obtain patents, to protect trade secrets, to operate without infringing upon the proprietary rights of others and to prevent others from infringing on our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. As of February 14, 2014, we held over 50 unexpired issued U.S. patents and over 300 unexpired issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have over 50 pending U.S. patent applications and over 100 foreign applications pending in Europe, Australia, Japan, Canada and other countries.

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 typically 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, derivation, post-grant oppositions, and similar proceedings may be necessary to determine rights to inventions in our patents and patent applications. Litigation or similar 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 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 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.

On April 19, 2011, the Office of National Drug Control Policy (ONDCP) released the Obama Administration's *Epidemic: Responding to America's Prescription Drug Abuse Crisis*—a comprehensive action plan to address the national prescription drug abuse epidemic. This plan includes action in four major areas to reduce prescription drug abuse: education, monitoring, proper disposal, and enforcement. In support of the action plan, the FDA announced the elements of a Risk Evaluation and Mitigation Strategy (REMS) that will require all manufacturers of long-acting and extended-release opioids to ensure that training is provided to prescribers of these medications and to develop information that prescribers can use when counseling patients about the risks and benefits of opioid use. The FDA wants drug makers to work together to develop a single system for implementing the REMS strategies.

Many of our drug candidates including REMOXY, our other ORADUR-based 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, which could negatively impact us and our collaborators.

Competition

We may face competition from other companies in numerous industries including pharmaceuticals, medical devices and drug delivery. POSIDUR, TRANSDUR-Sufentanil, ELADUR, Relday, REMOXY and other ORADUR-based drug candidates, if approved, will compete with currently marketed oral opioids, transdermal opioids, local anesthetic patches, anti-psychotics, 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, Knoll, Janssen, Medtronic, Endo, AstraZeneca, Arrow International, Tricumed, Kimberly-Clark, Cumberland Pharmaceuticals, Cadence Pharmaceuticals, Pacira, Acorda Therapeutics, Mallinckrodt, Shire, Johnson & Johnson, Eli Lilly, Pfizer, Novartis and others. Our ORADUR-ADHD product candidates, if approved, will compete with currently marketed or approved products by Shire, Johnson & Johnson, UCB, Novartis, Noven, Celgene, Eli Lilly, Pfizer and others. Relday, if approved, will compete with currently marketed products by Johnson & Johnson, Eli Lilly, Astra Zeneca, Pfizer, Bristol-Myers Squibb 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, Immune Pharmaceuticals, Innocoll, Nektar, Kimberly-Clark, Acorda Therapeutics, Flamel, Alexza, Cadence Pharmaceuticals, Hospira, Cumberland Pharmaceuticals, Egalet, Acura, Elite Pharmaceuticals, Phosphagenics, Intellipharmaceutics, Collegium Pharmaceutical, Heron Therapeutics 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.

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 10260 Bubb Road, Cupertino, California, 95014. Our telephone number is (408) 777-1417, and our website 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 website 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 14, 2014 we had 101 employees, including 54 in research and development, 21 in manufacturing and 26 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 14, 2014 are as follows:

Name	Age	Position
Felix Theeuwes, D.Sc.	76	Chairman, Chief Scientific Officer and Director
James E. Brown, D.V.M.	57	President, Chief Executive Officer and Director
Matthew J. Hogan, M.B.A.	54	Chief Financial Officer
Su Il Yum, Ph.D.	74	Executive Vice President, Pharmaceutical Systems Research and Development

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

James E. Brown, D.V.M. co-founded DURECT in February 1998 and has served as our President, Chief Executive Officer and a Director since June 1998. He previously worked at ALZA Corporation as Vice President of Biopharmaceutical and Implant Research and Development from June 1995 to June 1998. Prior to that, Dr. Brown held various positions at Syntex Corporation, a pharmaceutical company, including Director of Business Development from May 1994 to May 1995, Director of Joint Ventures for Discovery Research from April 1992 to May 1995, and held a number of positions including Program Director for Syntex Research and Development from October 1985 to March 1992. Dr. Brown holds a B.A. from San Jose State University and a D.V.M. (Doctor of Veterinary Medicine) from the University of California, Davis where he also conducted post-graduate work in pharmacology and toxicology.

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

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

Pfizer may discontinue development of REMOXY

We rely on Pfizer and its subsidiaries to devote time and resources to the development, manufacturing and commercialization of REMOXY. Pfizer has indicated that they would not expect to resubmit the NDA in response to the Complete Response Letter before mid-2015. There can be no assurance that Pfizer will continue development of REMOXY. Pfizer and its subsidiaries and affiliates may commercialize, develop or acquire drugs or drug candidates that may compete directly or compete for resources with REMOXY. For instance, Pfizer is developing ALO-02 (an extended release abuse resistant formulation of oxycodone that would compete with REMOXY) and owns Embeda® (an extended-release oral formulation of morphine sulfate), and Avinza® (a once-daily morphine treatment for moderate to severe pain). If Pfizer does not continue development of REMOXY, rights to REMOXY may revert to Pain Therapeutics, which may not continue REMOXY development either. If Pfizer continues development of REMOXY, there can be no assurance that their resubmission of the NDA will be timely, or that it will satisfy the FDA's requirements. Any discontinuation or delay in the development of REMOXY will significantly harm our prospects and would be likely to have a negative effect on the price of our common stock.

Regulatory approval of POSIDUR has been delayed, and regulatory approval of our other product candidates is subject to delay or may be denied, which could harm our business

In February 2014, we received a Complete Response Letter to our NDA for POSIDUR from the FDA. Based on its review, the FDA has determined that they cannot approve the NDA in its present form, stating the NDA does not contain sufficient information to demonstrate that POSIDUR is safe when used in the manner described in the proposed label, and the FDA has indicated that additional clinical safety studies need to be conducted. The failure to adequately demonstrate the safety and effectiveness of a pharmaceutical product candidate under development to the satisfaction of FDA and other regulatory agencies has, with respect to POSIDUR and could with respect to other product candidates delay or prevent regulatory clearance of the potential product candidate, resulting in delays to the commercialization of our product candidate, 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 product candidates, and thus our product candidates may not be approved for marketing. During the review process, the FDA may request more information regarding the safety of our product candidates, as they have in their Complete Response Letter for POSIDUR, and answering such questions could require significant additional work and expense, and take a significant amount of time, resulting in a material delay of approval or the failure to obtain approval. During the review process, the FDA may also request more information regarding the chemistry, manufacturing or controls related to our product candidates, as they have in their Complete Response Letter for REMOXY, and answering such questions could require significant additional work and expense, and take a significant amount of time, resulting in a material delay of approval or the failure to obtain approval.

Development of our pharmaceutical product candidates is not complete, and we cannot be certain that our product candidates 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 product candidates under development. For each product candidate 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 a drug delivery technology to deliver the proper dose of drug over the desired period of time;
- determining the appropriate drug dosage for use in the pharmaceutical product candidate;
- 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 product candidate in commercial quantities and at acceptable cost.

The time frame necessary to achieve these developmental milestones for any individual product is long and uncertain, and we may not successfully complete these milestones for any of our products in development. We have not yet completed development of POSIDUR, TRANSDUR-Sufentanil, ELADUR, Relday, REMOXY and our other ORADUR-based drug candidates, and we have limited experience in developing such products. We may not be able to finalize the design or formulation of any of these product candidates. In addition, we may select components, solvents, excipients or other ingredients to include in our product candidates 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 product candidates. Even after we complete the design of a product candidate, the product candidate must still complete required clinical trials and additional safety testing in animals before approval for commercialization. We are continuing testing and development of our product candidates and may explore possible design or formulation changes to address issues of safety, manufacturing efficiency and performance. We or our collaborators may not be able to complete development of any product candidates 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, Relday, REMOXY and our other ORADUR-based drug candidates, or other product candidates, we will not be able to earn revenue from them, which would materially harm our business.

We or our third-party collaborators must show the safety and efficacy of our drug candidates in animal studies and human clinical trials to the satisfaction of regulatory authorities before they can be sold; failure to obtain approvals for REMOXY, POSIDUR or our other product candidates would significantly harm our business, prospects and financial condition

Before we or our third-party collaborators can obtain government approval to sell any of our pharmaceutical product candidates, 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 2010, King (now Pfizer) resubmitted the NDA in response to a Complete Response Letter received in December 2008 by Pain Therapeutics. On June 23, 2011, a Complete Response Letter from the FDA was received by Pfizer on the resubmission to the NDA for REMOXY. The issues raised in the Complete Response Letter relate primarily to manufacturing. Pfizer has efforts underway to resolve these issues. In October 2013, Pfizer stated that, having achieved technical milestones related to manufacturing, they will continue the development program for REMOXY®. Following guidance received from the FDA earlier in 2013, Pfizer announced that they will proceed with the additional clinical studies and other actions required to address the Complete Response Letter. These new clinical studies will include, in part, a pivotal bioequivalence study with the modified REMOXY formulation to bridge to the clinical data related to the original REMOXY formulation, and an abuse-potential study with the modified formulation. As previously disclosed, the complete response submission is not expected to occur prior to mid-2015.
- POSIDUR—A total of 15 clinical trials in subjects undergoing various surgical procedures have been conducted with POSIDUR. In all, 1,060 subjects have been studied in the POSIDUR Phase 2 and 3 clinical development program, of which 668 have been treated with POSIDUR, 268 with SABER-Placebo (SABER vehicle without drug), and 124 with bupivacaine HCl solution. In July 2012, we completed pre-NDA communications with the FDA regarding POSIDUR. Through this process, we have received guidance and thoughtful comments from the FDA covering various chemistry, manufacturing, non-clinical, clinical pharmacology, clinical, statistical and product labeling topics based on our pre-NDA meeting questions. In April 2013, we submitted a new drug application as a 505(b)(2) application, which relies in part on the FDA's findings of safety and effectiveness of a reference drug. In June 2013, we announced that our NDA submission

had been accepted by the FDA indicating that the application is sufficiently complete to permit a substantive review. In February 2014, we received a Complete Response Letter from the FDA. Based on its review, the FDA has determined that they cannot approve the NDA in its present form, stating the NDA does not contain sufficient information to demonstrate that POSIDUR is safe when used in the manner described in the proposed label, and the FDA has indicated that additional clinical safety studies need to be conducted. We are evaluating the issues and recommendations described in the Complete Response Letter and plan to have further discussions with the FDA around them. There can be no assurance that we will be able to adequately address all of FDA's concerns regarding the POSIDUR NDA or there could be a delay in addressing such concerns, the FDA may not grant regulatory approval of POSIDUR, adverse effects may arise from additional testing or use of POSIDUR, and the data that we have generated or may generate may not be deemed sufficient by FDA or other regulatory agencies to support regulatory approval of POSIDUR.

- ELADUR—A Phase IIa clinical trial in post-herpetic neuralgia (PHN or post-shingles pain) was completed and positive efficacy trends were reported in the fourth quarter of 2007. King, which assumed worldwide development and commercialization rights for ELADUR through its acquisition of Alpharma, conducted a Phase II clinical trial to evaluate ELADUR for the treatment of chronic low back pain and reported in April 2011 that the primary efficacy endpoint for the trial was not met. In February 2012, Pfizer, which assumed worldwide development and commercialization rights to ELADUR through its acquisition of King, notified us that they were returning their worldwide development and commercialization rights to ELADUR. In January 2014, we and Impax entered into an agreement, pursuant to which we have granted Impax an exclusive worldwide license to our proprietary TRANSDUR® transdermal delivery technology and other intellectual property to develop and commercialize ELADUR. There can be no assurance that Impax will be able to successfully develop ELADUR to obtain marketing approval by the FDA or other regulatory agencies.
- TRANSDUR-Sufentanil Patch—In February 2009, an end-of-Phase II meeting with the FDA was conducted for this program outlining a potential regulatory pathway for the Phase III program and NDA submission. In 2011, we had discussions with the FDA and regulatory agencies in several major European countries to better understand development requirements for U.S. and European countries. We are in discussions with potential partners regarding licensing development and commercialization rights to this program to which we hold worldwide rights. 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.
- ORADUR-based opioids—Phase I clinical trials have been conducted for two of these ORADUR-based product candidates (hydrocodone and hydromorphone), and an IND has been accepted by the FDA for the third ORADUR-based opioid (oxymorphone). In October 2013, Pain Therapeutics stated that it had regained all rights from Pfizer with respect to the three ORADUR-based opioid drug candidates (hydrocodone, hydromorphone and oxymorphone). Pain Therapeutics stated that they have not yet made a decision to develop or out-license these three product candidates. There can be no assurance that we or our collaborators will be able to successfully develop ORADUR-based formulations of hydrocodone, hydromorphone or oxymorphone to obtain marketing approval by the FDA or other regulatory agencies.
- ORADUR-ADHD—Since 2010, we and Orient Pharma have conducted several Phase I studies to evaluate multiple formulations of ORADUR-Methylphenidate. We and Orient Pharma recently selected a lead formulation containing the active pharmaceutical ingredient methylphenidate. This formulation was chosen based on its potential for rapid onset of action, long duration for once-a-day dosing and target pharmacokinetic profile as demonstrated in a recent Phase 1 trial. In addition, this product candidate will utilize a small capsule size relative to the leading existing long-acting products on the market. Orient Pharma has met with the Taiwan Food and Drug Administration (TFDA) to discuss the Phase 3 program in that market and is developing its plans for further development in the defined Asian and South Pacific countries to which it has rights from us. DURECT retains rights to all other territories in the world and is initiating licensing discussions with other companies now that the lead formulation has been selected. There can be no assurance that we will be able to successfully develop ORADUR-methylphenidate to obtain marketing approval by the TFDA or the U.S. FDA or other regulatory agencies, nor is there any assurance that we will be able to find a collaborator with respect to the development and commercialization of this drug candidate for the territories not currently licensed to Orient Pharma.
- Relday—In January 2013, Zogenix announced positive single-dose pharmacokinetic (PK) results from the Phase 1 clinical trial of Relday. Per Zogenix, based on the favorable safety and PK profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, Zogenix extended the study to include a 100 mg dose of the same formulation. In May 2013, Zogenix announced positive results with the 100 mg arm, demonstrating dose proportionality across the full dose range that would be anticipated to be used in clinical practice. According to Zogenix, the positive results from this study extension positions Zogenix to begin a multi-dose clinical trial, which would provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies, and Zogenix plans to commence this multi-dose clinical trial in the second half of 2014. There can be no assurance that Zogenix will commence the multi-dose clinical trial in the second half of 2014 or that the results of such a trial will warrant continued development of Relday.

We are currently in the clinical, preclinical or research stages with respect to all our other product candidates 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 product candidates. 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 data supportive of the safety or efficacy of our drug candidates or required for regulatory approval.

Early clinical trial results may not predict the results of later trials, and our clinical trials or those of our collaborators for POSIDUR or REMOXY may not satisfy regulatory agencies

While some clinical trials of our product candidates have shown indications of safety and efficacy of our product candidates, there can be no assurance that these results will be confirmed in subsequent clinical trials or provide a sufficient basis for regulatory approval. In addition, side effects observed in clinical trials, or other side effects that appear in later clinical trials, may adversely affect our or our collaborators' ability to obtain regulatory approval or market our product candidates. For example, in the Phase IIb hysterectomy trial and the BESST Phase III abdominal surgery trial of POSIDUR, transient local hematoma-like discolorations were observed near the surgical site. Side effects such as these, toxicity or other safety issues associated with the use of our drug candidates could require us to perform additional studies or halt development of our drug candidates. 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 product candidates which we have not planned or anticipated. For example, the FDA's Complete Response Letter raised concerns related to, among other matters, the Chemistry, Manufacturing, and Controls section of the NDA for REMOXY. There can be no assurance that Pfizer will resolve these issues to the satisfaction of the FDA in a timely manner or ever, which could harm our business, prospects and financial condition. Further, the FDA's Complete Response Letter for POSIDUR raised concerns that insufficient safety data had been provided and FDA has indicated that additional clinical safety trials for POSIDUR need to be conducted, which would be expensive and could delay product approval, harming our business, prospects and financial condition.

Regulatory action or failure to obtain product approvals could delay or limit development and commercialization of our product candidates and result in failure to achieve anticipated revenues

The manufacture and marketing of our pharmaceutical product candidates 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, 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 studies 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 product candidates. 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 product candidates.

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

Many of our drug candidates under development, including REMOXY, our other ORADUR-based opioids and TRANSDUR-Sufentanil are subject to mandatory Risk Evaluation and Mitigation Strategy (REMS) programs, which could delay the approval of these drug candidates, reduce demand for them, and increase the cost, burden and liability associated with their commercialization

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.

On April 19, 2011, the Office of National Drug Control Policy (ONDCP) released the Obama Administration's *Epidemic: Responding to America's Prescription Drug Abuse Crisis*—a comprehensive action plan to address the national prescription drug abuse epidemic. This plan includes action in four major areas to reduce prescription drug abuse: education, monitoring, proper disposal, and enforcement. In support of the action plan, the FDA announced the elements of a Risk Evaluation and Mitigation Strategy (REMS) that will require all manufacturers of long-acting and extended-release opioids to ensure that training is provided to prescribers of these medications and to develop information that prescribers can use when counseling patients about the risks and benefits of opioid use. The FDA wants drug makers to work together to develop a single system for implementing the REMS strategies.

On July 9, 2012 the FDA approved a REMS for extended-release (ER) and long-acting (LA) opioids. The REMS is part of a federal initiative to address the prescription drug abuse, misuse, and overdose epidemic. The REMS introduces new safety measures designed to reduce risks and improve the safe use of ER/LA opioids, while ensuring access to needed medications for patients in pain. The new ER/LA opioid REMS will affect more than 20 companies that manufacture these opioid analgesics. Under the new REMS, companies will be required to make education programs available to prescribers based on an FDA Blueprint. It is expected that companies will meet this obligation by providing educational grants to continuing education (CE) providers, who will develop and deliver the training. The REMS also will require companies to make available FDA-approved patient education materials on the safe use of these drugs. The companies will be required to perform periodic assessments of the implementation of the REMS and the success of the program in meeting its goals. The FDA will review these assessments and may require additional elements to achieve the goals of the program.

On September 10, 2013, the FDA announced safety labeling changes and post-market study requirements for extended-release and long-acting opioid analgesics (ER/LA opioids). The updated class-wide labeling changes state that ER/LA opioids are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The updated indication further clarifies that, because of the risks of addiction, abuse, and misuse, even at recommended doses, and because of the greater risks of overdose and death, these drugs should be reserved for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain; ER/LA opioid analgesics are not indicated for as-needed pain relief. Recognizing that more information is needed to assess the serious risks associated with long-term use of ER/LA opioids, the FDA is requiring the drug companies that make these products to conduct further post-market studies and clinical trials. These changes may result in a decrease in prescriptions for this class of drugs and will increase the costs borne by manufacturers of ER/LA opioids.

Many of our drug candidates including REMOXY, our other ORADUR-opioid drug candidates and TRANSDUR-Sufentanil are subject to the REMS requirement. The FDA's REMS requirements have been evolving, and 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, as well as decreased demand resulting from new labeling requirements, which could negatively impact the commercial benefits to us and our collaborators from the sale of these drug candidates.

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 product candidates 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 product candidates. We have entered into agreements with Pain Therapeutics, King (now Pfizer), Orient Pharma, Zogenix, Impax 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, Relday, Eladur and other product candidates, 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 product candidates, 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. Enforcing any of these agreements in the event of a breach by the other party could require the expenditure of significant resources and consume a significant amount of management time and attention. Our collaborators may also conduct their activities in a manner that is different from the manner we would have chosen, had we been developing such product candidates ourselves. Further, our collaborators may elect not to develop or commercialize product candidates arising out of our collaborative arrangements or not devote sufficient resources to the development, clinical trials, regulatory approval, manufacture, marketing or sale of these product candidates. If any of these events occur, we may not recognize revenue from the commercialization of our product candidates 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 product candidates. We may not be able to control public disclosures made by some of our third-party collaborators, which could negatively impact our stock price.

Cancellation of our collaboration agreements may impact our near-term revenues and adversely affect potential economic benefits

Our collaboration agreements with third parties typically allow the third party to terminate the agreement by providing notice to us. For example, in January 2012, we were notified that Nycomed was terminating the Development and License Agreement between Nycomed and us relating to the development and commercialization of POSIDUR in Europe and their other licensed territories. In February 2012, we were notified that Pfizer was terminating the worldwide Development and License Agreement between Alpharma (acquired by King which subsequently was acquired by Pfizer) and us relating to the development and commercialization of ELADUR. In March 2012, we were notified that Hospira was terminating the Development and License Agreement between Hospira and us relating to the development and commercialization of POSIDUR in the United States and Canada. Termination of such agreements can lead to a near-term increase in our reported revenues resulting from the immediate recognition of payments that would otherwise have been recognized over time. Termination deprives us of potential future economic benefits under such agreements, and may make it more difficult to enter into agreements with other third parties for use of the assets that were subject to the terminated agreement. Termination of our agreements with Pain Therapeutics, Zogenix or Impax, or Pfizer's agreement with Pain Therapeutics, could have similar effects.

Our 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. Acquisitions of our collaborators can be disruptive

Our 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 product candidates, or can lead to lengthy, expensive litigation or arbitration. In general, our collaboration agreements, including our

agreements with Pain Therapeutics and King (now Pfizer) with respect to REMOXY, Pain Therapeutics with respect to the other ORADUR-based products incorporating specified opioids, Orient Pharma with respect to ORADUR-Methylphenidate, Zogenix with respect to Relday, and Impax with respect to Eladur, 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. From time to time, our licensees may be the subject of an acquisition by another company. For example, Alpharma was acquired by King in December 2008, in February 2011 King was acquired by Pfizer and, in October 2011 Nycomed was acquired by Takeda. Such transactions can lead to turnover of program staff, a review of development programs and strategies by the acquirer, and other events that can disrupt a program, resulting in program delays or discontinuations.

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

Our cash flows are likely to differ from our reported revenues

Our revenues will likely differ from our cash flows from revenue-generating activities. Upfront payments received upon execution of collaborative agreements are recorded as deferred revenue and generally recognized on a straight-line basis over the period of our continuing involvement with the third-party collaborator pursuant to the applicable agreement. The period of continuing involvement may also be revised on a prospective basis. For example, in the first quarter of 2012, we revised the period of continuing involvement related to the termination of our collaborations with Nycomed, Hospira, and Pfizer, resulting in the accelerated recognition of approximately $35.4 million in revenue from upfront payments received in earlier periods; this recognition of revenue in the first quarter of 2012 had no impact on cash flow during the period. As of December 31, 2013, we had $1.6 million of deferred revenue which will be recognized in future periods and may cause our reported revenues to be greater than cash flows from our ongoing revenue-generating activities.

Our 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 development activities or sales accomplishments. While our involvement is necessary to the achievement of development-based milestones, the performance of our third-party collaborators is also required to achieve those milestones. Under our third-party collaborative agreements, our third party collaborators will take the lead in commercialization activities and we are typically not involved in the achievement of sales-based milestones. Therefore, we are even more dependent upon the performance of our third-party collaborators in achieving sales-based milestones. To the extent we and our third-party collaborators do not achieve such development-based milestones or our third-party collaborators do not achieve sales-based 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 product candidates. The negotiation and consummation of these types 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 will require and 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 product candidates. 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 product candidates. 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:

- regulatory actions with respect to our product candidates;
- 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 product candidates;
- costs involved in establishing manufacturing capabilities for clinical and commercial quantities of our product candidates;
- competing technological and market developments;
- market acceptance of our product candidates;
- 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 product candidates 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 delays in generating future product revenue.

We and our third-party collaborators may not be able to manufacture sufficient quantities of our pharmaceutical product candidates 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 product candidates 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 product candidates are complex. We and our third-party collaborators, where relevant, have not yet completed development of the manufacturing process for any product candidates or components, including REMOXY and our other ORADUR-based drug candidates, POSIDUR, ELADUR, Relday, and TRANSDUR-Sufentanil. If we and our third-party collaborators, where relevant, fail to timely complete the development of the manufacturing process for our product candidates, we and our third-party collaborators, where relevant, will not be able to timely produce product for clinical trials and commercialization of our product candidates. We have also committed to manufacture and supply product candidates 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 product candidate or component at an acceptable cost, then we and our third-party collaborators may not be able to commercialize that product candidate 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 product candidates, including POSIDUR, REMOXY and our other ORADUR-based drug candidates, ELADUR, Relday and TRANSDUR-Sufentanil. We have not manufactured commercial quantities of any of our product candidates. In the future, we intend to develop additional manufacturing capabilities for our product candidates and components to meet our demands and those of our third-party collaborators by contracting with third-party manufacturers and by potentially constructing additional manufacturing space at our facilities in California and Alabama. We have limited experience building and validating manufacturing facilities, and we may not be able to accomplish these tasks in a timely or cost effective manner.

If we and our third-party collaborators, where relevant, are unable to manufacture our pharmaceutical product candidates 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 product candidates 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 product candidates and those of our third-party collaborators.

We have entered into a supply agreement with Hospira Worldwide, Inc. for clinical and commercial supplies of POSIDUR and a supply agreement with Corium International, Inc. for clinical and commercial supplies of ELADUR. 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 product candidates or supply required components for our product candidates. 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 our pharmaceutical product candidates 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 product candidates 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 product candidates, 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 product candidates under development; or
- FDA required product withdrawals or warnings arising from identification of serious and unanticipated adverse side effects in our product candidates.

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 product candidates. If we, our third-party collaborators or our respective suppliers do not achieve compliance for our product candidates 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 product candidates.

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, 2013, had an accumulated deficit of approximately $360.8 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 product candidates, obtain the required regulatory clearances, and manufacture and market our proposed product candidates. Development of pharmaceutical product candidates 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 product candidates. The license fees for these technologies or rights would increase the costs of our product candidates.

To date, we have not generated significant revenue from the commercial sale of our pharmaceutical product candidates and do not expect to do so in the near future. Our current revenues are from the sale of the ALZET product line, the sale of LACTEL biodegradable polymers and certain excipient sales, and from payments under collaborative research and development agreements with third parties. In the year ended December 31, 2012, we had a one-time increase in revenues resulting from the recognition of previously deferred revenues associated with upfront payments from terminated agreements. These revenues represented the recognition of deferred revenue for cash received in earlier periods and we do not expect this to recur. 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 product candidates 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 and commercial group to market future products but we have limited sales and marketing experience with respect to pharmaceuticals and may not be able to do so effectively

We have a small sales and marketing group focused on our ALZET and LACTEL product lines. We may choose to develop our own sales force and commercial group to market products that we may develop in the future, or to market POSIDUR if we do not enter into an agreement with a third party to commercialize POSIDUR. Developing a sales force and commercial group will require substantial expenditures and the hiring of qualified personnel. We have limited sales and marketing experience, and may not be able to effectively recruit, train or retain sales personnel. If we are not able to put in place an appropriate sales force and commercial group for POSIDUR, we may not be able to effectively launch the product. We may not be able to effectively sell our product candidates, 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 product candidates 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 product candidates;
- 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 product candidates; or
- build up inventory in excess of demand thereby limiting future purchases of our product candidates resulting in significant quarter-to-quarter variability in our sales.

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

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

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 product candidates. For example, we currently depend on third-party vendors to manage and monitor our clinical trials and to perform critical manufacturing steps for our product candidates. These third parties may not execute their responsibilities and tasks competently in compliance with applicable laws and regulations or in a timely fashion. We rely on third-parties to manufacture or perform manufacturing steps relating to our product candidates 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 product candidates. 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 product candidates 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 product candidates (including POSIDUR, REMOXY, our other ORADUR-based drug candidates, ELADUR, Relday and TRANSDUR-Sufentanil) 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-based drug candidates, ELADUR, Relday 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 product candidate 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 pharmaceutical product candidates, but do not have in place long term supply agreements with respect to all of the components of any of our product 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 product candidates 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 product candidates, causing us to lose sales, incur additional costs, delay new product introductions and could harm our reputation.

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 ability to commercially exploit our products will depend significantly on our ability to obtain and maintain patents, maintain trade secret protection and operate without infringing the proprietary rights of others.

The patent status of our lead drug candidates, REMOXY and POSIDUR, are as follows:

In the U.S., REMOXY is covered by six patent families. Three patent families include granted patents expiring in at least 2015, 2025, and 2031, respectively. The patent family providing protection until at least 2025 includes six granted patents. The other three patent families include pending patent applications, which if granted, could result in patents expiring in 2028, 2034, and 2034, respectively, plus any eligible patent term adjustments and extensions. We currently have pending U.S. applications for these six patent families. There can be no assurance that the pending patent applications will be granted. In Europe, REMOXY is covered by two granted patents expiring in 2016 and 2023, respectively, plus any eligible patent term extensions.

In the U.S., POSIDUR is covered by two patent families, which include granted patents expiring in at least 2015 and 2025, respectively. In Europe, POSIDUR is covered by two granted patents expiring in 2016 and 2025, respectively, plus any eligible patent term extensions.

As of February 14, 2014, we held over 50 unexpired issued U.S. patents and over 300 unexpired issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have over 50 pending U.S. patent applications and over 100 foreign applications pending in Europe, Australia, Japan, Canada and other countries.

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. 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. Decisions of the U.S. Supreme Court and other courts 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, the America Invents Act was signed into law in September 2011, which among other changes to the U.S. patent laws, changes patent priority from "first to invent" to "first to file," implements a post-grant opposition system for patents and provides a prior user defense to infringement. These judicial and legislative changes 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 also rely upon trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. We require our employees, consultants, advisors and collaborators to execute appropriate confidentiality and assignment-of-inventions agreements with us. These agreements typically provide that all materials and confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances, and that all inventions arising out of the individual's relationship with us 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, derivation, post-grant oppositions, and similar proceedings may be necessary to determine rights to inventions in our patents and patent applications. Enforcing or defending our proprietary rights is expensive, could cause diversion of our resources and may be unsuccessful. 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.

Our collaboration agreements may depend on our intellectual property

We are party to collaborative agreements with Pain Therapeutics, King (now Pfizer), Zogenix and Impax among others. 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 v. Genentech* 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 may be sued by third parties claiming that our product candidates infringe on their intellectual property rights, particularly because there is substantial uncertainty about the validity and breadth of medical patents

We or our collaborators may be exposed to future litigation by third parties based on claims that our product candidates 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 product candidates 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 product candidates, which would be costly and time-consuming.

Technologies and businesses which we acquire or license may be difficult to integrate, disrupt our business, dilute stockholder value or divert management attention

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 product candidates 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 product candidates 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 certain other product candidates 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 product candidates 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 product candidates containing controlled substances and subject us to enforcement action. In addition, because of their restrictive nature, these regulations could limit our commercialization of our product candidates 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, inventories and other non-cash charges, as well as stock-based compensation expenses may adversely impact or delay our profitability

We may incur significant non-cash charges related to impairment write-downs of our long-lived assets, including goodwill and other intangible assets. We will continue to incur non-cash charges related to amortization of other intangible assets. For example, we had a $13.5 million non-cash write-down of deferred royalties and commercial rights related to CHRONOGESIC in the fourth quarter of 2008. We are required to perform periodic impairment reviews of our goodwill at least annually. The carrying value of goodwill on our balance sheet was $6.4 million at December 31, 2013. 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 2013 and determined that goodwill was not impaired as of December 31, 2013. 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.

Inventories include certain excipients that are sold to a customer and included in products awaiting regulatory approval. These inventories are capitalized based on management's judgment of probable sale prior to their expiration date which in turn is based on non-binding forecasts from our customer. The valuation of inventory requires us to estimate the value of inventory that may become expired prior to use. We may be required to expense previously capitalized inventory costs upon a change in our judgment, due to, among other potential factors, a denial or delay of approval of our customer's product by the necessary regulatory bodies, or new information that suggests that the inventory will not be saleable. In addition, these circumstances may cause us to record a liability related to minimum purchase agreements that we have in place for raw materials.

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 remaining maturities of 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, 2013, no assurance can be given that 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 product candidates, we are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. Although we believe that we have complied with the applicable laws, regulations and policies in all material respects and have not been required to correct any material noncompliance, we may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development involves the use, generation and disposal of hazardous materials, including but not limited to certain hazardous chemicals, solvents, agents and biohazardous materials. The extent of our use, generation and disposal of such substances has increased substantially since we started manufacturing and selling biodegradable polymers. Although we believe that our safety procedures for storing, handling and disposing of such materials comply with the standards prescribed by state and federal regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. We currently contract with third parties to dispose of these substances generated by us, and we rely on these third parties to properly dispose of these substances in compliance with applicable laws and regulations. If these third parties do not properly dispose of these substances in compliance with applicable laws and regulations, we may be subject to legal action by governmental agencies or private parties for improper disposal of these substances. The costs of defending such actions and the potential liability resulting from such actions are often very large. In the event we are subject to such legal action or we otherwise fail to comply with applicable laws and regulations governing the use, generation and disposal of hazardous materials and chemicals, we could be held liable for any damages that result, and any such liability could exceed our resources.

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

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

Risks Related To Our Industry

The market for our pharmaceutical product candidates 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 product candidates 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, Relday, REMOXY and other ORADUR-based drug candidates, if approved, will compete with currently marketed oral opioids, transdermal opioids, local anesthetic patches, anti-psychotics, 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, Knoll, Janssen, Medtronic, Endo, AstraZeneca, Arrow International, Tricumed, Kimberly-Clark, Cumberland Pharmaceuticals, Cadence Pharmaceuticals, Pacira, Acorda Therapeutics, Mallinckrodt, Shire, Johnson & Johnson, Eli Lilly, Pfizer, Novartis and others. Our ORADUR-ADHD product candidates, if approved, will compete with currently marketed or approved products by Shire, Johnson & Johnson, UCB, Novartis, Noven, Celgene, Eli Lilly, Pfizer and others. Relday, if approved, will compete with currently marketed products by Johnson & Johnson, Eli Lilly, Astra Zeneca, Pfizer, Bristol-Myers Squibb 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, Immune Pharmaceuticals, Innocoll, Nektar, Kimberly-Clark, Acorda Therapeutics, Flamel, Alexza, Cadence Pharmaceuticals, Hospira, Cumberland Pharmaceuticals, Egalet, Acura, Elite Pharmaceuticals, Phosphagenics, Intellipharmaceutics, Collegium Pharmaceutical, Heron Therapeutics 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' research and development, financial, marketing, manufacturing and other resources.

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

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we would market, sell and distribute our products. As a biotechnology company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. The Federal healthcare Anti-Kickback Statute will constrain our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, persons from knowingly and willfully

soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. Federal civil and criminal false claims laws and civil monetary penalty laws impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. The federal physician sunshine requirements under the Affordable Care Act requires manufacturers of drugs, devices, biologics and medical supplies to report annually to HHS information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations. Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Healthcare reform measures could hinder or prevent our product candidates' commercial success.

In the United States, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future revenue and profitability and the future revenue and profitability of our collaborators or potential collaborators. Federal and state lawmakers regularly propose and, at times, enact legislation that results in significant changes to the healthcare system, some of which is intended to contain or reduce the costs of medical products and services. For example, in March 2010, the President signed one of the most significant healthcare reform measures in decades, the Affordable Care Act. It contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which will impact existing government healthcare programs and will result in the development of new programs. The Affordable Care Act, among other things:

- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs";
- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- requires collection of rebates for drugs paid by Medicaid managed care organizations;
- addresses new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extension products;
- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and
- mandates a further shift in the burden of Medicaid payments to the states.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, automatic reductions to several government programs were enacted during "sequestration". These reductions included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additional state and federal healthcare reform measures may be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates once approved or additional pricing pressures.

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 product candidates 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 product candidates, 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 product candidates, 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 product candidates. A product liability claim could also significantly harm our reputation and delay market acceptance of our product candidates.

Acceptance of our pharmaceutical product candidates 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 products in research and development, including REMOXY and other ORADUR-based drug candidates, POSIDUR, ELADUR, Relday and TRANSDUR-Sufentanil. Even if approved for marketing, our product candidates may not achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including:

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

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

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

The continuing efforts of government and insurance companies, health maintenance organizations and other payors of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and third-party collaborators and the availability of capital. For example, in certain foreign markets, pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, recent federal and state government initiatives have been directed at lowering the total cost of health care, and the U.S. Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid systems. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of such proposals could materially harm our business, financial condition and results of operations.

The successful commercialization of our product candidates will depend in part on the extent to which appropriate reimbursement levels for the cost of our product candidates 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 product candidates to treat patients' diseases or medical conditions, we may incur delays in market acceptance of our products

Broad use of our product candidates will require extensive training of numerous physicians on the proper and safe use of our product candidates. 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 product candidates may be unable to rapidly train physicians in numbers sufficient to generate adequate demand for our product candidates. Any delay in training would materially delay the demand for our product candidates 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 high 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.

Risks Related To Our Common Stock

Our stock price has in the past and may in the future not meet the minimum bid price for continued listing on the Nasdaq Global Market. Our ability to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if we are delisted from The Nasdaq Global Market or if we are unable to transfer our listing to another stock market

On January 16, 2013, we received written notification from Nasdaq informing us that because the closing bid price of our common stock was below $1.00 for 30 consecutive trading days, our shares no longer complied with the minimum closing bid price requirement for continued listing on the Nasdaq Global Market under Nasdaq Marketplace Rule 5450(a)(1). We were given a 180-day period, until July 15, 2013, to regain compliance with Nasdaq's listing requirements by having the closing bid price of our common stock listed on Nasdaq be at least $1.00 for at least 10 consecutive trading days.

While we regained compliance within the applicable time period as of February 1, 2013, if our shares again no longer comply with the minimum closing bid price requirement for continued listing on the Nasdaq Global Market under Nasdaq Marketplace Rule 5450(a)(1) and we do not regain compliance within the applicable 180-day time period, we may transfer our common stock listing to The Nasdaq Capital Market, provided that the Company (i) meets the applicable market value of publicly held shares requirement for continued listing and all other applicable requirements for initial listing on The Nasdaq Capital Market (except for the closing bid price requirement) based on the Company's most recent public filings and market information and (ii) notifies Nasdaq of its intent to cure this deficiency. Following a transfer to The Nasdaq Capital Market, the Company would be afforded the remainder of an additional 180 calendar day grace period in order to regain compliance with the minimum closing bid price requirement of $1.00 per share under The Nasdaq Capital Market, unless it does not appear to NASDAQ that it would be possible for the Company to cure the deficiency.

If compliance is not demonstrated within the applicable compliance period, Nasdaq will notify the Company that its securities will be subject to delisting. The Company may appeal Nasdaq's determination to delist its securities to a Hearings Panel. During any appeal process, shares of the Company's common stock would continue to trade on the Nasdaq Global Market or Nasdaq Capital Market, as applicable.

There can be no assurance that we will maintain or regain compliance with the requirements for listing our common stock on the Nasdaq Global Market or that our common stock would be eligible for transfer to the Nasdaq Capital Market and remain in compliance with the requirements for listing on that market. Delisting from Nasdaq could adversely affect our ability to raise additional financing through the public or private sale of equity securities, would significantly affect the ability of investors to trade our securities and would negatively affect the value and liquidity of our common stock. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities.

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 product candidates, 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 product candidates 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. In December 2013, we filed a new shelf registration statement on Form S-3 with the SEC, which upon being declared effective in January 2014, allowed us to offer up to $100.9 million of securities from time to time in one or more public offerings of our common stock. In addition, we entered into a Controlled Equity Offering℠ sales agreement with Cantor Fitzgerald & Co., (Cantor Fitzgerald), under which we may sell, subject to certain limitations, up to $25 million of common stock through Cantor Fitzgerald, acting as agent. 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 to successfully develop and commercialize the respective product candidates they are developing;
- adverse results (including adverse events or failure to demonstrate safety or efficacy) or delays in our clinical and non-clinical trials of POSIDUR, REMOXY or our other ORADUR-based drug candidates, ELADUR, Relday, TRANSDUR-Sufentanil or other product candidates;
- announcements of FDA non-approval of our product candidates, 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 product candidates, clinical trials, manufacturing processes or sales and marketing activities, or those of our third party collaborators;
- announcements of technological innovations, patents, product approvals or new products by our competitors;
- regulatory, judicial and patent developments in the United States and foreign countries;
- any lawsuit involving us or our product candidates 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;
- 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;

- potential failure to meet continuing listing standards from The NASDAQ Global Market;
- loss or disruption of facilities due to natural disasters;
- 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, could 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 and Delaware law contain provisions that could discourage another company from acquiring us

Provisions of Delaware law, our certificate of incorporation and bylaws 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 classified board of directors with staggered terms;
- requiring supermajority stockholder voting to effect certain amendments to our certificate of incorporation and bylaws;
- eliminating the ability of stockholders to call special meetings of stockholders;
- prohibiting stockholder action by written consent; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

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

Location	Approximate Square Feet	Operation	Expiration
Cupertino, CA	30,000 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2019 (with an option to renew for an additional five years)
Cupertino, CA	20,000 sq. ft.	Office and Laboratory	Lease expires 2019 (with an option to renew for an additional five years)
Vacaville, CA	24,634 sq. ft.	Manufacturing	Lease expires 2018
Birmingham, AL	21,540 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2021 (with an option to terminate after August 2017 and with two options to renew the lease term for an additional five years each after the current lease expires)

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. Mine Safety Disclosures.

Not applicable.

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, 2012	**Low**	**High**
First Quarter	$ 0.71	$ 1.23
Second Quarter	0.68	0.96
Third Quarter	0.82	1.49
Fourth Quarter	0.61	1.71

Year ended December 31, 2013	**Low**	**High**
First Quarter	$ 0.90	$ 1.48
Second Quarter	0.76	1.85
Third Quarter	0.98	1.45
Fourth Quarter	1.20	1.77

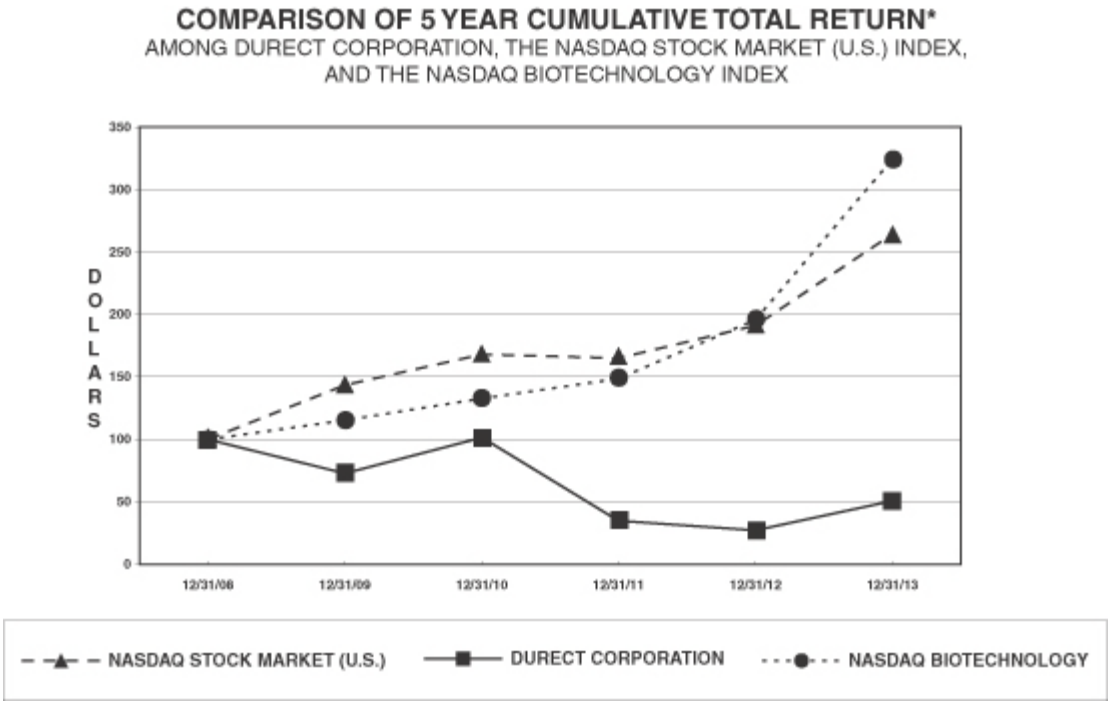
The closing sale price of our common stock as reported on the NASDAQ Global Market on February 14, 2014 was $1.65 per share. As of that date there were approximately 122 holders of record of the common stock. This does not include the number of persons whose stock is in nominee or "street name" accounts 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.

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, 2008. The graph assumes that $100 was invested on December 31, 2008. The stock price performance on the following graph is not necessarily indicative of future stock price performance.



* $100 Invested on 12/31/08 in stock or index—including reinvestment of dividends. Fiscal year ending December 31.

DURECT CORPORATION

	Cumulative Total Return					
	12/31/08	12/31/09	12/31/10	12/31/11	12/31/12	12/31/13
DURECT CORPORATION	100.00	72.86	101.77	34.81	27.14	51.03
NASDAQ STOCK MARKET (U.S.)	100.00	143.89	168.22	165.19	191.47	264.84
NASDAQ BIOTECHNOLOGY	100.00	115.63	132.98	148.69	196.12	324.80

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. Selected Financial Data.

The following selected 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, 2013, 2012 and 2011 and the balance sheet data at December 31, 2013 and 2012 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, 2010 and 2009, and the balance sheet data at December 31, 2011, 2010 and 2009 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,				
	2013	2012	2011	2010	2009
	(in thousands, except per share data)				
Statement of Operations Data:					
Collaborative research and development and other revenue (1)	$ 3,590	$ 42,494	$ 22,360	$ 20,091	$ 12,347
Product revenue, net	11,736	10,576	11,127	11,500	12,113
Total revenue	15,326	53,070	33,487	31,591	24,460
Operating expenses:					
Cost of revenue	4,837	4,654	4,713	4,275	5,311
Research and development	18,945	20,265	34,053	36,214	34,801
Selling, general and administrative	12,706	12,095	13,574	14,937	15,020
Total operating expenses	36,488	37,014	52,340	55,426	55,132
Income (loss) from operations	(21,162)	16,056	(18,853)	(23,835)	(30,672)
Other income (expense):					
Interest and other income (expenses)	(284)	151	93	943	420
Interest expense	(6)	(7)	(5)	(6)	(36)
Net other income (expense)	(290)	144	88	937	384
Net income (loss)	$ (21,452)	$ 16,200	$ (18,765)	$ (22,898)	$ (30,288)
Basic net income (loss) per share	$ (0.21)	$ 0.18	$ (0.21)	$ (0.26)	$ (0.36)
Diluted net income (loss) per share	$ (0.21)	$ 0.18	$ (0.21)	$ (0.26)	$ (0.36)
Shares used in computing basic net income (loss) per share	103,078	88,433	87,410	86,868	83,427
Shares used in computing diluted net income (loss) per share	103,078	88,589	87,410	86,868	83,427

	As of December 31,				
	2013	2012	2011	2010	2009
			(in thousands)		
Balance Sheet Data:					
Cash, cash equivalents and investments	$ 24,391	$ 28,932	$ 30,829	$ 49,572	$ 41,552
Working capital	21,143	29,428	22,410	36,936	34,796
Total assets	40,820	45,935	49,196	67,560	58,151
Other long-term liabilities	1,618	1,197	738	315	508
Stockholders' equity	30,721	36,331	3,477	14,487	27,843

(1) The 2012 figure includes the accelerated recognition of $35.4 million in deferred revenue associated with upfront fees previously received under terminated collaboration agreements with Nycomed, Pfizer and Hospira.

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, 2013, 2012 and 2011 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:

- potential regulatory filings for or approval of REMOXY, POSIDUR or any of our other product candidates;
- the progress of our third-party collaborations, including estimated milestones;
- our intention to seek, and ability to enter into strategic alliances and collaborations;
- the potential benefits and uses of our products;
- responsibilities of our collaborators, including the responsibility to make cost reimbursement, milestone, royalty and other payments to us, and our expectations regarding our collaborators' plans with respect to our products;
- our responsibilities to our collaborators, including our responsibilities to conduct research and development, clinical trials and manufacture products;
- our ability to protect intellectual property, including intellectual property licensed to our collaborators;
- market opportunities for products in our product pipeline;
- 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 possible 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, EMEA and other government regulation on our business;
- the impact of potential Risk Evaluation and Mitigation Strategies (REMS) on our business;
- uncertainties associated with obtaining and protecting patents and other intellectual property rights, as well as avoiding the intellectual property rights of others;
- 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;
- the possibility that we may develop additional manufacturing capabilities;
- our employees, including the number of employees and the continued services of key management, technical and scientific personnel;
- our future performance, including our anticipation that we will not derive meaningful revenues from our pharmaceutical systems for at least the next twelve months and our expectations regarding our ability to achieve profitability;
- sufficiency of our cash resources, anticipated capital requirements and capital expenditures and our need for additional financing;
- our expectations regarding marketing expenses, research and development expenses, and selling, general and administrative expenses;
- the composition of future revenues; 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 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 a specialty pharmaceutical company focused on the development of pharmaceutical products based on our proprietary drug delivery technology platforms. Our product pipeline currently consists of eight 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) for which a Complete Response Letter was received in June 2011, another program the subject of a NDA with the FDA for which a Complete Response Letter was received in February 2014, two programs in Phase II and four programs in Phase I. The more advanced programs are 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 programs underway in fields outside of pain management, including central nervous system disorders, metabolic disorders, cardiovascular disease and other chronic diseases.

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 which over time may provide a pathway for us to develop our own commercial, sales and marketing organization.

Collaborative Research and Development and Other Revenues

Collaborative research and development and other revenues consist of three broad categories: (a) the recognition 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 Pain Therapeutics, Pfizer (King), Hospira, Nycomed, Zogenix, and others.

Product Revenues

We have historically generated 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 and one excipient that is included in a currently marketed animal health product.

In the future, we expect to generate modest revenue related to an animal health product which was approved and launched by our licensee in 2011. 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.

Operating Results

Since our inception in 1998, we have generally had a history of operating losses. At December 31, 2013, we had an accumulated deficit of $360.8 million. Our net losses were $21.5 million and $18.8 million for the years ended December 31, 2013 and 2011, respectively, while we generated net income of $16.2 million for the year ended December 31, 2012 related to the termination of certain of our collaboration agreements. 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 2014 compared to 2013. We expect selling, general and administrative expenses to increase in 2014 compared to 2013. 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

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, inventories and stock-based compensation. Actual amounts could differ significantly from these estimates.

Inventories

Inventories, in part, include certain excipients that are sold to a customer and included in products awaiting regulatory approval. These inventories are capitalized based on management's judgment of probable sale prior to their expiration date which in turn is primarily based on non-binding forecasts from our customer as well as management's internal estimates. The valuation of inventory requires us to estimate the value of inventory that may become expired prior to use. We may be required to expense previously capitalized inventory costs upon a change in our judgment, due to, among other potential factors, a denial or delay of approval of our customer's product by the necessary regulatory bodies, or new information that suggests that the inventory will not be saleable. In addition, these circumstances may cause us to record a liability related to minimum purchase agreements that we have in place for raw materials. As of December 31, 2013, we had $1.2 million in inventory as well as $1.0 million of prepaid assets related to excipients that are included in REMOXY and other programs. In addition, we have future purchase commitments totaling $500,000 per year through 2018. In the event that we determine that we will not utilize all of these materials, there could be a potential write-off related to this inventory and a reserve for future purchase commitments.

Revenue Recognition

We enter into license and collaboration agreements under which we may receive upfront license fees, research funding and contingent milestone payments and royalties. We evaluate the accounting treatment under these agreements including whether multiple deliverables exist, how the deliverables should be separated and how the consideration should be allocated to one or more units of accounting. For our collaborations with multiple deliverables, we have concluded that the deliverables are not separable and the arrangements should be accounted for as a combined unit of accounting. As a combined unit of accounting we recognized the consideration for the combined unit of accounting in the same manner as the revenue was recognized for the final deliverable, which was generally ratably over the longest period of involvement. For example, 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 longer of the estimated research and development period or other continuing obligation period defined in the respective agreements between us and our third-party collaborators. If we determine that the expected timeline for a project and therefore our continuing involvement is materially different than we previously assumed, we will adjust the period over which we recognize the deferred revenue. In the first quarter of 2012, we were notified by Hospira, Pfizer, and Nycomed that they were terminating certain license and collaboration agreements. As a result, the related deferred revenue from up-front payments for those license and collaboration agreements was recognized as revenue during 2012 as our performance obligations were relieved. During 2012, we recognized $35.4 million from the recognition of deferred revenue related to terminated license and collaboration agreements.

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,

net reimbursements of research and development expenses by our partners incurred are recorded as collaborative research and development revenue. Net payments of research and development expenses to our partners are recorded as an addition to our research and development expenses in the period incurred.

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.

Goodwill is periodically assessed for impairment. Goodwill is evaluated for impairment at the reporting unit level. The Company operates in one operating segment and one reporting unit, which is the research, development and manufacturing of pharmaceutical products. We assess the impairment of goodwill at least annually and 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 decline in our stock price for a sustained period;
- our market capitalization relative to net book value;
- new information affecting the commercial value of the asset;
- 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; and
- significant negative industry or economic trends.

If we determine that the carrying value of our 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. We would also reconcile our estimate of total enterprise value to our market capitalization. As of December 31, 2013, the carrying value of goodwill was approximately $6.4 million. No impairment of goodwill has been recorded through December 31, 2013. 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

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.

We estimate the volatility of our common stock at the date of grant based on the historical volatility of our common stock. 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. We 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.

Results of Operations

Comparison of years ended December 31, 2013, 2012 and 2011

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 net 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, revenue recognized from ratable recognition of upfront fees, and milestone payments in connection with our collaborative agreements.

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,		
	2013	2012	2011
Collaborator			
Zogenix, Inc. (Zogenix) (1)	$ 918	$ 1,872	$ 2,928
Pain Therapeutics, Inc. (Pain Therapeutics)	750	750	750
Pfizer Inc. (Pfizer) (2)	42	11,721	5,203
Hospira, Inc. (Hospira) (3)	—	23,726	11,419
Nycomed Danmark ApS (Nycomed) (4)	—	3,705	1,235
Others	1,880	720	825
Total collaborative research and development and other revenue	$ 3,590	$ 42,494	$ 22,360

(1) Amounts related to ratable recognition of upfront fees were $241,000 in 2013, $312,000 in 2012, and $147,000 in 2011. A development and license agreement with Zogenix was entered into in July 2011; we and Zogenix had previously been working together under a feasibility agreement pursuant to which our research and development costs were reimbursed by Zogenix.

(2) Amounts related to ratable recognition of upfront fees were zero in 2013, $9.9 million in 2012, and $2.7 million in 2011. In February 2011, Pfizer acquired King and thereby assumed the rights and obligations of King under the agreements we formerly had in place with King; accordingly amounts attributed to King are now shown as Pfizer figures. In February 2012, we were notified that Pfizer was terminating the worldwide Development and License Agreement between Alpharma (acquired by King which subsequently was acquired by Pfizer) and us dated September 19, 2008 relating to the development and commercialization of ELADUR. As a result, we recognized as revenue all of the remaining upfront fees in 2012 that had previously been deferred.

(3) Amounts related to ratable recognition of upfront fees were zero in 2013, $3.7 million in 2012, and $1.2 million in 2011. Takeda Pharmaceutical Company Limited acquired Nycomed and thereby assumed the rights and obligations of Nycomed under the agreements we formerly had in place with Nycomed. In January 2012, we were notified that Nycomed was terminating the Development and License Agreement between Nycomed and us dated November 26, 2006, as amended, relating to the development and commercialization of POSIDUR (SABER-Bupivacaine) in Europe and their other licensed territories. As a result, we recognized as revenue all of the remaining upfront fees in 2012 that had previously been deferred.

(4) Amounts related to ratable recognition of upfront fees were zero in 2013, $21.8 million in 2012 and $3.6 million in 2011. In March 2012, we were notified that Hospira was terminating the Development and License Agreement between Hospira and us dated June 1, 2010 relating to the development and commercialization of POSIDUR in the United States and Canada. As a result, we recognized as revenue all of the remaining upfront fees in 2012 that had previously been deferred.

We recorded $3.6 million, $42.5 million and $22.4 million of collaborative research and development revenue in 2013, 2012, and 2011, respectively. The decrease in collaborative research and development revenue in 2013 compared with 2012 was primarily attributable to revenue of $35.4 million recognized as a result of the termination of our agreements with Nycomed (with respect to POSIDUR), Pfizer (with respect to ELADUR) and Hospira (with respect to POSIDUR) in the first quarter of 2012; the termination of the agreements and the related recognition of deferred revenue did not reflect additional cash proceeds to us in 2012. Excluding the impact of recognition of the upfront fees from our agreements with collaborative partners in 2013 and 2012, collaborative research and development revenue decreased by $3.5 million in 2013 due to lower revenue recognized from our agreements with Zogenix and Pfizer as our role in the development activities for both Relday and REMOXY decreased in 2013, and lower revenue from our agreements with Hospira and Pfizer due to terminated agreements with respect to POSIDUR and ELADUR, partially offset by higher collaborative research and development revenue recognized in connection with our feasibility agreements with other companies compared with 2012.

The increase in collaborative research and development revenue in 2012 compared with 2011 was primarily attributable to revenue of $35.4 million recognized as a result of the termination of our agreements with Nycomed, Pfizer and Hospira in the first quarter of 2012. Excluding the impact of recognition of the upfront fees from our agreements with collaborative partners in 2012 and 2011, collaborative research and development revenue decreased by $7.8 million in 2012 due to lower revenue recognized from our agreements with Hospira, Pfizer (with respect to ELADUR) and Zogenix as the development activities for POSIDUR, ELADUR, Relday and other feasibility partners decreased in 2012 compared with 2011, partially offset by higher collaborative research and development revenue recognized in connection with our agreements with Pfizer (with respect to REMOXY) in 2012.

We received a $2.25 million upfront fee in connection with the development and license agreement signed with Zogenix in July 2011 relating to Relday. The $2.25 million upfront fee is recognized as collaborative research and development revenue ratably over the term of our continuing involvement with Zogenix with respect to Relday. At December 31, 2013, $699,000 of the $2.25 million upfront fee had been recognized as revenue.

We also received a $27.5 million upfront fee in connection with the development and license agreement signed with Hospira in June 2010 relating to POSIDUR. The $27.5 million upfront fee had been recognized as collaborative research and development revenue ratably over the term of our continuing involvement with Hospira with respect to POSIDUR. Our estimate of the remaining term of our continuing involvement was revised in the first quarter of 2012 as a result of Hospira's termination notice received by us in March 2012. At December 31, 2013, all of the $27.5 million upfront fee had been recognized as revenue.

We also received a $20.0 million upfront fee in connection with the development and license agreement signed with Alpharma (acquired by King which was subsequently acquired by Pfizer) in September 2008 relating to ELADUR. The $20.0 million upfront fee had been 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 revised in the first quarter of 2012 as a result of Pfizer's termination notice received by us in February 2012. At December 31, 2013, all of the $20.0 million upfront fee had been recognized as revenue.

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 had been recognized as 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 revised in the first quarter of 2012 as a result of Nycomed's termination notice received by us in January 2012. At December 31, 2013, all of the $14.0 million upfront fee had been recognized as revenue.

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 $11.7 million, $10.6 million and $11.1 million in 2013, 2012 and 2011, respectively.

The increase in product revenue in 2013 was primarily attributable to higher product revenue from our ALZET mini pump product line as a result of higher units sold and higher prices, higher revenue from our LACTEL polymer product line as a result of higher units sold as well as higher product revenue from the sale of certain excipients included in REMOXY and another product compared to 2012.The decrease in product revenue in 2012 compared to 2011 was primarily attributable to lower product revenue from the sale of certain excipients included in REMOXY to Pfizer and from our ALZET mini pump product line as a result of fewer units sold, partially offset by higher product revenue from our LACTEL polymer product line due to higher units sold compared to 2011. Revenues in 2013, 2012 and 2011 included $273,000, $48,000 and $490,000 in product revenue related to the shipments of excipients included in REMOXY.

Cost of product revenues

Cost of product revenues was $4.8 million, $4.7 million and $4.7 million in 2013, 2012 and 2011, respectively. Cost of product revenues include the cost of product revenue from our ALZET product line, our LACTEL product line and certain excipients that are included in REMOXY and another product.

The increase in the cost of product revenues in 2013 was primarily the result of higher cost of product revenues related to the sale of certain excipients to Pfizer and from our LACTEL product line, partially offset by slightly lower cost of product revenues from our ALZET product line arising from lower manufacturing costs for products sold in 2013 compared to 2012. The cost of product revenue in 2012 and 2011 was comparable primarily due to lower cost of goods sold related to the sale of certain excipients to Pfizer and related to our ALZET product line arising from lower units sold, partially offset by the result of higher manufacturing costs associated with our LACTEL product line due to higher units sold in 2012 compared to 2011. Cost of product revenue and gross profit margin will fluctuate from period to period depending upon the product mix in a particular period.

Stock-based compensation expense recognized related to cost of product revenues was $170,000, $244,000 and $328,000 in 2013, 2012 and 2011, respectively.

As of December 31, 2013, 2012 and 2011, we had 21, 24 and 24 manufacturing employees, respectively. As of February 14, 2014, we had 21 employees in manufacturing, which we expect will remain comparable in the near future.

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. Research and development expenses were $18.9 million, $20.3 million and $34.1 million in 2013, 2012 and 2011, respectively. Stock-based compensation expense recognized related to research and development personnel was $2.0 million, $2.6 million and $4.2 million in 2013, 2012 and 2011, respectively.

Research and development expenses decreased by $1.4 million in 2013 compared to 2012. The decreases in 2013 were primarily attributable to lower development costs associated with REMOXY, Relday, POSIDUR and TRANSDUR-Sufentanil, partially offset by higher research and development costs associated with depot injectable programs, other research programs, ORADUR-ADHD and ELADUR compared to 2012 as more fully discussed below.

Research and development expenses decreased by $13.8 million in 2012 compared to 2011. The decrease in 2012 was primarily attributable to lower development costs associated with POSIDUR, depot injectable programs, REMOXY, Relday, ORADUR-ADHD, TRANSDUR-Sufentanil and ELADUR, partially offset by higher development costs associated with other research programs compared to 2011 as more fully discussed below.

Research and development expenses associated with our major development programs are as follows (in thousands):

	Year Ended December 31,		
	2013	2012	2011
POSIDUR (1)	$ 8,966	$ 9,700	$ 18,691
Depot Injectable Programs	3,932	2,503	4,658
Relday (1)	734	1,638	2,515
ORADUR-ADHD	689	596	1,492
REMOXY and other ORADUR-based opioid products (1)	397	2,164	2,684
ELADUR(1)	208	200	1,456
TRANSDUR-Sufentanil (1)	68	254	812
Others	3,951	3,210	1,745
Total research and development expenses	$ 18,945	$ 20,265	$ 34,053

(1) See Note 2 Strategic Agreements in the financial statements for more details about our agreements with Hospira, Nycomed, Pfizer, Pain Therapeutics and Zogenix.

POSIDUR

Our research and development expenses for POSIDUR decreased to $9.0 million in 2013 from $9.7 million in 2012, primarily due to lower external development costs for POSIDUR, partially offset by higher employee-related costs for POSIDUR compared with 2012.

Our research and development expenses for POSIDUR decreased to $9.7 million in 2012 from $18.7 million in 2011, primarily due to lower clinical trial expenses related to POSIDUR in 2012 as we largely completed the Phase III clinical study for POSIDUR in the fourth quarter of 2011.

Depot Injectable programs

Our research and development expenses for depot injectable programs increased to $3.9 million in 2013 from $2.5 million in 2012 primarily due to higher employee-related costs and higher costs related to research supplies as well as non-clinical studies for these programs compared with 2012.

Our research and development expenses for depot injectable programs decreased to $2.5 million in 2012 from $4.7 million in 2011 primarily due to lower employee-related costs and lower external costs for these programs in 2012 compared to 2011.

Relday

Our research and development expenses for Relday decreased to $734,000 in 2013 from $1.6 million in 2012 primarily due to decreased formulation development activities and non-clinical studies associated with Relday in 2013.

Our research and development expenses for Relday decreased to $1.6 million in 2012 from $2.5 million in 2011 primarily due to decreased formulation development activities and non-clinical studies associated with Relday as Zogenix filed an IND for Relday in the second quarter of 2012.

ORADUR-ADHD

Our research and development expenses for ORADUR-ADHD increased to $689,000 in 2013 from $596,000 in 2012, primarily due to higher employee-related costs and higher outside expenses for these drug candidates compared with 2012.

Our research and development expenses for ORADUR-ADHD decreased to $596,000 in 2012 from $1.5 million in 2011, primarily due to lower employee-related costs incurred for this program.

REMOXY and other ORADUR-based opioid products

Our research and development expenses for REMOXY and other ORADUR-based opioids decreased to $397,000 in 2013 from $2.2 million in 2012, primarily due to lower employee-related costs as well as lower costs related to research supplies for REMOXY, as our role in assisting Pfizer diminished in 2013 compared with 2012.

Our research and development expenses for REMOXY and other ORADUR-based opioids decreased to $2.2 million in 2012 from $2.7 million in 2011, primarily due to decreased development support activities for REMOXY in 2012.

ELADUR

Our research and development expenses for ELADUR increased to $208,000 in 2013 from $200,000 in 2012, primarily due to higher employee-related costs related to this product candidate in 2013 compared with 2012.

Our research and development expenses for ELADUR decreased to $200,000 in 2012 from $1.5 million in 2011, primarily due to lower employee-related costs, non-clinical studies and contract manufacturing expenses related to this drug candidate.

TRANSDUR-Sufentanil

Our research and development expenses for TRANSDUR-Sufentanil decreased to $68,000 in 2013 from $254,000 in 2012, primarily due to decreased non-clinical costs and employee-related costs for this drug candidate compared with 2012.

Our research and development expenses for TRANSDUR-Sufentanil decreased to $254,000 in 2012 from $812,000 in 2011, primarily due to decreased external costs and employee-related costs for this drug candidate in 2012 compared with 2011.

Other DURECT Research Programs

Our research and development expenses for all other activities increased to $4.0 million in 2013 from $3.2 million in 2012, primarily due to higher employee-related costs and higher external contract research and non-clinical studies costs for these research programs compared with 2012.

Our research and development expenses for all other activities increased to $3.2 million in 2012 from $1.7 million in 2011, primarily due to increased contract research costs and higher employee-related costs for these research programs in 2012 compared with 2011.

As of December 31, 2013, 2012 and 2011, we had 54, 54 and 72 research and development employees respectively. As of February 14, 2014, we had 54 employees in research and development, which we expect will remain comparable in the near future. We expect research and development expenses to increase in 2014 compared to 2013.

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.

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 $12.7 million, $12.1 million and $13.6 million in 2013, 2012 and 2011, respectively. Stock-based compensation expense recognized related to selling, general and administrative personnel was $1.3 million, $1.5 million and $2.1 million in 2013, 2012 and 2011, respectively.

Selling, general and administrative expenses increased by $611,000 in 2013 compared to 2012, primarily due to higher employee related costs and marketing related expenses incurred in 2013 compared to 2012. Selling, general and administrative expenses decreased by $1.5 million in 2012 compared to 2011, primarily due to lower stock-based compensation expenses related to selling, general and administrative personnel as well as lower other employee-related costs and patent related expenses incurred in 2012 compared to 2011.

As of December 31, 2013, 2012 and 2011, we had 26, 26 and 28 selling, general and administrative personnel, respectively. As of February 14, 2014, we had 26 selling, general and administrative employees, which we expect will remain comparable in the near future. We expect selling, general and administrative expenses to increase in 2014 compared to 2013.

Other Income (Expense). Interest and other income (expense) was ($284,000), $151,000 and $134,000 in 2013, 2012 and 2011, respectively. In 2013, other expense included income tax expense of $320,000 related to the cumulative impact of recording a deferred tax liability associated with goodwill related to an asset acquisition in 2000. In 2012, we received a payment of $83,000 from selling of certain used lab equipment. In 2011, we had higher average cash and investment balances compared with 2012. Interest expense was $6,000, $7,000 and $46,000 in 2013, 2012 and 2011, respectively.

Income taxes. As of December 31, 2013, we had net operating loss (NOL) carryforwards for federal income tax purposes of approximately $258.6 million, which expire in the years 2019 through 2033, and federal research and development tax credits of approximately $8.4 million, which expire at various dates beginning in 2018 through 2033, if not utilized. As of December 31, 2013, we had NOL carryforwards for state income tax purposes of approximately $186.0 million, which expire in the years 2014 through 2033, and state research and development tax credits of approximately $9.1 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, 2013 and 2012, we had net deferred tax assets of $122.0 million and $110.3 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 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, 2013 and 2012. 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 approximately 19.0 million shares of our common stock. We also issued approximately 4.4 million shares of our common stock to an institutional investor in connection with an equity financing in September 2009. In December 2012 and November 2013, we completed an underwritten public offering in which we sold an aggregate of approximately

14.0 million shares and approximately 8.2 million shares, respectively, of our common stock pursuant to an effective registration statement. These transactions may also have resulted in a change of control as defined by Section 382 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. Tax years 1998 to 2013 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 $24.4 million and $28.9 million at December 31, 2013 and 2012, respectively. This includes $450,000 and $400,000 of interest-bearing marketable securities classified as restricted investments on our balance sheet as of December 31, 2013 and 2012, respectively, which primarily serve as collateral for letters of credit securing our leased facilities in Alabama and California. The letter of credit for our leased facility in Alabama will expire in July 2021 and the letter of credit for our leased facility in California will expire in February 2019.

We used $15.4 million, $13.4 million and $17.4 million cash in operating activities in the year ended December 31, 2013, 2012 and 2011, respectively. The cash used for operations was primarily to fund operations as well as our working capital requirements. Our cash used in operating activities differs from our net income (loss) primarily due to the timing and recognition of up-front payments under collaborative agreements. Upfront payments received upon execution of collaborative agreements are recorded as deferred revenue and generally recognized on a straight-line basis over the period of our continuing involvement with the third-party collaborator pursuant to the applicable agreement. The net income of $16.2 million in 2012 was largely a result of the accelerated recognition of $35.4 million in deferred revenue associated with up-front fees previously received from terminated collaboration agreements; such revenue is non-recurring and has no cash flow impact on our financial statements in 2012. The increase in cash used in operations in 2013 compared with 2012 was primarily attributable to the increases in accounts payable and prepaid expenses, offset by the decreases in contract research liability in 2013 compared with 2012. The decrease in cash used for operations was mainly attributable to the increase in accounts receivable, partially offset by the decrease in contract research liability and deferred revenue in 2012 compared to 2011.

We generated $1.1 million, $3.9 million and $14.7 million of cash from investing activities in the years ended December 31, 2013, 2012 and 2011, respectively. The decrease in cash received from investing activities in 2013 compared to 2012 was primarily due to a decrease in net proceeds from maturities of available-for-sale securities, partially offset by a decrease in purchases of property and equipment in 2013 compared to 2012. The decrease in cash received from investing activities in 2012 compared to 2011 was primarily due to a decrease in net proceeds from maturities of available-for-sale securities, partially offset by a decrease in purchases of property and equipment in 2012 compared to 2011. We anticipate incurring capital expenditures of approximately $100,000 over the next 12 months. The actual amount and timing of other capital expenditures will depend, among other things, on the success of clinical trials for our product candidates and our collaborative research and development activities.

We generated $11.0 million, $11.8 million and $1.1 million of cash from financing activities in the years ended December 31, 2013, 2012 and 2011, respectively. The decrease in cash provided by financing activities in 2013 compared to 2012 was primarily due to lower cash proceeds received from an equity financing in 2013 compared with 2012, partially offset by higher proceeds from exercises of stock options in 2013 compared to 2012. The increase in cash provided by financing activities in 2012 compared to 2011 was primarily due to approximately $11.6 million of cash received from an equity financing in 2012, partially offset by lower proceeds from exercises of stock options in 2012 compared to 2011.

In May 2012, we filed a new shelf registration statement on Form S-3 with the SEC, which upon being declared effective in May 2012, allowed us to offer up to $50 million of securities from time to time in one or more public offerings of our common stock. In December 2012, we completed an underwritten public offering in which we sold an aggregate of 14,000,000 shares of our common stock pursuant to an effective registration statement at a price to the public of $0.90 per share. We received net proceeds of approximately $11.6 million after deducting underwriting discounts and commissions and estimated offering expenses. In November 2013, we completed an underwritten public offering in which we sold an aggregate of 8,214,287 shares of our common stock pursuant to an effective registration statement at a price to the public of $1.40 per share. We received net proceeds of approximately $10.6 million after deducting underwriting discounts and commissions and estimated offering expenses. In December 2013, we filed a new shelf registration statement on Form S-3 with the SEC, which upon being declared effective in January 2014, allowed us to offer up to $100.9 million of securities from time to time in one or more public offerings of our common stock. In addition, we entered into a Controlled Equity Offering ^{SM} sales agreement with Cantor Fitzgerald & Co., (Cantor Fitzgerald), under which we may sell, subject to certain limitations, up to $25 million of common stock through Cantor Fitzgerald, acting as agent.

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 term as a higher proportion of our research and development efforts are self-funded rather than covered by collaborative partners. In aggregate, we are required to make future payments pursuant to our existing contractual obligations as follows (in thousands):

Contractual Obligations	2014	2015	2016	2017	2018	2019 and thereafter	Total
Capital lease (1)	$ 14	$ 14	$ 7	$ —	$ —	$ —	$ 35
Purchase commitments	500	500	500	500	500	—	2,500
Operating lease obligations	1,871	1,941	1,970	2,000	1,948	1,056	10,786
Total contractual cash obligations	$ 2,385	$ 2,455	$ 2,477	$ 2,500	$ 2,448	$ 1,056	$ 13,321

(1) Includes principal and interest payments.

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 Risk

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, 2013, approximately 60% of our investment portfolio is composed of investments with original maturities of one year or less and approximately 24% of our investment portfolio matures less than 90 days from the date of purchase.

The following table presents the amounts of our cash equivalents and investments that may be subject to interest rate risk and the average interest rates as of December 31, 2013 by year of maturity (dollars in thousands):

	2014	2015	Total
Cash equivalents:			
Fixed rate	$ 5,300	$ —	$ 5,300
Average fixed rate	0.17%	—	0.17%
Variable rate	$ 34	$ —	$ 34
Average variable rate	0.01%	—	0.01%
Short-term investments:			
Fixed rate	$ 12,753	$ —	$ 12,753
Average fixed rate	0.21%	—	0.21%
Long-term investments:			
Fixed rate	$ —	$ 3,352	$ 3,352
Average fixed rate	—	0.26%	0.26%
Restricted investments:			
Fixed rate	$ 450	$ —	$ 450
Average fixed rate	0.10%	—	0.10%
Total investment securities	$ 18,537	$ 3,352	$ 21,889
Average rate	0.20%	0.26%	0.20%

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, 2012 by year of maturity (dollars in thousands):

	2013	2014	Total
Cash equivalents:			
Fixed rate	$ 5,663	$ —	$ 5,663
Average fixed rate	0.18%	—	0.18%
Variable rate	$ 4,204	$ —	$ 4,204
Average variable rate	0.04%	—	0.04%
Short-term investments:			
Fixed rate	$ 17,337	$ —	$ 17,337
Average fixed rate	0.27%	—	0.27%
Restricted investments:			
Fixed rate	$ 400	$ —	$ 400
Average fixed rate	0.10%	—	0.10%
Total investment securities	$ 27,604	$ —	$ 27,604
Average rate	0.26%	—	0.26%

Item 8. Financial Statements and Supplementary Data.

DURECT CORPORATION
INDEX TO FINANCIAL STATEMENTS

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, 2013 and 2012, and the related statements of operations and comprehensive income (loss), stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2013. 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, 2013 and 2012, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2013, 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, 2013, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 Framework) and our report dated February 28, 2014 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Redwood City, California
February 28, 2014

DURECT CORPORATION

BALANCE SHEETS
(in thousands, except per share amounts)

	December 31, 2013	December 31, 2012
ASSETS		
Current assets:		
Cash and cash equivalents	$ 7,836	$ 11,195
Short-term investments	12,753	17,337
Accounts receivable (net of allowances of $144 at December 31, 2013 and $154 at December 31, 2012)	2,349	2,166
Inventories	3,502	3,399
Prepaid expenses and other current assets	1,888	2,258
Total current assets	28,328	36,355
Property and equipment, net	1,985	2,457
Goodwill	6,399	6,399
Intangible assets, net	18	36
Long-term investments	3,352	—
Long-term restricted investments	450	400
Other long-term assets	288	288
Total assets	$ 40,820	$ 45,935
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 736	$ 1,785
Accrued liabilities	5,865	3,997
Contract research liabilities	329	483
Deferred revenue, current portion	255	662
Total current liabilities	7,185	6,927
Deferred revenue, non-current portion	1,296	1,480
Other long-term liabilities	1,618	1,197
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value: 10,000 shares authorized; none issued and outstanding	—	—
Common stock, $0.0001 par value: 200,000 shares authorized; 110,409 and 101,880 shares issued and outstanding at December 31, 2013 and 2012, respectively	11	10
Additional paid-in capital	391,504	375,658
Accumulated other comprehensive income	1	6
Accumulated deficit	(360,795)	(339,343)
Stockholders' equity	30,721	36,331
Total liabilities and stockholders' equity	$ 40,820	$ 45,935

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

DURECT CORPORATION

STATEMENTS OF OPERATIONS AND COMPREHENSIVE INCOME (LOSS)
(in thousands, except per share amounts)

	Year ended December 31,		
	2013	2012	2011
Collaborative research and development and other revenue	$ 3,590	$ 42,494	$ 22,360
Product revenue, net	11,736	10,576	11,127
Total revenues	15,326	53,070	33,487
Operating expenses:			
Cost of product revenues	4,837	4,654	4,713
Research and development	18,945	20,265	34,053
Selling, general and administrative	12,706	12,095	13,574
Total operating expenses	36,488	37,014	52,340
Income (loss) from operations	(21,162)	16,056	(18,853)
Other income (expense):			
Interest and other income (expenses)	(284)	151	93
Interest expense	(6)	(7)	(5)
Net other income (expense)	(290)	144	88
Net income (loss)	(21,452)	16,200	(18,765)
Net change in unrealized gain (loss) on available-for-sale securities, net of tax	(5)	1	(1)
Total comprehensive income (loss)	$ (21,457)	$ 16,201	$ (18,766)
Net income (loss) per share			
Basic	$ (0.21)	$ 0.18	$ (0.21)
Diluted	$ (0.21)	$ 0.18	$ (0.21)
Weighted-average shares used in computing net income (loss) per share			
Basic	103,078	88,433	87,410
Diluted	103,078	88,589	87,410

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

DURECT CORPORATION

STATEMENT OF STOCKHOLDERS' EQUITY
(in thousands)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2010	87,053	$ 8	$ 351,251	$ 6	$ (336,778)	$ 14,487
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	494	1	1,125	—	—	1,126
Stock-based compensation expense from stock options and ESPP shares	—	—	6,630	—	—	6,630
Net loss	—	—	—	—	(18,765)	(18,765)
Change in unrealized gain on available-for-sale securities, net of tax	—	—	—	(1)	—	(1)
Balance at December 31, 2011	87,547	9	359,006	5	(355,543)	3,477
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	333	—	231	—	—	231
Issuance of common stock upon equity financing, net of issuance cost of $983	14,000	1	11,616	—	—	11,617
Stock-based compensation expense from stock options and ESPP shares	—	—	4,805	—	—	4,805
Net income	—	—	—	—	16,200	16,200
Change in unrealized gain on available-for-sale securities, net of tax	—	—	—	1	—	1
Balance at December 31, 2012	101,880	10	375,658	6	(339,343)	36,331
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	315	—	315	—	—	315
Issuance of common stock upon equity financing, net of issuance cost of $825	8,214	1	10,674	—	—	10,675
Stock-based compensation expense from stock options and ESPP shares	—	—	4,857	—	—	4,857
Net loss	—	—	—	—	(21,452)	(21,452)
Change in unrealized gain on available-for-sale securities, net of tax	—	—	—	(5)	—	(5)
Balance at December 31, 2013	110,409	$ 11	$ 391,504	$ 1	$ (360,795)	$ 30,721

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

DURECT CORPORATION

STATEMENTS OF CASH FLOWS
(in thousands)

	Year ended December 31,		
	2013	2012	2011
Cash flows from operating activities			
Net income (loss)	$ (21,452)	$ 16,200	$ (18,765)
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Depreciation and amortization	558	964	1,176
Stock-based compensation	3,426	4,320	6,641
Loss (gain) on impairment and disposal of fixed assets	—	(73)	8
Inventory write-off	574	193	242
Changes in assets and liabilities:			
Accounts receivable	(183)	1,282	268
Inventories	(681)	(353)	(670)
Prepaid expenses and other assets	370	(372)	1,099
Accounts payable	(1,049)	511	293
Accrued liabilities	3,734	78	(1,464)
Contract research liability	(154)	(878)	(748)
Deferred revenue	(591)	(35,320)	(5,466)
Total adjustments	6,004	(29,648)	1,379
Net cash used in operating activities	(15,448)	(13,448)	(17,386)
Cash flows from investing activities			
Purchases of property and equipment	(69)	(290)	(2,467)
Purchases of available-for-sale securities	(20,403)	(25,155)	(30,320)
Proceeds from sales of available-for-sale securities	—	—	349
Proceeds from maturities of available-for-sale securities	21,580	29,352	47,172
Net cash provided by investing activities	1,108	3,907	14,734
Cash flows from financing activities			
Payments on equipment financing obligations	(9)	(8)	(15)
Net proceeds from issuances of common stock upon exercise of stock options and purchases of ESPP shares	315	231	1,126
Net proceeds from issuance of common stock in connection with equity financing	10,675	11,617	—
Net cash provided by financing activities	10,981	11,840	1,111
Net increase (decrease) in cash and cash equivalents	(3,359)	2,299	(1,541)
Cash and cash equivalents at beginning of year	11,195	8,896	10,437
Cash and cash equivalents at end of year	$ 7,836	$ 11,195	$ 8,896
Supplemental disclosure of cash flow information			
Cash paid for interest	$ 6	$ 7	$ 5

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

DURECT CORPORATION

NOTES TO FINANCIAL STATEMENTS

1. Summary of Significant Accounting Policies

Nature of Operations

DURECT Corporation (the Company) was incorporated in the state of Delaware on February 6, 1998. The Company is a pharmaceutical company developing therapies based on its proprietary drug formulations and delivery platform technologies. The Company has several products under development by itself and with third party collaborators. The Company also manufactures and sells osmotic pumps used in laboratory research, and designs, develops and manufactures a wide range of standard and custom biodegradable polymers and excipients for pharmaceutical and medical device clients for use as raw materials in their products. In addition, the Company conducts research and development of pharmaceutical products in collaboration with third party pharmaceutical and biotechnology companies.

Basis of Presentation and Use of Estimates

The Company's financial statements have been prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP). Certain other expense balances on the statements of operations and comprehensive income (loss) have been reclassified to conform to the current period presentation. The preparation of financial statements in conformity with U.S. GAAP 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 date of the financial statements and the reported amounts of revenue and expenses during the reported period. Actual results could differ materially from those estimates.

Cash, Cash Equivalents and Investments

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

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

Concentrations of Credit Risk

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

Pharmaceutical companies and academic institutions account for a substantial portion of the Company's trade receivables. The Company provides credit in the normal course of business to its customers and collateral for these receivables is generally not required. The risk associated with this concentration is limited due to the large number of accounts and their geographic dispersion. The Company monitors the creditworthiness of its customers to which it grants credit terms in the normal course of business. The Company maintains reserves for estimated credit losses and, to date, such losses have been within management's expectations.

Customer and Product Line Concentrations

A portion of the Company's revenue is derived from its ALZET mini pump product line, LACTEL biodegradable polymer product line and the sale of certain excipients for REMOXY and another product. In 2013, revenue from the ALZET product line and the LACTEL product line accounted for 48% and 26% of total revenue, respectively. In 2012, revenue from the ALZET product line and the LACTEL product line accounted for 13% and 7% of total revenue, respectively. In 2011, revenue from the ALZET product line and the LACTEL product line accounted for 22% and 9% of total revenue, respectively. Total revenue in 2012 reflected one-time recognition of $35.4 million of collaborative research and development revenue as a result of the termination of the Company's agreements with Nycomed, Pfizer and Hospira.

In 2013, Tolmar Inc. accounted for 15% of the Company's total revenues. In 2012, Hospira and Pfizer accounted for 45% and 22% of the Company's total revenues, respectively. In 2011, Hospira and Pfizer accounted for 34% and 16% of the Company's total revenues, respectively.

Total revenue by geographic region for the years 2013, 2012 and 2011 are as follows (in thousands):

	Year ended December 31,		
	2013	2012	2011
United States	$ 11,087	$ 44,687	$ 27,782
Europe	2,089	6,285	3,651
Japan	1,104	1,151	1,183
Other	1,046	947	871
Total	$ 15,326	$ 53,070	$ 33,487

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

Inventories

Inventories are stated at the lower of cost or market, with cost determined on a first-in, first-out basis. Inventories, in part, include certain excipients that are sold to a customer and included in products awaiting regulatory approval. These inventories are capitalized based on management's judgment of probable sale prior to their expiration date which in turn is primarily based on non-binding forecasts from our customers as well as management's internal estimates. The valuation of inventory requires management to estimate the value of inventory that may become expired prior to use. The Company may be required to expense previously capitalized inventory costs upon a change in management's judgment, due to, among other potential factors, a denial or delay of approval of a customer's product by the necessary regulatory bodies, or new information that suggests that the inventory will not be saleable. In addition, these circumstances may cause the Company to record a liability related to minimum purchase agreements that the Company has in place for raw materials. As of December 31, 2013, the Company had $1.2 million in inventory and $1.0 million of prepaid assets related to excipients that are included in REMOXY and other programs. In addition, the Company has future purchase commitments totaling $500,000 per year through 2018. In the event that management determines that the Company will not utilize all of these materials, there could be a potential write-off related to this inventory and a reserve for future purchase commitments.

The Company's inventories consisted of the following (in thousands):

	December 31,	
	2013	2012
Raw materials	$ 1,404	$ 1,149
Work in-process	1,063	1,011
Finished goods	1,035	1,239
Total inventories	$ 3,502	$ 3,399

Property and Equipment

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

Acquired Intangible Assets and Goodwill

Acquired intangible assets consist of patents, developed technology, trademarks and customer lists related to the Company's acquisitions accounted for using the purchase method. Amortization of these purchased intangibles is calculated on a straight-line basis over the respective estimated useful lives of the assets ranging from four to seven years. The Company assesses goodwill for impairment at least annually.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, including property and equipment, intangible assets, and other long-term assets, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable.

An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition is less than its carrying amount. Impairment, if any, is calculated as the amount by which an asset's carrying value exceeds its fair value, typically using discounted cash flows to determine fair value. Through December 31, 2013, there have been no material impairment losses.

Stock-Based Compensation

The Company accounts for share-based payments using a fair-value based method for costs related to all share-based payments, including stock options and stock issued under the Company's employee stock purchase plan (ESPP). The Company estimates the fair value of share-based payment awards on the date of grant using an option-pricing model. See Note 8 for further information regarding stock-based compensation.

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 on the Company's part exists, the price is fixed or determinable and the collectability of the amounts owed is reasonably assured. The Company enters into license and collaboration agreements under which it may receive upfront license fees, research funding and contingent milestone payments and royalties. The Company's deliverables under these arrangements typically consist of granting licenses to intellectual property rights and providing research and development services. The accounting standards contain a presumption that separate contracts entered into at or near the same time with the same entity or related parties were negotiated as a package and should be evaluated as a single agreement.

In the first quarter of 2011, the Company adopted ASU No. 2009-13, Revenue Recognition—*Multiple Deliverable Revenue Arrangements* (ASU 2009-13) for multiple deliverable revenue arrangements, on a prospective basis, for applicable transactions originating or materially modified on or subsequent to January 1, 2011. ASU 2009-13 provides application guidance on whether multiple deliverables exist, how the deliverables should be separated and how the consideration should be allocated to one or more units of accounting. This update changes the requirements for establishing separate units of accounting in a multiple element arrangement and establishes a selling price hierarchy for determining the selling price of a deliverable. The selling price used for each deliverable is based on vendor-specific objective evidence, if available, third-party evidence if vendor-specific objective evidence is not available, or estimated selling price if neither vendor-specific nor third-party evidence is available. Implementation of ASU 2009-13 has had no impact on the Company's reported revenue as compared to revenue under previous guidance. Under ASU 2009-13, the Company may be required to exercise considerable judgment in determining the estimated selling price of delivered items under new agreements and the Company's revenue under new agreements may be more accelerated as compared to the prior accounting standard.

For multiple element arrangements entered into prior to January 1, 2011, the Company determined whether the elements had value on a stand-alone basis and whether there was objective and reliable evidence of fair value. When the delivered element did not have stand-alone value or there was insufficient evidence of fair value for the undelivered element(s), the Company recognized the consideration for the combined unit of accounting in the same manner as the revenue was recognized for the final deliverable, which was generally ratably over the longest period of involvement. For example, upfront payments received upon execution of collaborative agreements are recorded as deferred revenue and recognized as collaborative research and development revenue based on a straight-line basis over the period of the Company's continuing involvement with the third-party collaborator pursuant to the applicable agreement. Such period generally represents the longer of the estimated research and development period or other continuing obligation period defined in the respective agreements between the Company and its third-party collaborators. Returns or credits related to the sale of products have not had a material impact on the Company's revenues or net loss.

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

Milestone payments under collaborative arrangements are triggered either by the results of the Company's research and development efforts or by specified sales results by a third-party collaborator. Milestones related to the Company's development-based activities may include initiation of various phases of clinical trials, successful completion of a phase of development or results from a clinical trial, acceptance of a New Drug Application by the FDA or an equivalent filing with an equivalent regulatory agency in another territory, or regulatory approval by the FDA or by an equivalent regulatory agency in another territory. Due to the uncertainty involved in meeting these development-based milestones, the development-based milestones are considered to be substantial (i.e., not just achieved through passage of time) at the inception of the collaboration agreement. In addition, the amounts of the payments assigned thereto are considered to be commensurate with the enhancement of the value of the delivered intellectual property as a result of the Company's performance. The Company's involvement is necessary to the achievement of development-based milestones. The Company would account for development-based milestones as revenue upon achievement of the substantive milestone events. Milestones related to sales-based activities may be triggered upon events such as the first commercial sale of a product or when sales first achieve a defined level. Under the Company's collaborative agreements, the Company's third-party collaborators will take the lead in commercialization activities and the Company is typically not involved in the achievement of sales-based milestones. These sales-based milestones would be achieved after the completion of the Company's development activities. The Company would account for the sales-based milestones in the same manner as royalties, with revenue recognized upon achievement of the milestone. In addition, upon the achievement of either development-based or sales-based milestone events, the Company has no future performance obligations related to any milestone payments.

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

Research and Development Expenses

Research and development expenses are primarily comprised of salaries and benefits associated with research and development personnel, overhead and facility costs, preclinical and non-clinical development costs, clinical trial and related clinical manufacturing costs, contract services, and other outside costs. Research and development costs are expensed as incurred. Research and development costs paid to third parties under sponsored research agreements are recognized as the related services are performed. In addition, net reimbursements of research and development expenses incurred by the Company's partners are recorded as collaborative research and development revenue. Net payments of research and development expenses to the Company's partners are recorded as an addition to research and development expenses in the period incurred.

Comprehensive Income (Loss)

Accumulated other comprehensive income as of December 31, 2013, 2012 and 2011 is entirely comprised of unrealized gains or losses on available-for-sale securities.

Segment Reporting

The Company operates in one operating segment, which is the research, development and manufacturing of pharmaceutical products.

Net Income (Loss) Per Share

Basic net income (loss) per share is calculated by dividing net income (loss) by the weighted-average number of common shares outstanding. Diluted net income (loss) per share is computed using the weighted-average number of common shares outstanding and common stock equivalents (i.e., options and warrants to purchase common stock) outstanding during the period, if dilutive, using the treasury stock method for options and warrants. The numerators and denominators in the calculation of basic and diluted net income (loss) per share were as follows (in thousands except per share amounts):

	Year Ended December 31,		
	2013	2012	2011
Numerators:			
Net income (loss)	$ (21,452)	$ 16,200	$ (18,765)
Denominators:			
Weighted average shares used to compute basic net income (loss) per share	103,078	88,433	87,410
Effect of dilutive securities:			
Dilution from stock options	—	150	—
Dilution from ESPP	—	6	—
Dilutive common shares	—	156	—
Weighted average shares used to compute basic net income (loss) per share	103,078	88,589	87,410
Net income (loss) per share:			
Basic	$ (0.21)	$ 0.18	$ (0.21)
Diluted	$ (0.21)	$ 0.18	$ (0.21)

The computation of diluted net income (loss) per share for the years ended December 31, 2013, 2012 and 2011 excludes the impact of options to purchase 19.6 million, 20.7 million and 21.3 million shares of common stock outstanding, respectively, at December 31, 2013, 2012 and 2011, as such impact would be antidilutive.

Shipping and Handling

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

Operating Leases

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

2. Strategic Agreements

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

	Year ended December 31,		
	2013	2012	2011
Collaborator			
Zogenix, Inc. (Zogenix) (1)	$ 918	$ 1,872	$ 2,928
Pain Therapeutics, Inc. (Pain Therapeutics)	750	750	750
Pfizer Inc. (Pfizer) (2)	42	11,721	5,203
Hospira, Inc. (Hospira) (3)	—	23,726	11,419
Nycomed Danmark ApS (Nycomed) (4)	—	3,705	1,235
Others	1,880	720	825
Total collaborative research and development and other revenue	$ 3,590	$ 42,494	$ 22,360

(1) Amounts related to ratable recognition of upfront fees were $241,000 in 2013, $312,000 in 2012, and $147,000 in 2011. A development and license agreement with Zogenix was entered into in July 2011; the Company and Zogenix had previously been working together under a feasibility agreement pursuant to which the Company's research and development costs were reimbursed by Zogenix.

(2) Amounts related to ratable recognition of upfront fees were zero in 2013, $9.9 million in 2012, and $2.7 million in 2011. In February 2011, Pfizer acquired King and thereby assumed the rights and obligations of King under the agreements the Company formerly had in place with King; accordingly amounts attributed to King are now shown as Pfizer figures. In February 2012, the Company was notified that Pfizer was terminating the worldwide Development and License Agreement between Alpharma (acquired by King which subsequently was acquired by Pfizer) and the Company dated September 19, 2008 relating to the development and commercialization of ELADUR. As a result, the Company recognized as revenue all of the remaining upfront fees in 2012 that had previously been deferred.

(3) Amounts related to ratable recognition of upfront fees were zero in 2013, $3.7 million in 2012, and $1.2 million in 2011. Takeda Pharmaceutical Company Limited acquired Nycomed and thereby assumed the rights and obligations of Nycomed under the agreements the Company formerly had in place with Nycomed. In January 2012, the Company was notified that Nycomed was terminating the Development and License Agreement between Nycomed and the Company dated November 26, 2006, as amended, relating to the development and commercialization of POSIDUR (SABER-Bupivacaine) in Europe and their other licensed territories. As a result, the Company recognized as revenue all of the remaining upfront fees in 2012 that had previously been deferred.

(4) Amounts related to ratable recognition of upfront fees were zero in 2013, $21.8 million in 2012 and $3.6 million in 2011. In March 2012, the Company was notified that Hospira was terminating the Development and License Agreement between Hospira and the Company dated June 1, 2010 relating to the development and commercialization of POSIDUR in the United States and Canada. As a result, the Company recognized as revenue all of the remaining upfront fees in 2012 that had previously been deferred.

As of February 14, 2014, the Company had potential milestones of up to $171.6 million that the Company may receive in the future under its collaborative arrangements, of which $66.6 million are development-based milestones and $105.0 million are sales-based milestones. Within the category of development-based milestones, $3.1 million are related to early stage clinical testing (defined as Phase 1 or 2 activities), $9.8 million are related to late stage clinical testing (defined as Phase III activities), $17.7 million are related to regulatory filings, and $36.0 million are related to regulatory approvals.

Agreement with Pain Therapeutics, Inc.

In December 2002, the Company entered into an exclusive agreement with Pain Therapeutics, Inc. (“Pain Therapeutics”) to develop and commercialize on a worldwide basis REMOXY and other oral sustained release, abuse deterrent opioid products incorporating four specified opioid drugs, using the ORADUR technology. The agreement also provides Pain Therapeutics with the exclusive right to commercialize products developed under the agreement on a worldwide basis. In connection with the execution of the agreement, Pain Therapeutics paid the Company upfront fees of $900,000 in December 2002 and $100,000 in October 2003. In December 2005, the Company amended its agreement with Pain Therapeutics in order to specify its obligations with respect to the supply of key excipients for use in the licensed products. Under the agreement, as amended, the Company is responsible for formulation development, supply of selected key excipients used in the manufacture of licensed products and other specified tasks. Under the agreement with Pain Therapeutics, subject to and upon the achievement of predetermined development and regulatory milestones for the four drug candidates currently in development, the Company is entitled to receive milestone payments of up to $9.3 million in the aggregate. As of December 31, 2013, the Company had received $1.7 million in cumulative milestone payments. In addition, if commercialized, the Company will receive royalties for REMOXY and other licensed products which do not contain an opioid antagonist of between 6.0% to 11.5% of net sales of the product depending on sales volume. This agreement can be terminated by either party for material breach by the other party and by Pain Therapeutics without cause. Under the agreement, Pain Therapeutics reimburses the Company for qualified expenses incurred by the Company in connection with the development program.

The Company recognizes collaborative research and development revenue related to research and development activities for REMOXY and other development programs based on reimbursement of qualified expenses as defined in the collaborative agreement and related amendment with Pain Therapeutics. Total collaborative research and development revenue recognized under the agreements with Pain Therapeutics was $750,000 in 2013, 2012 and 2011. The cumulative aggregate payments received by the Company as of December 31, 2013 were $34.2 million under this agreement.

Under the terms of this agreement, Pain Therapeutics paid the Company an upfront license fee of $1.0 million, with the potential for an additional $9.3 million in performance milestone payments based on the successful development and approval of the four ORADUR-based opioids. Of these potential milestones, $9.3 million are development-based milestones (of which $1.7 million have been achieved as of December 31, 2013). There are no sales-based milestones under the agreement.

In March 2009, King assumed the responsibility for further development of REMOXY from Pain Therapeutics. As a result of this change, the Company continues to perform REMOXY-related activities in accordance with the terms and conditions set forth in the license agreement between the Company and Pain Therapeutics. Now King is substituted in lieu of Pain Therapeutics with respect to interactions with the Company in its performance of those activities including the obligation to pay the Company with respect to all REMOXY-related costs incurred by the Company. In February 2011, Pfizer acquired King and thereby assumed the rights and obligations of King with respect to REMOXY; accordingly, amounts attributed to King are now shown as Pfizer figures.

Total collaborative research and development revenue recognized for REMOXY-related work performed by the Company for Pfizer was $42,000, $1.7 million and $1.3 million for the years ended December 31, 2013, 2012 and 2011, respectively. Prior to March 2009, the Company recognized collaborative research and development revenue for REMOXY-related work under the agreements with Pain Therapeutics. The cumulative aggregate payments received by the Company from Pfizer as of December 31, 2013 were $7.1 million under this agreement.

Long Term Supply Agreement with King (now Pfizer)

During 2008, the Company 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, the Company 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, the Company signed an exclusive long term excipient supply agreement with respect to REMOXY with King. In February 2011, Pfizer acquired King and thereby assumed the rights and obligations of King with respect to this long term supply agreement. This agreement stipulates the terms and conditions under which the Company will supply to King, based on the Company's 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 Company 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 the Company, in which case termination will be effective one year after notice by King. The Company may terminate the agreement if the Company is 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 the Company 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.

In 2013, 2012 and 2011, the Company recognized $273,000, $48,000 and $490,000 of product revenue, respectively, related to key excipients for REMOXY and the associated cost of goods sold was $165,000, $33,000 and $302,000, respectively.

Agreement with Zogenix, Inc.

On July 11, 2011, the Company and Zogenix, Inc., (Zogenix), entered into a Development and License Agreement (the Zogenix Agreement). The Company and Zogenix had previously been working together under a feasibility agreement pursuant to which the Company's research and development costs were reimbursed by Zogenix. Under the Zogenix Agreement, Zogenix will be responsible for the clinical development and commercialization of a proprietary, long-acting injectable formulation of risperidone using the Company's SABER controlled-release formulation technology in combination with Zogenix's DosePro® needle-free, subcutaneous drug delivery system. DURECT will be responsible for non-clinical, formulation and CMC development activities. The Company will be reimbursed by Zogenix for its research and development efforts on the product.

Zogenix paid a non-refundable upfront fee to the Company of $2.25 million in July 2011. The Company's research and development services are considered integral to utilizing the licensed intellectual property and, accordingly, the deliverables are accounted for as a single unit of accounting. The $2.25 million upfront fee will be recognized as collaborative research and development revenue ratably over the term of the Company's continuing research and development involvement with Zogenix with respect to this product candidate. Zogenix is obligated to pay the Company up to $103 million in total future milestone payments with respect to the product subject to and upon the achievement of various developments, regulatory and sales milestones. Of these potential milestones, $28 million are development-based milestones (none of which has been achieved as of December 31, 2013), and

$75 million are sales-based milestones (none of which has been achieved as of December 31, 2013). Zogenix is also required to pay a mid single-digit to low double-digit percentage patent royalty on annual net sales of the product determined on a jurisdiction-by-jurisdiction basis. The patent royalty term is equal to the later of the expiration of all DURECT technology patents or joint patent rights in a particular jurisdiction, the expiration of marketing exclusivity rights in such jurisdiction, or 15 years from first commercial sale in such jurisdiction. After the patent royalty term, Zogenix will continue to pay royalties on annual net sales of the product at a reduced rate for so long as Zogenix continues to sell the product in the jurisdiction. Zogenix is also required to pay to the Company a tiered percentage of fees received in connection with any sublicense of the licensed rights.

The Company granted to Zogenix an exclusive worldwide license, with sub-license rights, to the Company's intellectual property rights related to the Company's proprietary polymeric and non-polymeric controlled-release formulation technology to make and have made, use, offer for sale, sell and import risperidone products, where risperidone is the sole active agent, for administration by injection in the treatment of schizophrenia, bipolar disorder or other psychiatric related disorders in humans. The Company retains the right to supply Zogenix's Phase III clinical trial and commercial product requirements on the terms set forth in the Zogenix Agreement.

The Company retains the right to terminate the Zogenix Agreement with respect to specific countries if Zogenix fails to advance the development of the product in such country, either directly or through a sublicensee. In addition, either party may terminate the Zogenix Agreement upon insolvency or bankruptcy of the other party, upon written notice of a material uncured breach or if the other party takes any act impairing such other party's relevant intellectual property rights. Zogenix may terminate the Zogenix Agreement upon written notice if during the development or commercialization of the product, the product becomes subject to one or more serious adverse drug experiences or if either party receives notice from a regulatory authority, independent review committee, data safety monitory board or other similar body alleging significant concern regarding a patient safety issue. Zogenix may also terminate the Zogenix Agreement with or without cause, at any time upon prior written notice.

The following table provides a summary of collaborative research and development revenue recognized under the agreements with Zogenix (in thousands). The cumulative aggregate payments received by the Company as of December 31, 2013 were $10.6 million under these agreements.

	Year Ended December 31,		
	2013	2012	2011
Ratable recognition of upfront payment	$ 241	$ 312	$ 146
Research and development expenses reimbursable by Zogenix	677	1,560	2,782
Total collaborative research and development revenue	$ 918	$ 1,872	$ 2,928

Agreement with Hospira, Inc.

In June 2010, the Company and Hospira, Inc. (Hospira) entered into a license agreement to develop and market POSIDUR (SABER-bupivacaine) in the U.S. and Canada. POSIDUR is the Company's investigational post-operative pain relief depot currently in Phase III clinical development in the U.S. that utilizes the Company's patented SABER technology to deliver bupivacaine to provide up to three days of pain relief after surgery.

Under the terms of the agreement, Hospira made an upfront payment of $27.5 million. In March 2012, the Company was notified that Hospira was terminating the agreement effective September 28, 2012, or, as permitted under the agreement, at an earlier date elected by the Company. Hospira's termination returned to the Company the U.S. and Canadian rights to develop and commercialize POSIDUR and as such the Company now holds worldwide rights to POSIDUR. As a result of the termination of the Hospira agreement for POSIDUR, the Company recognized as revenue during the first quarter of 2012 the remaining $21.8 million of deferred revenue related to the upfront fee of the development and license agreement as the Company has no remaining performance obligations under the agreement; this recognition of revenue did not result in additional cash proceeds to the Company.

The following table provides a summary of amounts comprising the Company's net share of the research and development costs for POSIDUR under the agreement with Hospira (in thousands):

	Year Ended December 31,		
	2013	2012	2011
Research and development expenses reimbursable by Hospira	$ —	$ 1,968	$ 7,792
Research and development expenses reimbursable by the Company	—	—	—
Net payable to Hospira	—	—	—
Net receivable from Hospira	$ —	$ 1,968	$ 7,792

The following table provides a summary of collaborative research and development revenue recognized under the agreement with Hospira (in thousands). The cumulative aggregate payments received by the Company as of December 31, 2013 were $40.7 million under this agreement.

	Year Ended December 31,		
	2013	2012	2011
Recognition of upfront payment (1)	$ —	$ 21,758	$ 3,627
Research and development expenses reimbursable by Hospira	—	1,968	7,792
Total collaborative research and development revenue	$ —	$ 23,726	$ 11,419

(1) The Company's estimate of the term of its continuing performance obligation was revised in the first quarter of 2012 as a result of the termination of the POSIDUR agreement by Hospira. As a result of the termination of the Hospira agreement for POSIDUR, the Company recorded as revenue during the first quarter of 2012 the remaining $21.8 million deferred revenue related to the upfront fee of the development and license agreement.

Agreement with Nycomed

In November 2006, the Company entered into a development and license agreement with Nycomed, which was amended in February 2010 and February 2011. Under the terms of the agreement, as amended, the Company licensed to Nycomed the exclusive commercialization rights to POSIDUR for the European Union (E.U.) and certain other countries.

Under the terms of the agreement as amended, Nycomed paid the Company an upfront license fee of $14.0 million and an $8.0 million development-based milestone payment. In October 2011, Takeda Pharmaceutical Company Limited (Takeda) acquired Nycomed and thereby assumed the rights and obligations of Nycomed under the agreements the Company formerly had in place with Nycomed. In January 2012, the Company was notified that Takeda (through Nycomed) was terminating the license agreement with us, and thereby returning their right to develop and commercialize POSIDUR (SABER® -Bupivacaine) in Europe and their other licensed territories to us. As a result of the termination of the Nycomed agreement for POSIDUR, the Company recognized revenue during the first quarter of 2012 for the remaining $3.7 million of deferred revenue related to the upfront fee of the development and license agreement as the Company had no remaining performance obligations under the agreement; this recognition of revenue did not result in additional cash proceeds to the Company.

The Company's net share of the research and development costs for POSIDUR under the Company's agreement with Nycomed was zero in 2013, 2012 and 2011.

The following table provides a summary of collaborative research and development revenue recognized under the agreement with Nycomed with regard to POSIDUR (in thousands). The cumulative aggregate payments received by the Company from Nycomed as of December 31, 2013 were $37.3 million under this agreement. In addition, the cumulative aggregate payments paid by the Company to Nycomed were $9.0 million as of December 31, 2013.

	Year Ended December 31,		
	2013	2012	2011
Recognition of upfront payment (1)	$ —	$ 3,705	$ 1,235
Research and development expenses reimbursable by Nycomed	—	—	—
Total collaborative research and development revenue	$ —	$ 3,705	$ 1,235

(1) The Company's estimate of the term of its continuing performance obligation was revised in the first quarter of 2012 as a result of the termination of the agreement by Nycomed. As a result of the termination of the Nycomed agreement for POSIDUR, the Company recorded as revenue during the first quarter of 2012 the remaining $3.7 million deferred revenue related to the upfront fee of the development and license agreement.

Agreement with Alpharma Ireland Limited, an affiliate of Alpharma Inc. (Alpharma) (acquired by King which subsequently was acquired by Pfizer)

Effective October 2008, the Company and Alpharma, entered into a development and license agreement granting Alpharma the exclusive worldwide rights to develop and commercialize ELADUR, DURECT's investigational transdermal bupivacaine patch. As a result of the acquisition of Alpharma by King in December 2008, King assumed the rights and obligations of Alpharma under the agreement. As a result of the acquisition of King by Pfizer in February 2011, Pfizer assumed the rights and obligations of King under the agreement; accordingly, amounts contributed to King are now shown as Pfizer figures.

Under the terms of the agreement, Alpharma paid the Company an upfront license fee of $20.0 million. The $20.0 million upfront fee had been recognized as collaborative research and development revenue ratably over the term of the Company's continuing involvement with Pfizer with respect to ELADUR. The Company's estimate of the remaining term of its continuing involvement was adjusted in the third quarter of 2011 as a result of an updated development plan for ELADUR.

In February 2012, the Company was notified that Pfizer was terminating the agreement, effective August 30, 2012, or, as permitted under the agreement, at an earlier date elected by the Company. Pfizer's termination returned to the Company worldwide rights to develop and commercialize ELADUR. As a result of the termination of the agreement for ELADUR, the Company recognized revenue during the first quarter of 2012 for the remaining $9.9 million of deferred revenue related to the upfront fee of the development and license agreement as the Company has no remaining performance obligations under the agreement; this recognition of revenue did not result in additional cash proceeds to the Company.

The following table provides a summary of collaborative research and development revenue recognized under the agreement with King with regard to ELADUR (in thousands). The cumulative aggregate payments received by the Company as of December 31, 2013 were $29.2 million under this agreement.

	Year Ended December 31,		
	2013	2012	2011
Recognition of upfront payment (1)	$ —	$ 9,895	$ 2,708
Research and development expenses reimbursable by King	—	124	1,150
Total collaborative research and development revenue	$ —	$ 10,019	$ 3,858

(1) The Company's estimate of the term of our continuing performance obligation was revised in the first quarter of 2012 as a result of the termination of the agreement by Pfizer. As a result of the termination of this agreement for ELADUR, the Company recorded as revenue during the first quarter of 2012 the remaining $9.9 million deferred revenue related to the upfront fee of the development and license agreement.

3. Intangible Assets and Goodwill

Intangible assets recorded in connection with the Company's acquisitions consist of the following (in thousands):

	December 31, 2013		
	Gross Intangibles	Accumulated Amortization	Net Intangibles
Developed technology	$ 3,600	$ (3,600)	$ —
Patents	591	(573)	18
Other intangible assets	3,260	(3,260)	—
Total	$ 7,451	$ (7,433)	$ 18

	December 31, 2012		
	Gross Intangibles	Accumulated Amortization	Net Intangibles
Developed technology	$ 3,600	$ (3,600)	$ —
Patents	591	(555)	36
Other intangible assets	3,260	(3,260)	—
Total	$ 7,451	$ (7,415)	$ 36

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

The net amount of intangible assets at December 31, 2013 was $18,000, which will be amortized as follows: $17,900 in 2014 and $100 in 2015. Should any intangible assets become impaired, the Company will write them down to their estimated fair value.

Goodwill totaled $6.4 million at December 31, 2013. The Company evaluates goodwill for impairment at least annually. In 2013, 2012 and 2011 goodwill was evaluated and no indicators of impairment were noted. Should goodwill become impaired, the Company may be required to record an impairment charge. To date, the Company has not recorded any impairment charge to goodwill.

4. Financial Instruments

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The Company's valuation techniques used to measure fair value maximize the use of observable inputs and minimize the use of unobservable inputs. The Company follows a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value. These levels of inputs are the following:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company's financial instruments are valued using quoted prices in active markets or based upon other observable inputs. The following table sets forth the fair value of the Company's financial assets that were measured at fair value on a recurring basis as of December 31, 2013 (in thousands):

	Level 1	Level 2	Level 3	Total
Money market funds	$ 34	$ —	$ —	$ 34
Certificates of deposit	—	450	—	450
Commercial paper	—	1,249	—	1,249
Corporate debt	—	3,258	—	3,258
U.S. Government agencies	—	16,898	—	16,898
Total	$ 34	$ 21,855	$ —	$ 21,889

The following table sets forth the fair value of our financial assets that were measured at fair value on a recurring basis as of December 31, 2012 (in thousands):

	Level 1	Level 2	Level 3	Total
Money market funds	$ 4,204	$ —	$ —	$ 4,204
Certificates of deposit	—	550	—	550
Commercial paper	—	8,993	—	8,993
Corporate debt	—	3,807	—	3,807
U.S. Government agencies	—	10,050	—	10,050
Total	$ 4,204	$ 23,400	$ —	$ 27,604

Money market funds are classified as Level 1 financial assets. Certificates of deposit, commercial paper, corporate debt securities, and U.S. Government agency securities are classified as Level 2 financial assets. The fair value of the Level 2 assets is estimated using pricing models using current observable market information for similar securities. The Company's Level 2 investments include U.S. government-backed securities and corporate securities that are valued based upon observable inputs that may include benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications. The fair value of the Company's commercial paper is based upon the time to maturity and discounted using the three-month treasury bill rate. The average remaining maturity of the Company's Level 2 investments as of December 31, 2013 is less than twelve months and these investments are rated by S&P and Moody's at AAA or AA- for securities and A1 or P1 for commercial paper.

The following is a summary of available-for-sale securities as of December 31, 2013 and 2012 (in thousands):

	December 31, 2013			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value
Money market funds	$ 34	$ —	$ —	$ 34
Certificates of deposit	450	—	—	450
Commercial paper	1,249	—	—	1,249
Corporate debt	3,257	1	—	3,258
U.S. Government agencies	16,898	1	(1)	16,898
	$ 21,888	$ 2	$ (1)	$ 21,889
Reported as:				
Cash and cash equivalents	$ 5,334	$ —	$ —	$ 5,334
Short-term investments	12,752	2	(1)	12,753
Long-term investments	3,352	—	—	3,352
Long-term restricted investments	450	—	—	450
	$ 21,888	$ 2	$ (1)	$ 21,889

	December 31, 2012			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value
Money market funds	$ 4,204	$ —	$ —	$ 4,204
Certificates of deposit	550	—	—	550
Commercial paper	8,993	—	—	8,993
Corporate debt	3,806	1	—	3,807
U.S. Government agencies	10,045	5	—	10,050
	$ 27,598	$ 6	$ —	$ 27,604
Reported as:				
Cash and cash equivalents	$ 9,867	$ —	$ —	$ 9,867
Short-term investments	17,331	6	—	17,337
Long-term restricted investments	400	—	—	400
	$ 27,598	$ 6	$ —	$ 27,604

The following is a summary of the cost and estimated fair value of available-for-sale securities at December 31, 2013, by contractual maturity (in thousands):

	December 31, 2013	
	Amortized Cost	Estimated Fair Value
Mature in one year or less	$ 18,502	$ 18,503
Mature after one year through five years	3,352	3,352
	$ 21,854	$ 21,855

There were no securities that have had an unrealized loss for more than 12 months as of December 31, 2013 or 2012.

As of December 31, 2013, unrealized losses on available-for-sale investments are not attributed to credit risk and are considered to be temporary. The Company believes that it is more-likely-than-not that investments in an unrealized loss position will be held until maturity or the recovery of the cost basis of the investment. To date, the Company has not recorded any impairment charges on marketable securities related to other-than-temporary declines in market value.

5. Property and Equipment

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

	December 31,	
	2013	2012
Equipment	$ 12,438	$ 12,369
Leasehold improvement	9,855	9,755
Construction-in-progress	180	289
	22,473	22,413
Less accumulated depreciation and amortization	(20,488)	(19,956)
Property and equipment, net	$ 1,985	$ 2,457

Depreciation expense was $541,000, $948,000 and $1.2 million in 2013, 2012 and 2011, respectively. Amortization expense was $9,306, $9,307 and $9,844 in 2013, 2012 and 2011 for assets held under capital leases, respectively.

As of December 31, 2013, the Company has recorded $558,000 as a liability which was included in other long-term liabilities on its balance sheet for asset retirement obligations associated with the estimated restoration cost for its leased buildings.

6. Restricted Investments

As of December 31, 2013 and 2012, the Company had $450,000 and $400,000, respectively, recorded as restricted investments, which primarily served as collateral for letters of credit securing its leased facilities in Alabama and California.

7. Commitments

Operating Leases

The Company has lease arrangements for its facilities in California and Alabama. Under these leases, the Company is required to pay certain maintenance expenses in addition to monthly rent. Rent expense is recognized on a straight-line basis over the lease term for leases that have scheduled rental payment increases. Rent expense under all operating leases was $1.5 million, $1.6 million and $2.0 million, for the years ended December 31, 2013, 2012 and 2011, respectively.

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

Year ending December 31,	Operating Leases
2014	$ 2,385
2015	2,455
2016	2,477
2017	2,500
Thereafter	3,504
	$ 13,321

Other Purchase Commitments

In 2005, the Company entered into a supply agreement with a vendor. The remaining minimum purchase commitments under this agreement are $500,000 per year through 2018.

8. Stockholders' Equity

Common Stock

In December 2012, the Company completed an underwritten public offering through which was sold an aggregate of 14,000,000 shares of common stock pursuant to an effective registration statement at a price to the public of $0.90 per share. The Company received net proceeds of approximately $11.6 million after deducting underwriting discounts and commissions and offering expenses.

In November 2013, the Company completed an underwritten public offering through which was sold an aggregate of 8,214,287 shares of common stock pursuant to an effective registration statement at a price to the public of $1.40 per share. The Company received net proceeds of approximately $10.6 million after deducting underwriting discounts and commissions and estimated offering expenses.

In December 2013, the Company filed a new shelf registration statement on Form S-3 with the SEC, which upon being declared effective in January 2014, allows for the offer of up to $100.9 million of securities from time to time in one or more public offerings of common stock. In addition, the Company entered into a Controlled Equity Offering℠ sales agreement with Cantor Fitzgerald & Co., (Cantor Fitzgerald), under which it may sell, subject to certain limitations, up to $25 million of common stock through Cantor Fitzgerald, acting as agent.

Description of Stock-Based Compensation Plans

2000 Stock Plan (Incentive Stock Plan)

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

In April 2005, the Board of Directors approved certain amendments to the 2000 Stock Plan. At the Company's annual stockholders meeting in June 2005, the stockholders approved the amendments of the 2000 Stock Plan to: (i) expand the types of awards that the Company may grant to eligible service providers under the Stock Plan to include restricted stock units, stock appreciation rights and other similar types of awards (including other awards under which recipients are not required to pay any purchase or exercise price) as well as cash awards; and (ii) include certain performance criteria that may be applied to awards granted under the Stock Plan.

In April 2010, the Board of Directors approved certain amendments to the 2000 Stock Plan. At the Company's annual stockholders meeting in June 2010, the stockholders approved the amendments of the 2000 Stock Plan to: (i) provide that the number of shares that remain available for issuance will be reduced by two shares for each share issued pursuant to an award (other than an option or stock appreciation right) granted on or after the date of the 2010 Annual Meeting; (ii) expand the types of transactions that might be considered repricings and option exchanges for which stockholder approval is required; (iii) provide that shares tendered or withheld in payment of the exercise price of an option or withheld to satisfy a withholding obligation, and all shares with respect to which a stock appreciation right is exercised, will not again be available for issuance under the Stock Plan; (iv) require that options and stock appreciation rights have an exercise price or base appreciation amount that is at least fair market value on the grant date, except in connection with certain corporate transactions, and that stock appreciation rights may not have longer than a 10-year term; (v) add new performance goals that may be used to provide "performance-based compensation" under the 2000 Stock Plan; (vi) extend the term of the 2000 Stock Plan to the date that is ten (10) years following the stockholders meeting; and (vii) expand the treatment of outstanding awards in connection with certain changes of control of the Company to cover mergers in which the consideration payable to stockholders is not solely securities of the successor corporation.

In March 2011, the Board of Directors approved an amendment to the 2000 Stock Plan. At the Company's annual stockholders meeting in June 2011, the stockholders approved the amendment of the 2000 Stock Plan to increase the number of shares of the Company's common stock available for issuance by 5,500,000 shares. A total of 29,796,500 shares of common stock have been reserved for issuance under this plan. The plan expires in June 2020.

In April 2013, the Board of Directors approved certain amendments to the 2000 Stock Plan to: (i) increase the number of stock options granted to a non-employee director on the date which such person first becomes a director from 30,000 to 70,000 shares of common stock; each option shall have a ten-year term, become exercisable in installments of one-third of the total number of options granted on each anniversary of the grant and have a two-year period following termination of Director status in which the former director can exercise the option; (ii) modify the exercise period for future option grants to a non-employee director in which a former director can exercise the option following termination of Director status from a one year period to a two-year period.

Options granted under the 2000 Stock Plan expire no later than ten years from the date of grant. Options may be granted with different vesting terms from time to time not to exceed five years from the date of grant. The option price of an incentive stock option granted to an employee or of a nonstatutory stock option granted to any person who owns stock representing more than 10% of the total combined voting power of all classes of stock of the Company (or any parent or subsidiary) shall be no less than 110% of the fair market value per share on the date of grant. The option price of an incentive stock option granted to any other employee shall be no less than 100% of the fair market value per share on the date of grant.

As of December 31, 2013, 3,406,167 shares of common stock were available for future grant and options to purchase 23,114,331 shares of common stock were outstanding under the 2000 Stock Plan.

2000 Directors' Stock Option Plan

In March 2000, the Board of Directors adopted the 2000 Directors' Stock Option Plan. A total of 300,000 shares of common stock had been reserved initially for issuance under this plan. The directors' plan provides that each person who becomes a non-employee director of the Company after the effective date of the Company's initial public offering will be granted a non-statutory stock option to purchase 20,000 shares of common stock on the date on which the optionee first becomes a non-employee director of the Company. This plan also provides that each option granted to a new director shall vest at the rate of 33 1/3% per year and each annual option of 5,000 shares shall vest in full at the end of one year.

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

In April 2005, the Board of Directors approved certain amendments to the 2000 Directors' Stock Option Plan. At the Company's annual stockholders meeting in June 2005, the stockholders approved the amendments of the 2000 Directors' Stock Option Plan to: (i) increase the number of shares of common stock issuable under the Director's Plan by an additional 425,000 shares, to an aggregate of 925,000 shares; (ii) increase the number of option shares issued to nonemployee directors annually in connection with their continued service on the Board from 12,000 shares to 20,000 shares; and (iii) modify the vesting of such annual option grants so that such shares vest completely on the day before the first anniversary of the date of grant. The plan expired in September 2010. Awards to our non-employee directors have been granted under the 2000 Stock Plan following that date.

As of December 31, 2013, no shares of common stock were available for future grant and options to purchase 622,000 shares of common stock were outstanding under the 2000 Director's Stock Option Plan.

2000 Employee Stock Purchase Plan

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

In April 2010, the Board of Directors approved certain amendments to the 2000 Employee Stock Purchase Plan. At the Company's annual stockholders meeting in June 2010, the stockholders approved the amendments of the 2000 Employee Stock Purchase Plan to: (i) increase the number of shares of our common stock authorized for issuance under the ESPP by 250,000 shares; (ii) extend the term of the ESPP to the date that is ten (10) years following the stockholders meeting; (iii) provide for six-month consecutive offering periods beginning on November 1, 2010; (iv) revise certain provisions to reflect the final regulations issued under Section 423 of the Code by the Internal Revenue Service; and (v) provide for the cash-out of options outstanding under an offering period in effect prior to the consummation of certain corporate transactions as an alternative to providing for a final purchase under such offering period.

The plan expires in June 2020. A total of 2,200,000 shares of common stock have been reserved for issuance under this plan. As of December 31, 2013, 245,377 shares of common stock were available for future grant and 1,954,623 shares of common stock have been issued under the 2000 Employee Stock Purchase Plan.

As of December 31, 2013, shares of common stock reserved for future issuance consisted of the following:

	December 31, 2013
Stock options outstanding	23,736,331
Stock options available for grant	3,406,167
Employee Stock Purchase Plan	245,377
	27,387,875

A summary of stock option activity under all stock-based compensation plans is as follows:

	Number of Options	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value (in millions)
Outstanding at December 31, 2010	19,383,134	$ 3.68	6.36	$ —
Options granted	2,931,779	$ 3.17		
Options exercised	(300,809)	$ 2.71		
Options forfeited	(923,172)	$ 2.91		
Options expired	(625,868)	$ 7.21		
Outstanding at December 31, 2011	20,465,064	$ 3.55	5.65	$ —
Options granted	3,418,287	$ 0.79		
Options exercised	(179,067)	$ 0.78		
Options forfeited	(640,649)	$ 2.47		
Options expired	(2,161,479)	$ 4.37		
Outstanding at December 31, 2012	20,902,156	$ 3.07	5.41	$ —
Options granted	4,592,849	$ 1.21		
Options exercised	(187,014)	$ 1.01		
Options forfeited	(54,308)	$ 1.62		
Options expired	(1,517,352)	$ 3.17		
Outstanding at December 31, 2013	23,736,331	$ 2.73	5.60	$ 5.2
Exercisable at December 31, 2013	19,900,600	$ 2.97	5.04	$ 3.2
Vested and expected to vest at December 31, 2013	23,374,815	$ 2.75	5.54	$ 5.0

The aggregate intrinsic value in the table above represents the total pretax intrinsic value (i.e., the difference between the Company's closing stock price on the last trading day of 2013 and the exercise price, multiplied by the number of in-the-money options) that would have been received by the option holders had all option holders exercised their options on December 31, 2013. This amount changes based on the fair market value of the Company's common stock. The total intrinsic value of options exercised was $77,000, $103,000 and $248,000 for the years ended December 31, 2013, 2012 and 2011, respectively.

In February 2012 and February 2013, the Company granted its employees stock options to purchase 966,000 and 1.7 million shares, respectively, of the Company's common stock, which vested immediately on the grant date. The weighted-average grant-date fair value of all options granted with exercise prices equal to fair market value was $0.85 in 2013, $0.54 in 2012 and $2.13 in 2011 determined by the Black-Scholes option valuation method. There were no options granted with exercise prices lower than fair market value in 2013, 2012 and 2011.

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

As of December 31, 2013, the Company had three stock-based equity compensation plans, which are described above. The employee stock-based compensation cost that has been included in the statements of operations and comprehensive income (loss) is shown as below (in thousands):

	Year ended December 31,		
	2013	2012	2011
Cost of product revenues	$ 170	$ 244	$ 328
Research and development	1,999	2,602	4,181
Selling, general and administrative	1,257	1,474	2,132
	$ 3,426	$ 4,320	$ 6,641

Because the Company had a net operating loss carryforward as of December 31, 2013, no excess tax benefits for the tax deductions related to stock-based compensation expense were recognized in the statement of operations. Additionally, no incremental tax benefits were recognized from stock options exercised during 2013, which would have resulted in a reclassification to reduce net cash provided by operating activities with an offsetting increase in net cash provided by financing activities.

Determining Fair Value

Valuation and Expense Recognition. The Company estimates the fair value of stock options granted using the Black-Scholes option valuation model. For options granted before January 1, 2006, the Company recognized the expense on an accelerated basis. For options granted on or after January 1, 2006, the Company recognizes the expense on a straight-line basis. The expense for options is recognized over the requisite service periods of the awards, which is generally the vesting period.

Expected Term. The expected term of options granted represents the period of time that the options are expected to be outstanding. In 2011, 2012 and 2013, the Company determined the expected life using historical options experience. This develops the expected life by taking the weighted average of the actual life of options exercised and cancelled and assumes that outstanding options are exercised uniformly from the current holding period through the end of the contractual life.

Expected Volatility. The Company estimates the volatility of its common stock at the date of grant based on the historical volatility of the Company's common stock.

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

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

The Company used the following assumptions to estimate the fair value of options granted (including fully vested options issued in February 2012 and February 2013) and shares purchased under its stock plans and employee stock purchase plan for the years ended December 31, 2013, 2012 and 2011:

	Year ended December 31,		
	2013	2012	2011
Stock Options			
Risk-free rate	0.9-2.9%	0.9-1.5%	1.2-2.7%
Expected dividend yield	—	—	—
Expected term (in years)	5.3 – 10.0	5.5 – 6.5	6.3
Volatility	77-86%	78-81%	73-77%
Forfeiture rate	8.4%	7.7%	6.1%

	Year ended December 31,		
	2013	2012	2011
Employee Stock Purchase Plan			
Risk-free rate	0.1-0.2%	0.1-1.0%	0.1-1.0%
Expected dividend yield	—	—	—
Expected term (in years)	0.5	1.3	1.3
Volatility	64-81%	69-101%	50-163%

There were 128,433, 153,730 and 192,997 shares purchased under the Company's employee stock purchase plan during the years ended December 31, 2013, 2012 and 2011, respectively. Included in the statement of operations for the year ended December 31, 2013, 2012 and 2011 was $56,000, $36,000 and $63,000, respectively, in stock-based compensation expense related to the recognition of expenses related to shares purchased under the Company's employee stock purchase plan.

As of December 31, 2013, $2.9 million of total unrecognized compensation costs related to nonvested stock options is expected to be recognized over the respective vesting terms of each award through 2017. The weighted average term of the unrecognized stock-based compensation expense is 1.7 years.

The following table summarizes information about stock options outstanding at December 31, 2013:

Options Outstanding				Options Exercisable	
Range of Exercise Price	Number of Options Outstanding	Weighted-Average Remaining Contractual Life (In years)	Weighted-Average Exercise Price	Number of Options Exercisable	Weighted-Average Exercise Price
$0.73 – 0.73	20,000	8.28	$ 0.73	7,500	$ 0.73
$0.74 – 0.78	2,747,977	8.04	$ 0.78	1,859,091	$ 0.78
$0.82 – 1.20	501,105	9.05	$ 1.01	228,371	$ 0.94
$1.21 – 1.21	3,814,429	9.10	$ 1.21	2,315,220	$ 1.21
$1.24 – 2.13	1,840,314	6.08	$ 1.86	1,428,844	$ 2.02
$2.18 – 2.18	2,522,000	5.79	$ 2.18	2,411,057	$ 2.18
$2.22 – 3.11	3,295,880	4.17	$ 2.92	3,269,786	$ 2.92
$3.12 – 3.26	3,315,805	4.32	$ 3.24	2,722,535	$ 3.24
$3.29 – 4.43	2,405,285	3.07	$ 4.12	2,384,660	$ 4.13
$4.45 – 6.32	3,273,536	3.08	$ 5.56	3,273,536	$ 5.56
$0.73 – 6.32	23,736,331	5.60	$ 2.73	19,900,600	$ 2.97

The Company received $188,000, $140,000 and $815,000 in cash from option exercises under all stock-based compensation plans for the years ended December 31, 2013, 2012 and 2011, respectively.

9. Income Taxes

The Company accounts for income taxes using the liability method under ASC 740, *Income Taxes*. Under this method, deferred tax assets and liabilities are determined based on temporary differences resulting from the different treatment of items for tax and financial reporting purposes. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to reverse. Additionally, the Company must assess the likelihood that deferred tax assets will be recovered as deductions from future taxable income. The Company has provided a full valuation allowance on the Company's deferred tax assets because the Company believes it is more likely than not that its deferred tax assets will not be realized. The Company evaluates the realizability of its deferred tax assets on a quarterly basis. The Company recorded a deferred tax liability of $320,000 on its balance sheet at December 31, 2013 that arose from tax amortization of an indefinitely-lived intangible. The Company also recorded a deferred tax provision of $320,000 related to the deferred tax liability in the year ended December 31, 2013. There was no provision for income taxes in prior years as the Company has incurred losses to date.

The reconciliation of income tax expenses (benefit) at the statutory federal income tax rate of 34% to net income tax benefit included in the statements of operations for the years ended December 31, 2013, 2012 and 2011 is as follows (in thousands):

	Year Ended December 31,		
	2013	2012	2011
U.S. federal taxes provision (benefit) at statutory rate	$ (7,184)	$ 5,516	$ (6,377)
State taxes	—	—	—
Change in valuation allowance	9,517	(7,208)	5,355
Stock-based compensation	375	1,688	995
Change in deferreds	(1,718)	—	—
Other	(670)	4	27
Total income tax provision	$ 320	$ —	$ —

In 2013, 2012 and 2011, total income tax provision was $320,000, zero and zero, respectively. The Company has presented the $320,000 of deferred income tax provision in interest and other income (expenses) in its statements of operation and comprehensive income (loss) for the year ended December 31, 2013. Deferred tax assets and liabilities reflect the net tax effects of net operating loss and research and other credit carryforwards and the temporary differences between the carrying amounts of assets and liabilities for financial reporting and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2013	2012
Deferred tax assets:		
Net operating loss carryforwards	$ 98,425	$ 91,979
Research and other credits	10,127	9,191
Capitalized research and development expenses	498	179
Deferred revenue	584	624
Stock-based compensation	8,661	6,708
Other	3,724	1,600
Total deferred tax assets	122,019	110,281
Valuation allowance for deferred tax assets	(122,019)	(110,281)
Deferred tax liabilities—Intangibles	(320)	—
Net deferred tax assets and liabilities	$ (320)	$ —

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $11.7 million, decreased by $10.7 million and increased by $5.1 million during 2013, 2012 and 2011, respectively.

As of December 31, 2013, the Company had net operating loss carryforwards for federal income tax purposes of approximately $258.6 million, which expire in the years 2019 through 2033, and federal research and development tax credits of approximately $8.4 million which expire at various dates beginning in 2018 through 2033, if not utilized.

As of December 31, 2013, the Company had net operating loss carryforwards for state income tax purposes of approximately $186.0 million, which expire in the years 2014 through 2033, if not utilized, and state research and development tax credits of approximately $9.1 million, which do not expire.

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

At December 31, 2012 and December 31, 2013, the Company had unrecognized tax benefits of approximately $4.8 million and $5.3 million, respectively (none of which, if recognized, would affect the Company's effective tax rate). The Company does not believe there will be any material changes in its unrecognized tax positions over the next twelve months.

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

	December 31,	
	2013	2012
Balance at beginning of the year	$ 4,777	$ 4,644
Increases (decrease) related to prior year tax positions	88	—
Increases (decrease) related to current year tax positions	387	133
Settlements	—	—
Reductions due to lapse of applicable statute of limitations	—	—
Balance at end of the year	$ 5,252	$ 4,777

Interest and penalty costs related to unrecognized tax benefits, if any, are classified as a component of interest income and other income (expense), net in the accompanying Statements of Operations. The Company did not recognize any interest and penalty expense related to unrecognized tax benefits for the years ended December 31, 2013, 2012 and 2011.

The Company files income tax returns in the U.S. federal jurisdiction and various state jurisdictions. The Company is subject to U.S. federal and state income tax examination for calendar tax years ending 1998 through 2013 due to unutilized net operating losses and research credits.

10. Reduction in Force

In February 2012, the Company reduced the size of its workforce by 15 employees or approximately 12% of its headcount. The goal of this action was to better align the Company's cost structure with anticipated revenues and operating expenses, while not compromising the Company's key corporate objectives for the year. The Company completed this headcount reduction during the first quarter of 2012, and incurred approximately $336,000 in severance costs for the impacted employees, of which $195,000 was recorded in research and development expenses and $141,000 was recorded in selling, general and administrative expenses in the first quarter of 2012. All activities related to the restructuring were completed and the severance costs were paid during the first quarter of 2012.

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

	First Quarter		Second Quarter		Third Quarter		Fourth Quarter	
	2013	2012*	2013	2012	2013	2012	2013	2012
Revenue	$ 4,153	$ 41,185	$ 3,918	$ 4,796	$ 2,966	$ 3,828	$ 4,289	$ 3,262
Net income (loss)	$ (5,183)	$ 30,829	$ (5,145)	$ (4,328)	$ (6,024)	$ (4,803)	$ (5,100)	$ (5,498)
Basic net income (loss) per share	$ (0.05)	$ 0.35	$ (0.05)	$ (0.05)	$ (0.06)	$ (0.05)	$ (0.05)	$ (0.06)
Diluted net income (loss) per share	$ (0.05)	$ 0.35	$ (0.05)	$ (0.05)	$ (0.06)	$ (0.05)	$ (0.05)	$ (0.06)

* Revenue in the first quarter of 2012 included one-time recognition of $35.4 million of collaborative research and development revenue as a result of the termination of the Company's agreements with Nycomed, Pfizer and Hospira.

12. Subsequent Events

Agreement with Impax Laboratories, Inc.

On January 3, 2014, the Company and Impax Laboratories, Inc. (Impax) entered into a definitive agreement (the Impax Agreement). Pursuant to the Agreement, the Company has granted Impax an exclusive worldwide license to the Company's proprietary TRANSDUR transdermal delivery technology and other intellectual property to develop and commercialize ELADUR, the Company's investigational transdermal bupivacaine patch for the treatment of pain associated with post-herpetic neuralgia (PHN), in addition to selling certain assets and rights in and related to the product. Impax will control and fund the development and commercialization programs, and the parties will establish a joint management committee to oversee, review and coordinate the development and commercialization activities of the parties under the Impax Agreement. Impax will reimburse the Company for certain future research and development it may be requested to conduct on the product.

In connection with the asset transfer and license, Impax agreed to pay the Company an upfront fee of $2.0 million in cash and to make contingent cash payments to the Company of up to $61.0 million payable based upon the achievement of predefined milestones, of which $31.0 million are development-based milestones and $30.0 million are commercialization-based milestones. Upon the first commercialization of ELADUR by Impax, the Company would also receive a tiered mid single-digit to low double-digit royalty on annual net product sales determined on a country-by-country basis. Impax is also required to pay to the Company a percentage of fees received in connection with any sublicense of the licensed rights. Impax may terminate the Impax Agreement without cause at any time upon prior written notice, and either party may terminate the Impax Agreement upon certain circumstances including written notice of a material uncured breach.

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

Not applicable.

Item 9A. Controls and Procedures.

Disclosure Controls and Procedures

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

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Under the supervision of our Chief Executive Officer and Chief Financial Officer and with the participation of our management, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2013 based on the framework in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 Framework). Based on that evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2013.

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

Changes in Internal Control Over Financial Reporting

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

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of DURECT Corporation

We have audited DURECT Corporation's internal control over financial reporting as of December 31, 2013, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 Framework) (the COSO criteria). DURECT Corporation's management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

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

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

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

In our opinion, DURECT Corporation maintained, in all material respects, effective internal control over financial reporting as of December 31, 2013, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of DURECT Corporation as of December 31, 2013 and 2012, and the related statements of operations and comprehensive income (loss), stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2013 of DURECT Corporation and the financial statement schedule listed in the Index at Item 15(a)(2) and our report dated February 28, 2014 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Redwood City, California
February 28, 2014

Item 9B. Other Information.

None

PART III

The definitive proxy statement for our 2013 annual meeting of stockholders, when filed, pursuant to Regulation 14A of the Securities Exchange Act of 1934, will be incorporated by reference into this Form 10-K pursuant to General Instruction G (3) of Form 10-K and will provide the information required under Part III (Items 10-14), except for the information with respect to our executive officers, which is included in "Part I—Executive Officers of the Registrant."

PART IV

Item 15. Exhibits and Financial Statement Schedules.

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

(1) *Financial Statements*

See Item 8 of this Form 10-K

(2) *Financial Statement Schedules*

Schedule II—Valuation and Qualifying Accounts

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

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

Number	Description
2.1	Agreement and Plan of Merger dated April 18, 2001, among the Company, Target and Magnolia Acquisition Corporation (incorporated by reference to Exhibit 2.1 to our Current Report on Form 8-K (File No. 000-31615) filed on May 15, 2001).
2.2	Agreement and Plan of Merger dated August 15, 2003, among the Company, Birmingham Polymers, Inc., Absorbable Polymer Technologies, Inc. and the Principal Shareholders of Absorbable Polymer Technologies, Inc. (incorporated by reference to Exhibit 2.2 to our Registration Statement on Form S-3, as amended (File No. 333-108396), initially filed on August 29, 2003).
3.3	Amended and Restated Certificate of Incorporation of the Company (incorporated by reference to Exhibit 3.3 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
3.4	Certificate of Amendment of the Amended and Restated Certificate of Incorporation of the Company (incorporated by reference to Exhibit 3.4 to our Post-Effective Amendment No. 1 to our Registration Statement on Form S-3, filed on July 1, 2010.
3.5	Amended and Restated Bylaws of the Company (incorporated by reference to Exhibit 3.5 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
3.6	Certificate of Designation of Rights, Preferences and Privileges of Series A Participating Preferred Stock of DURECT Corporation (incorporated by reference to Exhibit 3.3 to our Registration Statement on Form S-3 (File No. 333-128979) initially filed on October 13, 2005).

Number	Description
3.7	Certificate of Amendment to Certificate of Designation of Rights, Preferences and Privileges of Series A Participating Preferred Stock of DURECT Corporation (incorporated by reference to Exhibit 3.7 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 5, 2010).
3.8	Amendment to Bylaws of the Company (incorporated by reference to Exhibit 3.8 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 5, 2011).
4.2	Second Amended and Restated Investors' Rights Agreement (incorporated by reference to Exhibit 4.2 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
4.3	Preferred Shares Rights Agreement, dated as of July 6, 2001, between the Company and EquiServe Trust Company, N.A. including the form of Certificate of Designation, the form of the Rights Certificate and the Summary of Rights attached thereto as Exhibits A, B and C, respectively (incorporated by reference to Exhibit 1 to our Registration Statement on Form 8-A (File No. 000-31615) filed on July 10, 2001).
10.1+	Form of Indemnification Agreement between the Company and each of its Officers and Directors (incorporated by reference to Exhibit 10.1 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.2+	1998 Stock Option Plan (incorporated by reference to Exhibit 10.2 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.3+	2000 Stock Plan, as amended and restated (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K (File No. 000-31615) filed on June 27, 2011).
10.4+	2000 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.4 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.5+	2000 Directors' Stock Option Plan (incorporated by reference to Exhibit 10.5 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.6**	Second Amended and Restated Development and Commercialization Agreement between the Company and ALZA Corporation effective April 28, 1999 (incorporated by reference to Exhibit 10.6 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.7**	Product Acquisition Agreement between the Company and ALZA Corporation dated as of April 14, 2000 (incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.8	Amended and Restated Loan and Security Agreement between the Company and Silicon Valley Bank dated as of October 28, 1998 (incorporated by reference to Exhibit 10.8 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.9**	Manufacturing and Supply Agreement between Neuro-Biometrix, Inc. and Novel Biomedical, Inc. dated as of November 24, 1997 (incorporated by reference to Exhibit 10.9 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.10**	Master Services Agreement between the Company and Quintiles, Inc. dated as of November 1, 1999 (incorporated by reference to Exhibit 10.10 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.11	Modified Net Single Tenant Lease Agreement between the Company and DeAnza Enterprises, Ltd. dated as of February 18, 1999 (incorporated by reference to Exhibit 10.11 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).

Number	Description
10.12	Sublease Amendment between the Company and Ciena Corporation dated as of November 29, 1999 and Sublease Agreement between Company and Lightera Networks, Inc. dated as of March 10, 1999 (incorporated by reference to Exhibit 10.12 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.13**	Project Proposal between the Company and Chesapeake Biological Laboratories, Inc. dated as of October 11, 1999 (incorporated by reference to Exhibit 10.13 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.17	Common Stock Purchase Agreement between the Company and ALZA Corporation dated April 14, 2000 (incorporated by reference to Exhibit 10.17 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.18	Warrant issued to ALZA Corporation dated April 14, 2000 (incorporated by reference to Exhibit 10.18 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.19	Amended and Restated Market Stand-off Agreement between the Company and ALZA Corporation dated as of April 14, 2000 (incorporated by reference to Exhibit 10.19 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.20**	Asset Purchase Agreement between the Company and IntraEAR, Inc. dated as of September 24, 1999 (incorporated by reference to Exhibit 10.20 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.21	Warrant issued to Silicon Valley Bank dated December 16, 1999 (incorporated by reference to Exhibit 10.21 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.22	Amendment to Second Amended and Restated Investors' Rights Agreement dated as of April 14, 2000 (incorporated by reference to Exhibit 10.22 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.23**	Master Agreement between the Company and Pacific Data Designs, Inc. dated as of July 6, 2000 (incorporated by reference to Exhibit 10.23 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.24**	Master Services Agreement between the Company and Clinimetrics Research Associates, Inc. dated as of July 11, 2000 (incorporated by reference to Exhibit 10.24 to our Registration Statement on Form S-1, as amended (File No. 333-35316), initially filed on April 20, 2000).
10.25**	Supply Agreement between the Company and Mallinckrodt, Inc. dated as of October 1, 2000 (incorporated by reference to Exhibit 10.25 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 30, 2001).
10.26	Lease between Sobrato Development Companies #850 and the Company (incorporated by reference to Exhibit 10.26 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 13, 2001).
10.27	Southern BioSystems, Inc. 1993 Stock Option Plan (as amended) (incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-8 (File No. 333-61224) filed on May 18, 2001).
10.28	Southern Research Technologies, Inc. 1995 Nonqualified Stock Option Plan (as amended) (incorporated by reference to Exhibit 4.2 to our Registration Statement on Form S-8 (File No. 333-61224) filed on May 18, 2001).

Number	Description
10.29**	Feasibility, Development and Commercialization Agreement between Southern BioSystems, Inc., an Alabama corporation and wholly-owned subsidiary of the Company (now merged into the Company), and Voyager Pharmaceutical Corporation dated as of July 22, 2002 (incorporated by reference to Exhibit 10.29 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 14, 2002).
10.30**	License & Option Agreement and Mutual Release between Southern BioSystems, Inc, an Alabama corporation and wholly-owned subsidiary of the Company (now merged into the Company), and Thorn BioScience LLC dated as of July 26, 2002 (incorporated by reference to Exhibit 10.30 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 14, 2002).
10.31**	Third Amended and Restated Development and Commercialization Agreement between the Company and ALZA Corporation dated as of October 1, 2002 (incorporated by reference to Exhibit 10.31 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 14, 2002).
10.32**	Development and License Agreement between the Company, Southern BioSystems, Inc, an Alabama corporation and wholly-owned subsidiary of the Company (now merged into the Company), and BioPartners, GmbH dated as of October 18, 2002 (incorporated by reference to Exhibit 10.32 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 14, 2003).
10.33**	Development, Commercialization and Supply License Agreement between the Company and Endo Pharmaceuticals Inc. dated as of November 8, 2002 (incorporated by reference to Exhibit 10.33 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 14, 2003).
10.34**†	Development and License Agreement between the Company, Southern BioSystems, Inc., an Alabama corporation and wholly-owned subsidiary of the Company (now merged into the Company), and Pain Therapeutics, Inc. dated as of December 19, 2002 (incorporated by reference to Exhibit 10.34 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 14, 2003).
10.35	Sublease between the Company and Norian Corporation with commencement date of January 1, 2004 (incorporated by reference to Exhibit 10.35 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 11, 2004).
10.36	Lease between the Company and Renault & Handley Employee Investments Co. with commencement date of January 1, 2005 (incorporated by reference to Exhibit 10.36 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 11, 2004).
10.37	Amendment to Development, Commercialization and Supply License Agreement between the Company and Endo Pharmaceuticals Inc. dated as of January 28, 2004 (incorporated by reference to Exhibit 10.37 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 11, 2004).
10.38	Indenture of Lease between the Company and the Board of Trustees of the University of Alabama dated as of May 1, 2004 (incorporated by reference to Exhibit 10.38 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 4, 2004).
10.39**	License and Commercial Agreement between the Company and NeuroSystec Corporation dated as of May 13, 2004 (incorporated by reference to Exhibit 10.39 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 4, 2004).
10.40	Commercial Lease between the Company and EWE, Inc. dated as of September 21, 2004 (incorporated by reference to Exhibit 10.40 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 5, 2004).
10.41**	License agreement between the Company and Endo Pharmaceuticals, Inc. dated as of March 10, 2005 (incorporated by reference to Exhibit 10.41 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on May 6, 2005).

Number	Description
10.42	Indenture of Lease between the Company and the Board of Trustees of the University of Alabama dated as of April 25, 2005 (incorporated by reference to Exhibit 10.42 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 4, 2005).
10.43	Third Addendum to Lease between the Company and Garaventa Properties dated as of July 8, 2005 (incorporated by reference to Exhibit 10.43 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on October 13, 2005).
10.44	Lease between the Company and RWC, LLC dated as of September 1, 2005 (incorporated by reference to Exhibit 10.44 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on October 13, 2005).
10.45**	Amendment dated December 21, 2005 to Development and License Agreement dated December 19, 2002 between the Company and Pain Therapeutics, Inc. (incorporated by reference to Exhibit 10.45 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 16, 2006).
10.46**	Sucrose Acetate Isobutyrate Pharmaceutical Grade Supply Agreement between the Company and Eastman Chemical Company dated as of December 30, 2005 (incorporated by reference to Exhibit 10.46 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 16, 2006).
10.47	Indenture of Lease between the Company and the Board of Trustees of the University of Alabama dated as of October 17, 2006 (incorporated by reference to Exhibit 10.47 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 15, 2007).
10.48**	Development and License Agreement between the Company and NYCOMED Danmark ApS dated as of November 29, 2006 (incorporated by reference to Exhibit 10.48 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 15, 2007).
10.49**	License Agreement between the Company and EpiCept Corporation dated as of December 20, 2006 (incorporated by reference to Exhibit 10.49 to our Annual Report on Form 10-K (File No. 000-31615) filed on March 15, 2007).
10.50	Lease between the Company and KLP Properties dated as of April 23, 2008 (incorporated by reference to Exhibit 10.50 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 8, 2008).
10.51	Amendment No. 1 to License Agreement between the Company and EpiCept Corporation dated as of September 12, 2008 (incorporated by reference to Exhibit 10.51 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 4, 2008).
10.52**	Development and License Agreement between the Company and Alpharma Ireland Limited dated as of September 19, 2008 (incorporated by reference to Exhibit 10.52 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 4, 2008).
10.53	Amendment to Commercial Lease between the Company and EWE, Inc. effective December 23, 2008 (incorporated by reference to Exhibit 10.53 to our Annual Report on Form 10-K (File No. 000-31615) filed with the SEC on March 10, 2009).
10.54	First Lease Extension between the Company and Renault & Handley Employee Investments Co. effective March 1, 2009 (incorporated by reference to Exhibit 10.54 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on May 7, 2009).
10.55**	Excipient Manufacturing and Supply Agreement between King Pharmaceuticals, Inc. and the Company dated as of August 5, 2009 (incorporated by reference to Exhibit 10.55 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 2, 2009).
10.56	Second Amendment to Lease between De Anza Enterprises and the Company dated as of August 6, 2009 (incorporated by reference to Exhibit 10.56 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 2, 2009).

Number	Description
10.57**	Amendment No. 1 to Development and License Agreement between the Company and Nycomed Danmark, ApS dated February 18, 2010 (incorporated by reference to Exhibit 10.57 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on May 10, 2010).
10.58	Amendment to Commercial Real Estate Lease between the Company and EWE, Inc. effective May 10, 2010 (incorporated by reference to Exhibit 10.58 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 5, 2010).
10.59**	Development and License Agreement between the Company and Hospira, Inc. dated June 1, 2010 (incorporated by reference to Exhibit 10.59 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 5, 2010).
10.60	Supply Agreement between the Company and Hospira, Inc. dated June 1, 2010 (incorporated by reference to Exhibit 10.60 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 5, 2010).
10.61	Common Stock Purchase Agreement between DURECT Corporation and Azimuth Opportunity Ltd., dated July 1, 2010 (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K (File No. 000-31615) filed on July 1, 2010).
10.62	Lease between the Company and DRA/CLP Riverchase Center Birmingham, LLC dated as of October 19, 2010 (incorporated by reference to Exhibit 10.62 to our Annual Report on Form 10-K (File No. 000-31615) filed with the SEC on March 3, 2011).
10.63	Third Amendment to Lease between De Anza Enterprises and the Company dated as of December 21, 2010 (incorporated by reference to Exhibit 10.63 to our Annual Report on Form 10-K (File No. 000-31615) filed with the SEC on March 3, 2011).
10.64**	Amendment No. 2 to Development and License Agreement between DURECT Corporation and Nycomed Danmark, APS dated February 8, 2011 (incorporated by reference to Exhibit 10.64 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on May 6, 2011).
10.65	Amendment to Commercial Lease between the Company and EWE, Inc. effective May 23, 2011 (incorporated by reference to Exhibit 10.65 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on August 5, 2011).
10.66**	Development and License Agreement between the Company and Zogenix, Inc. effective July 11, 2011 (incorporated by reference to Exhibit 10.66 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed on November 7, 2011).
10.67	Lease Termination Agreement between ECI TWO RESULTS LLC and the Company dated as of October 27, 2011 (incorporated by reference to Exhibit 10.67 to our Annual Report on Form 10-K (File No. 000-31615) filed with the SEC on March 2, 2012).
10.68	Amendment to Commercial Lease between the Company and EWE, Inc. effective December 19, 2011 (incorporated by reference to Exhibit 10.68 to our Annual Report on Form 10-K (File No. 000-31615) filed with the SEC on March 2, 2012).
10.69	Amendment to Commercial Lease between the Company and EWE, Inc. effective March 9, 2012 (incorporated by reference to Exhibit 10.69 to our Annual Report on Form 10-Q (File No. 000-31615) filed with the SEC on May 4, 2012).
10.70**	Amendment dated March 18, 2013 to Development and License Agreement dated July 11, 2011 between the Company and Zogenix, Inc (incorporated by reference to Exhibit 10.69 to our Annual Report on Form 10-Q (File No. 000-31615) filed with the SEC on May 3, 2013).
10.71	Fourth Amendment to Lease between De Anza Enterprises and the Company dated as of August 20, 2013(incorporated by reference to Exhibit 10.69 to our Annual Report on Form 10-Q (File No. 000-31615) filed with the SEC on November 5, 2013).

Number	Description
10.72	Addendum II to Lease between the Company and Northwest Asset Management Company dated as of August 27, 2013(incorporated by reference to Exhibit 10.69 to our Annual Report on Form 10-Q (File No. 000-31615) filed with the SEC on November 5, 2013).
10.73	Second Amendment to Lease between Handley Management Corporation, as successor-by-merger to Renault & Handley Employee Investments Co. and the Company dated November 11, 2013.
10.74	Executive Change of Control Policy, as amended December 12, 2013
12.1*	Ratio of Earnings to Fixed Charges.
23.1*	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (see signature page of this Form 10-K).
31.1*	Rule 13a-14(a) Section 302 Certification.
31.2*	Rule 13a-14(a) Section 302 Certification.
32.1*	Certificate pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certificate pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

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

† Refiled with additional disclosure previously treated as confidential.

\+ Indicates a management contract or compensatory plan or arrangement.

SCHEDULE II—VALUATION AND QUALIFYING ACCOUNTS

Year Ended December 31, 2013, 2012 and 2011
(in thousands)

	Balance at beginning of the year	Provision	Recoveries/ Write-Offs	Balance at end of the year
December 31, 2013				
Allowance for doubtful accounts	$ 154	$ (20)	$ 10	$ 144
December 31, 2012				
Allowance for doubtful accounts	$ 98	$ 73	$ (17)	$ 154
December 31, 2011				
Allowance for doubtful accounts	$ 107	$ (23)	$ 14	$ 98

SIGNATURES

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

DURECT CORPORATION

By: /S/ JAMES E. BROWN
James E. Brown
President and Chief Executive Officer

Date: February 28, 2014

POWER OF ATTORNEY

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

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ JAMES E. BROWN **James E. Brown**	President, Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2014
/s/ FELIX THEEUWES **Felix Theeuwes**	Chairman and Chief Scientific Officer	February 28, 2014
/s/ MATTHEW J. HOGAN **Matthew J. Hogan**	Chief Financial Officer (Principal Accounting Officer)	February 28, 2014
/s/ SIMON X. BENITO **Simon X. Benito**	Director	February 28, 2014
/s/ TERRENCE F. BLASCHKE **Terrence F. Blaschke**	Director	February 28, 2014
/s/ DAVID R. HOFFMANN **David R. Hoffmann**	Director	February 28, 2014
/s/ ARMAND P. NEUKERMANS **Armand P. Neukermans**	Director	February 28, 2014
/s/ JON S. SAXE **Jon S. Saxe**	Director	February 28, 2014
/s/ JAY SHEPARD **Jay Shepard**	Director	February 28, 2014

Exhibit 10.73

SECOND AMENDMENT TO LEASE

This Second Amendment to Lease ("Second Amendment"), dated November 11, 2013, by and between Handley Management Corporation ("Lessor"), as successor-by-merger to Renault & Handley Employees Investment Co. (the "Original Lessor"), and Durect Corporation, a Delaware corporation ("Lessee"), amends that certain Lease, dated May 14, 2003 (the "Original Lease"), by and between Original Lessor and Lessee, as amended by that certain First Lease Extension, dated December 15, 2008 (the "First Extension"), the Original Lease, as amended by the First Extension, is hereinafter referred to as the "Lease", for the Premises located at 10260 Bubb Road, Cupertino, California with reference to the following facts:

RECITALS

A. WHEREAS, Lessee exercised its Second Option to Extend for an additional five (5) year term commencing on March 1, 2014 and terminating February 28, 2019, as set forth in the Lease.

B. WHEREAS, Lessor and Lessee wish to set a new monthly rental rate for the extended term and provide for an additional five (5) year renewal option as set forth in this Second Amendment.

NOW, THEREFORE, for good and valuable consideration, receipt of which is hereby acknowledged, Lessor and Lessee agree as follows:

1. RECITALS; DEFINED TERMS: The recitals set forth above are incorporated by reference into this Second Amendment as though set forth at length. Capitalized terms used but not defined herein shall have the meanings given them in the Lease.

2. TERM: The Lease is hereby extended for a period of five (5) years, commencing on March 1, 2014 and terminating February 28, 2019 (the "Extension Term").

3. OPTION TO EXTEND: Provided that Lessee is not in default under the Lease after applicable notice and cure periods, and has faithfully performed its obligations under the Lease, Lessor hereby grants Lessee an option to extend the term of this Lease (the "Option to Extend") for a period of one (1) additional five(5) year term commencing March 1, 2019 and terminating February 29, 2024 (the "Option Period") on all the same terms and conditions of the Lease excepting that there shall be no additional options to extend and excepting the Base Monthly Rent which shall be at 100% of the then current fair market monthly rental value for the Premises as improved ("FMV") determined in accordance with Paragraph 36 of the Original Lease. Lessee shall exercise its Option to Extend by giving written notice to Lessor of its intent to do so not less than six (6) months nor more than nine (9) months prior to March 1, 2019.

4. RENTAL: Base Monthly Rent for the Extension Term shall be payable to Lessor without defense, deduction or offset at such place or places as may be designated from time to time by Lessor in the following amounts:

Commencing on March 1, 2014, and on the first day of each and every succeeding month to and including February 1, 2015 $45,426.00 shall be due.

Commencing on March 1, 2015, and on the first day of each and every succeeding month to and including February 1, 2016, $46,788.78 shall be due.

Commencing on March 1, 2016, and on the first day of each and every succeeding month to and including February 1, 2017, $48,192.44 shall be due.

Commencing on March 1, 2017, and on the first day of each and every succeeding month to and including February 1, 2018, $49,638.22 shall be due.

Commencing on March 1, 2018, and on the first day of each and every succeeding month to and including February 1, 2019, $51,127.36 shall be due.

5. SECURITY DEPOSIT: Lessor shall retain the existing Security Deposit as security for the full and faithful performance of each and every term, condition, covenant and provision of the Lease, as may be extended.

6. CONDITION OF PREMISES AND ALTERATIONS: Lessee has accepted possession of the Premises, and Lessor shall have no obligation to alter or improve the Premises, or to pay any costs of any such alterations or improvements.

7. FULL FORCE & EFFECT: As of the date hereof, the Lease is in full force and effect. From and after the date hereof, the term “Lease” shall mean the Lease as amended by this Second Amendment.

8. ENTIRETY: Except as provided in this Second Amendment, the Lease is the entire agreement between the parties and there are no agreements or representations between the parties except as expressed herein. Moreover, no subsequent change or modification of the Lease, as amended, shall be binding unless in writing and fully executed by Lessor and Lessee.

9. MISCELLANEOUS: Any inconsistencies or conflicts between the terms and provisions of the Lease and the terms and provisions of this Second Amendment shall be resolved in favor of the terms and provisions of this Second Amendment. This Second Amendment may be executed and delivered in any number of counterparts, including delivery by facsimile transmission, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

10. AUTHORITY: Lessor and Lessee each represent and warrant to the other that it has full authority to enter into and perform this Second Amendment without the consent or approval of any other person or entity including, without limitation, any mortgagees, partners, ground lessors, or other superior interest holders or interested parties. Each person signing this Second Amendment on behalf of Lessor or Lessee represents and warrants that he or she has the full and complete authority, corporate, partnership or otherwise, to bind Lessor or Lessee, as the case may be, to this Second Amendment.

[Remainder of Page Intentionally Blank Signatures on Following Page.]

IN WITNESS THEREOF, Lessor and Lessee have executed this Second Amendment to Lease as of the Effective Date.

Lessee:

Durect Corporation, a Delaware Corporation

By: Matt Hogan
Name: Matt Hogan
Its: Chief Financial Officer

Lessor:

Handley Management Corporation

By: Alice J. Holmes
Name: Alice J. Homes
Its: General Manager

Exhibit 10.74

DURECT CORPORATION
EXECUTIVE CHANGE OF CONTROL POLICY

This Executive Change of Control Policy (the "Policy") is effective as of April 7, 2004, as amended on September 25, 2008 and December 12, 2013.

POLICY GOALS

A. It is expected that the Company from time to time will consider the possibility of an acquisition by another company or other change of control transaction. The Board of Directors of the Company (the "Board") recognizes that such consideration can be a distraction to officers of the Company and can cause these individuals to consider alternative employment opportunities. The Board has determined that it is in the best interests of the Company and its stockholders to assure that the Company will have the continued dedication and objectivity of its officers, notwithstanding the possibility, threat or occurrence of a Change of Control (as defined below) of the Company.

B. Accordingly, the Board believes that it is in the best interests of the Company and its stockholders to provide officers with an incentive to continue their employment and to motivate such individuals to maximize the value of the Company upon a Change of Control for the benefit of its stockholders by providing them with certain benefits upon a Change of Control that provide them with enhanced financial security and incentive notwithstanding the possibility or occurrence of a Change of Control.

POLICY

1. ELIGIBILITY. This Policy shall be applicable to each individual who is an employee of the Company holding a position of Vice President (or equivalent position) or higher as of the effective date of a Change of Control or who held such a position with the Company within 90 days of such date but whose employment terminated under the conditions specified in Section 3 below (each, an "Officer"); provided, however, that the terms of this Policy will not apply to any Officer who is party to one or more agreements with the Company providing for specified benefits to the Officer upon or in connection with a Change of Control unless such Officer expressly consents (by executing the acknowledgment provided below) to becoming a participant eligible to receive benefits under this Policy and thereby expressly waiving and forfeiting any rights or claims he or she has or may have under any such prior agreement(s). Once acknowledged below, the terms of this Policy shall constitute the entire agreement between the Officer and the Company as to the subject matter covered by the Policy and such terms may thereafter be amended only by a written agreement signed by the Officer and, following approval by the Company's Board or a Committee thereof, a duly authorized officer of the Company.

2. AT-WILL EMPLOYMENT. Unless otherwise agreed to expressly by the Company and an Officer through a separate written agreement which remains in effect after the Officer becomes eligible to receive benefits under this Policy, each Officer's employment is and shall continue to be on an at-will basis, meaning that either the Officer or the Company (or its successor) can terminate their employment relationship with each other at any time for any or no reason. Nothing in this Policy shall give an Officer any benefits whatsoever in the event the Officer's employment terminates in a manner that is not in connection with a Change of Control.

3. SEPARATION BENEFITS UPON INVOLUNTARY TERMINATION FOLLOWING CHANGE OF CONTROL. If, in connection with and within 90 days prior to a Change of Control, or within twenty-four (24) months following the effective date of a Change of Control, the Officer's employment with the Company (or its successor) is terminated by the Company or the successor without Cause or the Officer experiences a Constructive Termination (in each case as defined below), then subject to Sections 3(c), 4 and 5 below the Officer will be entitled to the following benefits:

(a) Vesting Acceleration. The remaining unvested portion of any such stock options or shares of stock held by the Officer as of the effective date of the employment termination shall automatically be accelerated so as to become completely vested and exercisable (and any such right of repurchase or forfeiture provision shall lapse in full) as of the effective date of such termination; and

(b) Cash Benefits. The Officer will be entitled to payment of an amount equal in aggregate to his or her then-current annual base salary, payable in equal installments (on the Company's normal payroll schedule and subject to applicable withholdings) over the 12 months following the date of employment termination; provided however that this Section 3(b) shall be subject to Section 5(c) below; and provided further that the Company's obligations to make any payments under this Section 3(b) is subject to Section 3(c) below.

(c) Conditions to Payment of Benefits. Notwithstanding anything else to the contrary contained herein, no Officer shall be entitled to payment of any benefits provided under this Section 3 or otherwise under this Policy unless and until (1) the Company (or its successor) shall have received from the Officer an effective release releasing the Company (or its successor) from any and all claims Officer may have against such entities related to or arising in connection with his or her employment, the terms of such employment and termination thereof that becomes effective within sixty (60) days following the termination of employment (or if later, the Change of Control), and (2) the Officer is in compliance and continues to be in compliance with the covenants contained in Section 4 below (the "Covenants"), which Covenants shall be acknowledged and agreed to by the Officer upon his or her executing this Policy in the acknowledgment signature block below. The Officer further acknowledges that the benefits under this Policy are being provided to assist in the Officer's transition to other employment. Accordingly, to the extent that the Officer begins to engage in activities in violation of the Covenants during the period of the cash severance payments specified in Section 3(b) above, the Officer shall be entitled to retain any such payments received prior to the date he commences such activities but will cease to be eligible to receive any further payments or other benefits under the terms of this Policy or otherwise, and the Officer shall have no further claims, rights or entitlements to any severance payments or benefits in any respect.

4. COVENANTS. During his or her employment with the Company, the Officer agrees to devote his or her full time and best efforts to the business of the Company, and the Officer further agrees that during his or her employment with the Company and for any period thereafter for which he or she is receiving or has received payment of cash severance under Section 3(b) above (but in any event not exceeding two years), he or she will not, directly or indirectly, act as a partner, joint venturer, consultant, officer, director, employee, agent, independent contractor or stockholder of any company or business organization (including any unit or division of any company or organization) whose business is the development and marketing of products and services that are directly competitive with the products and services being developed and marketed by the Company immediately prior to the Change of Control; provided, however, that the record or beneficial ownership by the Officer of 5% or less of the outstanding publicly traded capital stock of any such company shall not be deemed, in and of itself, to be in violation of the Covenants set forth in this Section 4.

5. TAXES.

(a) General Withholding Tax Obligations. The Officer shall be responsible for any income, excise or other taxes imposed on the Officer under applicable law with respect to the benefits provided hereunder, including without limitation delivering to the Company (or its successor) any amounts necessary to timely satisfy any applicable withholding tax obligations. The Officer's receipt of any benefit hereunder is conditioned on his or her satisfaction of any applicable withholding or similar obligations that apply to such benefit, and any cash payment owed hereunder will be reduced to satisfy any such withholding or similar obligations that may apply.

(b) Limitation on Payments. In the event that the benefits provided for under this Policy (x) constitute "parachute payments" within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), and (y) but for this Section 4(b) would be subject to the excise tax imposed by Section 4999 of the Code (or any corresponding provisions of state income tax law), then such benefits shall be either (1) delivered in full to the Officer, or (2) delivered as to such lesser extent as would result in no portion of such severance benefits being subject to excise tax under Code Section 4999, whichever amount, taking into account the applicable federal, state and local income taxes and the excise tax imposed by Code Section 4999, results in the receipt by the Officer on an after-tax basis of the greater amount of benefits, notwithstanding that all or some portion of such benefits may be taxable under Code Section 4999. Any determination required under this Section 5(b) shall be made in writing by the Company's independent accountants, whose determination shall be conclusive and binding for all purposes on the Company and the Officer. In the event that (1) above applies, then the Officer shall be responsible for any excise taxes imposed with respect to such benefits. In the event that (2) above applies, then each benefit provided hereunder shall be proportionately reduced to the extent necessary to avoid imposition of such excise taxes.

(c) Code Section 409A. It is the parties' intent that this Policy and the benefits payable hereunder comply with the requirements of Code Section 409A and any final regulations and guidance promulgated thereunder (collectively "Section 409A") so that none of the severance payments and benefits to be provided hereunder will be subject to the additional tax imposed under Section 409A, and any ambiguities herein will be interpreted to so comply. Notwithstanding anything to the contrary in this Policy (or other agreement or arrangement referenced below in this Section 9(b)), if Officer is a "specified employee" within the meaning of Section 409A at the time of Officer's "separation from service" (as defined in Section 409A) (other than due to death), and if the amounts payable to Officer pursuant to Section 3(b) this Policy, when considered together with other severance payments or separation benefits, if any, to which Officer may be entitled under any other agreement or arrangement, would be considered deferred compensation under Section 409A (together, the "Deferred Compensation Separation Benefits"), then only that portion of the Deferred Compensation Separation Benefits which does not exceed the Section 409A Limit (as defined below) may be made within the first six (6) months following Officer's separation from service date in accordance with the payment schedule that otherwise applies to each payment or benefit. Any portion of the Deferred Compensation Separation Benefits in excess of the Section 409A Limit otherwise due to Officer on or within the six (6) month period following Officer's separation from service will accrue during such six (6) month period and will become payable in a lump sum payment on the date six (6) months and one (1) day following the separation from service date. All subsequent Deferred Compensation Separation Benefits, if any, will be payable in accordance with

the payment schedule otherwise applicable to each payment or benefit. For these purposes, each severance payment provided for under this Policy is hereby designated as a separate payment and will not collectively be treated with any other payments as a single payment. Notwithstanding anything herein to the contrary, if Officer dies following his or her separation from service but prior to the six (6) month anniversary of his or her separation from service date, then any payments delayed in accordance with this Section 5(c) will be payable in a lump sum as soon as administratively practicable after the date of Officer's death and all other Deferred Compensation Separation Benefits will be payable in accordance with the payment schedule applicable to each payment or benefit.

For purposes of this Policy, "Section 409A Limit" will mean the lesser of two (2) times: (i) Officer's annualized compensation based upon the annual rate of pay paid to Officer during the Company's taxable year preceding the Company's taxable year of Officer's termination of employment as determined under Treasury Regulation 1.409A-1(b)(9)(iii)(A)(1) and any Internal Revenue Service guidance issued with respect thereto; or (ii) the maximum amount that may be taken into account under a qualified plan pursuant to Code Section 401(a)(17) for the year in which Officer's separation from service occurs.

Notwithstanding anything to the contrary contained in this Policy, to the extent that any amendment to this Policy would constitute under Section 409A a delay or acceleration in payment of a Deferred Compensation Separation Benefit, or a change in the form of payment of a Deferred Compensation Separation Benefit, then such any amendment that effects a delay in a payment or a change in the form of payment must be done in a manner that complies with Section 409A(a)(4)(C) and any amendment that effects an acceleration of payment must be done in a manner that complies with Treas. Reg. §1.409A-3(j).

6. DEFINITION OF TERMS. The following terms referred to in this Policy shall have the following meanings:

(a) Change of Control. "Change of Control" means the occurrence of any of the following events:

(i) The closing of the sale of all or substantially all of the assets of the Company;

(ii) The closing of a merger or consolidation of the Company with any other corporation (other than a merger effected exclusively for the purpose of changing the domicile of the Company or a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity) at least fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity outstanding immediately after such merger or consolidation);

(iii) the direct or indirect acquisition (including by way of a tender or exchange offer) by any person, or persons acting as a group, of beneficial ownership or a right to acquire beneficial ownership of shares representing a majority of the voting power of the then-outstanding shares of capital stock of the Company;

(iv) a contested election of members of the Board (each, a "Director"), as a result of which or in connection with which the persons who were Directors before such election or their nominees cease to constitute a majority of the Board; or

(v) a dissolution or liquidation of the Company; provided however that a dissolution or liquidation of the Company will not constitute a "Change of Control" for purposes of this Policy if it is entered into in connection with proceedings by or against the Company under the United States Bankruptcy Code, or any other bankruptcy or insolvency law, including assignments for the benefit of creditors, compositions, extensions generally with its creditors, or proceedings seeking reorganization, arrangement, or other similar relief undertaken under U.S. federal, state or foreign law, including the Federal Bankruptcy Reform Act of 1978 (11 U.S.C. §101, et seq.), as amended.

(b) Cause. For purposes of this Policy, "Cause" for an Officer's termination will exist at any time after the happening of one or more of the following events:

(i) The Officer's deliberate material violation of any policy of the Company (or its successor) or deliberate refusal to comply in any material respect with the legal directives of his or her supervisor or the Board (so long as such directives are legal and consistent with the Officer's position and duties); or

(ii) The Officer's commission of any act of fraud, embezzlement, dishonesty or any other willful misconduct (including conviction of a felony) that has caused or is reasonably expected to cause material injury to the Company, its business or its reputation (or to its successor or its successor's business or reputation), or any act that constitutes fraud, or any knowing misrepresentation, involving or related to the Company's financial statements; or

(iii) Any unauthorized use or disclosure by the Officer of any proprietary information or trade secrets of the Company (or its successor) or any other party to whom the Officer owes an obligation of nondisclosure or use (through a written agreement or otherwise) as a result of his or her relationship with the Company (or its successor); or

(iv) The Officer's willful, material breach of any of his or her obligations under any written agreement or covenant with the Company (or its successor); or

(v) The Officer's failure to materially perform his or her duties or materially comply with the conditions applicable to his or her employment.

(c) Constructive Termination. "Constructive Termination" shall be deemed to occur if there is (i)(A) a material reduction in job title or responsibilities of the Officer (provided, however, that reassignment to a position, irrespective of title, that changes the Officer's responsibilities in a manner designed merely to reflect the fact that the Company has become a wholly-owned subsidiary or division of the counter-party to the Change of Control shall not constitute grounds for Constructive Termination); (B) a reduction of more than 20% of the Officer's base salary unless in connection with similar decreases of other similarly-situated officers of the Company or its successor entity; or (C) the Officer's refusal to relocate to a facility or location more than 50 miles from the Company's location at which the Officer works as of the effective date of the Change of Control; and (ii) immediately following any of the foregoing events, the Officer provides to his or her employer within 20 business days of such event written notice of his or her intent to terminate employment as a result of Constructive Termination, which written notice specifies the events or circumstances giving rise to the Officer's claim that Constructive Termination has occurred as well as the effective date of termination (which date shall be within 45 days of the date on which such notice is given); provided however that the Company shall have 30 days in which to cure the events or circumstances giving rise to the Constructive Termination claim and, if the Company is able to cure such events or circumstances within such 30-day period, then the Officer shall not have a basis to terminate his or her employment for Constructive Termination.

7. GOVERNING LAW. This policy shall be governed by the laws of the state in which the Officer performs or most recently performed his or her primary duties to the Company, without giving effect to the principles of conflicts of laws.

8. SEVERABILITY. By executing this Policy below, the Officer agrees with the Company that each provision herein will be treated as a separate and independent clause, and the unenforceability of any one clause shall in no way impair the enforceability of any of the other clauses. The parties intend that the Covenants will be construed as a series of separate covenants, one for each county, city, state, nation and other political subdivision of the territories in which the Company does business. If, in any judicial proceeding, a court refuses to enforce any of the separate covenants (or any part thereof) deemed included in the Covenants, then such unenforceable separate covenant (or such part) shall be deemed eliminated from this Policy for the purpose of those proceedings to the extent necessary to permit the remaining separate covenants (or portions thereof) to be enforced by the court. The parties intend that the Covenants be enforced to the maximum degree permitted by applicable law.

9. GENERAL. Any successor to the Company (whether direct or indirect, and whether by purchase, lease, merger, consolidation, liquidation or otherwise) to all or substantially all of the Company's business and/or assets will assume the Company's obligations under this Policy. Without the written consent of the Company, an Officer may not assign or transfer his or her rights under the Policy to any other person or entity. Notwithstanding the foregoing, the terms of the Policy and all rights of an Officer hereunder will inure to the benefit of, and be enforceable by, his or her personal or legal representatives, executors, administrators, successors, heirs, distributees, devisees and legatees.

Acknowledgment:

By signing below, the Officer indicates his or her agreement to and acceptance of the terms and conditions of the Durect Corporation Change of Control Policy, which include:

- waiving and forfeiting in full any benefits contingent upon or related to a Change of Control provided to the Officer under any agreement or arrangement, written or otherwise, with the Company made or entered into prior to the date hereof; and
- agreeing to the terms and conditions of, and the restrictions imposed by, the Covenants set forth Section 4 above.

Signature: _____

Name (print): _____

Date Executed: _____

SIGNATURE PAGE TO EXECUTIVE CHANGE OF CONTROL POLICY

Exhibit 12.1

COMPUTATION OF RATIO OF EARNINGS TO FIXED CHARGES

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

	Year Ended December 31,				
	2013	2012	2011	2010	2009
Earnings:					
Net income (loss)	$ (21,452)	$ 16,200	$ (18,765)	$ (22,898)	$ (30,288)
Fixed charges	607	620	828	805	934
Total Earnings	$ (20,845)	$ 16,820	$ (17,937)	$ (22,093)	$ (29,354)
Fixed Charges:					
Interest expense	$ 6	$ 7	$ 46	$ 6	$ 36
Portion of rent expense representative of interest	601	613	782	799	898
Total Fixed Charges	$ 607	$ 620	$ 828	$ 805	$ 934
Ratio of Earnings to Fixed Charges (1)	—	27.1	—	—	—

(1) For purposes of computing the ratio of earnings to fixed charges, earnings consist of net income (loss) plus fixed charges. Fixed charges consist of interest expense, amortization of debt expense and discount or premium related to indebtedness, whether expensed or capitalized, and that portion of rental payments under operating leases we believe to be representative of interest. Earnings were insufficient to cover fixed charges by $21.5 million, $18.8 million, $22.9 million and $30.3 million for the years ended December 31, 2013, 2011, 2010, and 2009, respectively. Earnings for the year ended December 31, 2012 included recognition of $35.4 million of collaborative research and development revenue as a result of the termination of the Company's agreements with Nycomed, Pfizer and Hospira. Excluding the recognition of $35.4 million of deferred revenue, earnings would have been insufficient to cover fixed charges by $19.2 million for the year ended December 31, 2012.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-8 Nos. 333-126990 and 333-98939) pertaining to the DURECT Corporation 2000 Directors' Stock Option Plan,

(2) Registration Statements (Form S-8 Nos. 333-166700, 333-161025, 333-152968, 333-124701 and 333-86110) pertaining to the DURECT Corporation 2000 Employee Stock Purchase Plan and the DURECT Corporation 2000 Stock Plan,

(3) Registration Statements (Form S-8 Nos. 333-176113, 333-120405 and 333-108390) pertaining to the DURECT Corporation 2000 Stock Plan,

(4) Registration Statements (Form S-8 No. 333-170349) pertaining to the DURECT Corporation 2000 Employee Stock Purchase Plan,

(5) Registration Statement (Form S-8 No. 333-47400) pertaining to the DURECT Corporation 2000 Employee Stock Purchase Plan, the DURECT Corporation 1998 Stock Option Plan, the DURECT Corporation 2000 Stock Plan and the DURECT Corporation 2000 Directors' Stock Option Plan,

(6) Registration Statement (Form S-8 No. 333-61224) pertaining to the DURECT Corporation 2000 Employee Stock Purchase Plan, the DURECT Corporation 2000 Stock Plan, the Southern BioSystems, Inc. 1993 Stock Option Plan and the Southern Research Technologies, Inc. 1995 Nonqualified Stock Option Plan,

(7) Registration Statement (Form S-8 No. 333-76622) pertaining to the Southern BioSystems, Inc. 1993 Stock Option Plan and the Southern Research Technologies, Inc. 1995 Nonqualified Stock Option Plan,

(8) Registration Statement (Form S-3 No. 333-128979) of DURECT Corporation,

(9) Registration Statement (Form S-3 No. 333-108398) of DURECT Corporation,

(10) Registration Statement (Form S-3 No. 333-108396) of DURECT Corporation,

(11) Registration Statement (Form S-3 No. 333-155042) of DURECT Corporation,

(12) Registration Statement (Form S-3 No. 333-181174) of DURECT Corporation, and

(13) Registration Statement (Form S-3 No. 333-193009) of DURECT Corporation

of our reports dated February 28, 2014, with respect to the financial statements and schedule of DURECT Corporation, and the effectiveness of internal control over financial reporting of DURECT Corporation included in this Annual Report (Form 10-K) of DURECT Corporation for the year ended December 31, 2013.

/s / ERNST & YOUNG LLP

Redwood City, California
February 28, 2014

Exhibit 31.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, James E. Brown, certify that:

1. I have reviewed this report on Form 10-K of DURECT Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   (a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   (c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

February 28, 2014

/S/ JAMES E. BROWN

James E. Brown
Chief Executive Officer

Exhibit 31.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Matthew J. Hogan, certify that:

1. I have reviewed this report on Form 10-K of DURECT Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   (a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   (c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

February 28, 2014

/S/ MATTHEW J. HOGAN

Matthew J. Hogan
Chief Financial Officer and Principal Accounting Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of DURECT Corporation (the "Company") on Form 10-K for the year ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, James E. Brown, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

February 28, 2014

/S/ JAMES E. BROWN

James E. Brown
Chief Executive Officer

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of DURECT Corporation (the "Company") on Form 10-K for the year ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Matthew J. Hogan, Chief Financial Officer and Principal Accounting Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

February 28, 2014

/S/ MATTHEW J. HOGAN

Matthew J. Hogan
Chief Financial Officer and Principal Accounting Officer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