DURECT CORP
Form 10-K
March 08, 2019

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, 2018

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	(The 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 every Interactive Data File required to be submitted 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 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, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
Emerging growth company	

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this

chapter).

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 $207,649,177 as of June 30, 2018 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 162,059,718 shares of the registrant's Common Stock issued and outstanding as of March 4, 2019.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference from the definitive Proxy Statement for the 2018 annual meeting of stockholders, which is expected to be filed not later than 120 days after the Registrant's fiscal year ended December 31, 2018.

DURECT CORPORATION

ANNUAL REPORT ON FORM 10-K

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2018

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PART I

Item 1. Business.

Overview

We are a biopharmaceutical company with research and development programs broadly falling into two categories: (i) new chemical entities derived from our Epigenetic Regulator Program, in which we attempt to discover and develop molecules which have not previously been approved and marketed as therapeutics, and (ii) proprietary pharmaceutical programs, in which we apply our formulation expertise and technologies largely to active pharmaceutical ingredients whose safety and efficacy have previously been established but which we aim to improve in some manner through a new formulation. We also manufacture and sell osmotic pumps used in laboratory research and design, and develop and manufacture 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.

Our product pipeline currently consists of multiple investigational drug candidates in development. DUR 928, a new chemical entity in Phase 1 and 2 development, is the lead candidate in DURECT's Epigenetic Regulator Program. An endogenous, orally bioavailable small molecule, DUR-928 has been shown in preclinical studies to play an important regulatory role in lipid homeostasis, inflammation, and cell survival. Human applications may include chronic metabolic diseases such as nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH) and other liver diseases, inflammatory skin conditions such as psoriasis and atopic dermatitis, and acute organ injury such as alcoholic hepatitis (AH) and acute kidney injury (AKI). DURECT's proprietary oral and injectable delivery technologies are designed to enable new indications and enhanced attributes for small-molecule and biologic drugs. One late-stage development program in this category is POSIMIR® (bupivacaine extended-release solution), an investigational analgesic product intended to deliver bupivacaine to provide up to 3 days of pain relief after surgery.

As a result of the assignment of certain patent rights, DURECT will receive single digit sales-based earn-out payments from U.S. net sales of Indivior's PERSERIS™ (risperidone) drug for schizophrenia, which was approved in July 2018. Indivior has indicated that it commenced the full commercial launch of PERSERIS in February 2019 and that it expects peak year net revenues to be $200-300 million. In addition, in September 2018, our licensee, Orient Pharma informed us that it had obtained marketing authorization for Methydur Sustained Release Capsules from the Ministry of Health and Welfare in Taiwan. Methydur Sustained Release Capsules use our ORADUR® technology and are indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in Taiwan. Orient Pharma also has stated that it expects to make Methydur Sustained Release Capsules commercially available in Taiwan in 2019, while seeking a partner in China and pursuing regulatory approvals in selected other countries where it has commercialization rights and a commercialization presence. We will receive a single digit royalty on sales of Methydur Sustained Release Capsules by Orient Pharma and retain rights to this product in North America, Europe, Japan and all other countries not specifically licensed to Orient Pharma.

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 royalties on product sales. At the same time, we have retained the rights to other programs, which are the basis of potential future collaborations and which over time may provide a pathway for us to develop our own commercial, sales and marketing organization.

NOTE: POSIMIR®, SABER®, CLOUD®, ORADUR ®, ALZET ® and LACTEL® are trademarks of DURECT Corporation. Other trademarks referred to belong to their respective owners. Full prescribing information for PERSERIS, including BOXED WARNING and Medication Guide can be found at www.perseris.com.

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Epigenetic Regulator Program and New Chemical Entities

Epigenetic regulation does not involve changes of the DNA sequence itself, but instead involve biochemical modification of either the DNA itself or of proteins that intimately associate with DNA as the key mediators of cellular function. These modifications facilitate the appropriate downstream biological effects through changes in gene expression.

DURECT's Epigenetic Regulator Program involves a multi-year collaborative effort with the Department of Internal Medicine at Virginia Commonwealth University (VCU), the VCU Medical Center and the McGuire VA Medical Center. The knowledge base supporting this program is a result of more than 30 years of lipid research by Shunlin Ren, M.D., Ph.D., Professor of Internal Medicine at the VCU Medical Center and a recipient of multiple grants from the National Institutes of Health (NIH) and other agencies for metabolic disease research. During the course of this program, a number of endogenous and synthetic compounds have been discovered that may have therapeutic utility for various diseases, disorders or syndromes. The lead compound from this program, DUR-928, is an endogenous, orally available small molecule that modulates the activity of various nuclear receptors that play important regulatory roles in lipid homeostasis, inflammation and cell survival. Under a license with Virginia Commonwealth University, we hold the exclusive worldwide right to develop and commercialize DUR-928 and related molecules discovered in the program.

The biological activity of DUR-928 has been demonstrated in over a dozen different animal disease models involving three animal species. Several of these disease models represent chronic metabolic disorders of hepatic lipid accumulation and dysfunction (e.g., NAFLD and NASH) and several represent acute organ injuries (e.g., endotoxin shock, acute oxidative damage, ischemic-reperfusion kidney injury, and stroke models).

Our major product research and development efforts planned for DUR-928 in 2019 are set forth in the following table:

In pharmacokinetic and toxicity studies conducted in mice, hamsters, rats, rabbits, dogs and monkeys, DUR-928 has been found to be orally available, locally tolerable and safe at all doses and in all routes of administration tested to date. These non-clinical results support the use of DUR-928 in the completed, ongoing and planned human safety, pharmacokinetics (PK) and proof-of-concept trials.

Chronic Liver Disease Program with Orally Administered DUR-928

Market Opportunity. Non-alcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease in both children and adults. It is estimated that NAFLD affects about 20% to 30% of adults and 10% of children in the United States. Non-alcoholic steatohepatitis (NASH), a more severe and progressive form of

NAFLD, is one of the most common chronic liver diseases worldwide, with an estimated prevalence of more than 10% of adults in the United States, Europe, Japan and other developed countries. No drug is currently approved for NAFLD or NASH. Moreover, alcoholic fatty liver disease (AFLD) and its more advanced stage, alcoholic steatohepatitis (ASH), develops in approximately 90% of individuals who drink more than 60 grams/day of alcohol, but may occur in individuals who drink less, and is a major contributor to the global burden of liver cirrhosis. In addition to these liver diseases, there are a number of orphan liver diseases for which we may seek to develop DUR-928.

Clinical Program. In January 2019 we announced plans to accelerate the start of a new DUR-928 Phase 1b trial in NASH patients and expect to begin enrolling patients in the first quarter of 2019. This will be a randomized and open-label study conducted in the U.S. to evaluate safety, pharmacokinetics and signals of biological activity of DUR-928. Three doses of DUR-928 (low, middle and high) will be administered orally for 28 consecutive days with approximately 20 patients per dose group for a total of approximately 60 patients in the trial. We expect to begin enrolling patients during the first quarter of 2019 and announce initial data from this study in the second half of 2019.

DURECT has completed multiple single-site Phase I trials in healthy subjects with orally administered DUR-928. One of the studies was a randomized, double-blinded, placebo-controlled, single-ascending-dose study that evaluated the safety, tolerability and PK of DUR-928. The 30-subject study evaluated DUR-928 in five cohorts of healthy volunteers receiving DUR-928 (n=20 on drug, 10 on placebo) at escalating doses that resulted in peak plasma concentrations greater than 100-fold higher than endogenous levels. DUR-928 was well-tolerated at all dose levels, with no serious treatment-related adverse events reported. Dose related increases in plasma concentrations were observed with peak plasma concentration at approximately 2-6 hours after dosing. We subsequently conducted a randomized, double-blinded, placebo-controlled, multiple-ascending-dose study in 20 healthy subjects (n=16 on drug, 4 on placebo). Following multiple dosing, DUR-928 was well-tolerated at all doses, with no serious drug-related adverse events reported and no accumulation in plasma concentrations observed with repeat dosing. We also conducted a food effect study with 8 healthy subjects and observed no food effect on DUR-928 absorption.

We also conducted a Phase 1b trial in cirrhotic and non-cirrhotic NASH patients and matched control subjects (MCS) (matched by age, body mass index and gender with normal liver function) utilizing orally administered DUR-928. This was an open-label, single-ascending-dose safety and PK study conducted in Australia in two successive dose cohorts (first a low dose of 50 mg and then a high dose of 200 mg). Both cohorts consisted of 10 NASH patients and 6 MCS. Data from this study was presented at the International Liver Congress™ 2017 organized by the European Association for the Study of the Liver (EASL) in Amsterdam on April 22, 2017. All patients and MCS in this study tolerated DUR-928 well. One patient (with a prior history of arrhythmia and an ongoing viral infection) in the high dose cohort experienced a serious adverse event (shortness of breath), which occurred without unusually abnormal biochemical changes and resolved without intervention but was considered possibly treatment related by the physician due to its temporal association with dosing. In both the low and high dose cohorts, the PK parameters were comparable between the NASH patients and the MCS. In addition, the systemic exposure following the low and high doses of DUR-928 was dose dependent.

While this study was not designed to assess efficacy, we observed significant reductions from baseline of several biomarkers after both doses of DUR-928. A single oral dose of DUR-928 statistically significantly reduced the levels of both full-length and cleaved cytokeratin-18 (CK-18), bilirubin, hsCRP, and IL-18 in these subjects. The mean decrease of full-length CK-18 (a generalized cell death marker) at the measured time point of greatest effect (12 hours after dosing) was 33% in the low dose cohort and 41% in the high dose cohort. The mean decrease of cleaved CK-18 (a cell apoptosis marker) at the measured time point of greatest effect (12 hours after dosing) was 37% in the low dose cohort and 47% in the high dose cohort. The mean reduction of total bilirubin (a liver function marker) at the measured time point of greatest effect (12 hours after dosing) was 27% in the low dose cohort and 31% in the high dose cohort. The mean decrease of high sensitivity C-Reactive Protein (hsCRP) (a marker of inflammation) at the measured time point of greatest effect (24 hours after dosing) was 8% in the low dose cohort and 13% in the high dose

cohort. The mean decrease of IL-18 (an inflammatory mediator) at the measured time point of greatest effect (8 hours after dosing) was 4% in the low dose cohort and 8% in the high dose cohort.

Collectively, the reduction of these biomarkers plus results from our animal and cell culture studies suggest potential therapeutic activity of DUR-928 for patients with liver diseases. However, additional studies are required to evaluate the safety and efficacy of DUR-928, and there is no assurance that these biomarker effects will be

associated with clinically relevant benefits, or that DUR-928 will demonstrate safety or efficacy in treating liver diseases in future controlled trials.

In 2018, we began conducting a Phase 2a trial in primary sclerosing cholangitis (PSC) with orally administered DUR-928. This Phase 2a trial was designed to be a randomized, open label study with a low dose cohort and a high dose cohort, in which patients (n = 15-20 per cohort) would receive daily oral dosing of DUR-928 for 4-weeks with follow-up for an additional four-weeks. The objectives of this study included safety, PK and pharmacodynamic (PD) markers, including the percent change from baseline of serum alkaline phosphatase (ALP) and other biomarkers. Since the initiation of the study, we dosed five PSC patients, and in January 2019 we decided to discontinue the trial primarily due to the slow enrollment rate and a desire to focus resources on other indications.

Acute Organ Injury Program with Injectable DUR-928

Market Opportunity. Acute organ injury is another area of major unmet medical need for which effective pharmaceutical treatment is often lacking. Alcoholic liver disease (ALD) is a syndrome characterized by progressive inflammatory liver injury associated with long-term heavy intake of alcohol, and involves a spectrum that ranges from mild injury to severe, life threatening injury. Alcoholic hepatitis (AH) is an acute, inflammatory form of ALD for which there are no effective therapeutics available. The prevalence of AH is believed to be 10-35% of heavy drinkers. There were over 320,000 hospitalizations related to alcoholic hepatitis in 2010, and the hospitalization costs amounted to nearly $50,000 per patient. Acute kidney injury (AKI), a sudden loss of kidney function due to renal failure or injury, affects approximately 2.8 million patients per year in the United States and is associated with increased mortality, prolonged hospital stays, kidney dialysis and progression to chronic kidney disease. There are various forms of acute organ injury affecting the liver, the kidney or other organs for which we may seek to develop DUR-928.

Clinical Program. The initial Phase 1 trial in healthy subjects was a single-site, randomized, double-blinded, placebo-controlled, single-ascending-dose study that evaluated the safety, tolerability and PK of intramuscular (IM) injected DUR-928. The 24-subject study (16 healthy volunteers on the drug and 8 on placebo) of four escalating dose levels resulted in dose proportional systemic exposure of DUR-928 with peak plasma concentrations greater than 1000-fold higher than endogenous levels. DUR-928 was well-tolerated at all dose levels, with no serious treatment-related adverse events reported. We also conducted a multiple-dose study involving 10 healthy subjects, in which participants received IM-injected DUR-928 for 5 consecutive days (8 subjects on the drug, 2 on placebo) using the next to highest dose from the single dose study. No serious treatment related adverse events were reported, no subjects withdrew from the study, no accumulation in plasma concentrations were observed with repeat dosing, and the pain scores and injection site reactions were minimal. We also conducted a single-ascending dose intravenous infusion (IV) study with 16 healthy subjects and observed no treatment-related serious adverse events. The systemic exposure following IV infusion was dose proportional.

A Phase 1 drug-drug interaction study conducted in healthy subjects demonstrated that neither orally administered nor intravenously injected DUR-928 at doses tested affected the safety and PK of midazolam, a drug metabolized by CYP3A4, which is one of the important enzymes associated with clinically relevant drug-drug interactions.

We have also conducted a Phase 1b study with injected DUR-928 in patients with impaired kidney function (stage 3 and 4 chronic kidney disease (CKD)) and matched control subjects (MCS), matched by age, body mass and gender with normal kidney function. This study was a single-site, open-label, single-ascending-dose study. in two successive cohorts (first a low dose of 30 mg and then a high dose of 120 mg) evaluating safety and PK of intramuscular injected DUR-928. The low dose cohort consisted of 6 patients with CKD and 3 MCS; the high dose cohort consisted of 5 CKD patients and 3 MCS. In this trial, DUR-928 was well tolerated among all subjects and the PK parameters between the kidney function impaired patients and the MCS were comparable. While the number of subjects involved was small and not designed to assess efficacy, we did observe decreases in bilirubin and CK-18 when those levels were elevated at baseline, although the results were not statistically significant. The results of this Phase 1b trial were

presented at Kidney Week 2018 in San Diego, CA.

In 2018, we began conducting a Phase 2a clinical trial with intravenously infused DUR-928 in patients with moderate and severe alcoholic hepatitis (AH). This is an open label, dose escalation, multi-center U.S. study, originally designed to be conducted in two sequential parts. Part A includes patients with moderate AH (as determined by the Model of End-Stage Liver Disease (MELD) scores, a common scoring system to assess the

severity and prognosis of AH patients), and Part B includes patients with severe AH. Three dose levels (30, 90 and 150 mg) were planned for testing in Part A. Dose escalation may occur following review of safety and pharmacokinetic (PK) results of the prior dose level by a Dose Escalation Committee (DEC). The target number of patients for the study was 4 per dose group. The objectives of this study include assessment of safety, PK and pharmacodynamic (PD) signals, including liver biochemistry and biomarkers. After completing dosing for the low-dose 30 mg cohort (n=4) of Part A (moderate AH patients), the DEC approved commencement of the 90 mg cohort in Part A while simultaneously commencing recruitment for Part B (severe AH patients) with the 30 mg dose. In January 2019 we announced that two severe AH patients had been treated and that after completing the 30 mg dose group in Part B, we plan to transition the study to Dr. Craig McClain at the University of Louisville, who was recently awarded an NIH grant to study DUR-928 in AH patients. We have now completed dosing of the 30 mg cohort (n=4) of Part B, the enrollment of which was much more rapid than Part A. After reviewing the safety and PK data, the DEC has approved commencement of the 90 mg cohort in Part B. Based on the encouraging data from both the moderate and severe 30 mg cohorts, the relatively rapid enrollment of severe AH patients, and strong encouragement from several of our key expert advisors and clinical trial investigators, we have decided to continue our trial by conducting the next cohort of severe AH patients at the 90 mg dose. In parallel with our recruitment of patient for both of the 90 mg cohorts in our trial, we are supporting Dr. Craig McClain's efforts to initiate his NIH-funded study at the University of Louisville.

Skin Inflammatory Disorder Program with Topical DUR-928

Market opportunity. Psoriasis is an inflammatory skin disease and an immune-mediated condition that causes the body to make new skin cells in days rather than weeks. In the United States, there are about 150,000 new cases of psoriasis every year and it affects more than 8 million Americans. According to the International Federation of Psoriasis Associations (IFPA), nearly 3% of the world's population has some form of psoriasis or about 125 million people. Psoriasis causes itchiness and irritation and may be painful. There is no cure for psoriasis, but treatment can ease symptoms.

Approximately 80% of patients with psoriasis have localized disease. Topical agents remain the mainstay of localized psoriasis treatment. Other inflammatory skin disorders, such as atopic dermatitis, which affects approximately 32 million Americans, represent significant unmet medical needs. Most currently available topical treatments, typically as first line therapy, either slow down excessive skin cell proliferation or reduce inflammation.

Clinical program. We have conducted an exploratory Phase 1b trial in psoriasis patients (9 evaluable patients) in Australia. The double-blinded and placebo-controlled trial was conducted using a micro-plaque assay with intralesional injections of DUR-928. We feel that the results were encouraging and warrant further investigation. As a result, we are conducting a Phase 2a, randomized, double-blind, vehicle-controlled proof-of-concept clinical trial, in which DUR-928 will be applied topically once-daily for 28 days in patients with mild to moderate plaque psoriasis. The trial will be conducted at multiple clinical sites in the U.S. Twenty patients are planned to be enrolled to obtain approximately 15 evaluable patients. Patients will serve as their own controls, applying DUR-928 to the plaque on one arm and the vehicle (placebo) to a similar plaque on the other arm. After the treatment period, patients will be followed for an additional four weeks. The primary efficacy endpoint will be change in local psoriasis scores from baseline in the DUR-928-treated plaques compared to that in the vehicle-treated plaques. We expect to begin enrolling patients during the first quarter of 2019 and announce top-line data from this study in the second half of 2019.

Additional Proprietary Pharmaceutical Programs

POSIMIR (bupivacaine extended-release solution)

Our post-operative pain relief depot, POSIMIR, is a sustained release injectable using our SABER® delivery system to deliver bupivacaine, an off-patent pharmaceutical agent. SABER is a controlled drug delivery technology that is administered via the parenteral (i.e., injectable) route to deliver drugs that act systemically or locally. POSIMIR is designed to be administered to a surgical site at the end of surgery for post-operative pain relief and is intended to provide local analgesia for up to 3 days, which we believe coincides with the time period of the greatest need for post-surgical pain control in most patients.

Status. In April 2013, we submitted an NDA as a 505(b)(2) application, which relied in part on the FDA's findings of safety and effectiveness of a reference drug. In February 2014, we received a Complete Response Letter (CRL) from the FDA. Based on the CRL and subsequent communications with the FDA, we conducted a new POSIMIR Phase 3 clinical trial (referred to as the PERSIST trial) consisting of patients undergoing laparoscopic cholecystectomy (gallbladder removal) surgery to further evaluate the benefits and risks of POSIMIR. We began recruiting patients for this trial in November 2015 comparing POSIMIR to placebo. Based on advice from the FDA received subsequent to the start of the trial, in April 2016 we amended the PERSIST trial. Starting in August 2016, we began implementing the amended trial (referred to as Part 2 of the PERSIST trial) to evaluate POSIMIR against standard bupivacaine HCl rather than placebo as we had been doing initially in the study. In October 2017, we reported that the PERSIST trial did not meet its primary efficacy endpoint of reduction in pain on movement over the first 48 hours after surgery as compared to standard bupivacaine HCl. While results trended in favor of POSIMIR versus the comparator, they did not achieve statistical significance.

In total, we have completed 16 clinical studies with POSIMIR, in seven different surgical procedures, 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 for extrapolation of the safety and efficacy data to a broad surgical population. Our POSIMIR clinical development program has been devised to establish the safety and efficacy of POSIMIR for the treatment of post-surgical pain for 3 days.

Efficacy

We believe that two of the completed clinical trials support the efficacy of POSIMIR in post-operative pain and meet the requirements to be considered as adequate and well-controlled pivotal clinical trials:

Hernia pivotal efficacy trial

The hernia pivotal efficacy clinical trial was designed to evaluate the tolerability, activity, dose response and pharmacokinetics of POSIMIR 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 POSIMIR 2.5 mL (n=43), POSIMIR 5 mL (n=47) and SABER 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 POSIMIR 5 mL reported thirty-one percent (31%) less pain versus placebo, and the result was statistically significant (p=0.0031). Fifty-three percent (53%) of the study patients in the POSIMIR 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 POSIMIR 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 POSIMIR 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 POSIMIR 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. In this study, 107 patients were randomly assigned to one of three treatment groups prior to undergoing elective arthroscopic shoulder surgery: POSIMIR 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 POSIMIR group experienced a statistically significant reduction in pain intensity of approximately 20% (p=0.012) versus SABER-Placebo. Applying the appropriate statistical test given the data distribution, the POSIMIR group showed a statistically significant reduction of approximately 67% (p=0.013) in median opioid use in favor of POSIMIR. No statistical differences were found when POSIMIR was compared to bupivacaine HCl.

Safety

Bupivacaine is a well-known drug with an extensive understanding of its risks and benefits. DURECT has completed 16 clinical trials involving POSIMIR. A total of 1463 patients participated in these trials, 1144 of whom were exposed to POSIMIR or SABER-Placebo in volumes ranging from 2.5 to 10 mL. A total of 876 patients were exposed to

POSIMIR with the dose of bupivacaine ranging from 330 to 990 mg. Our planned commercial dose is 5 mL (660 mg). In addition, a total of 272 patients were treated with bupivacaine HCl in control groups and 268 patients received SABER-Placebo in control groups.

Overall, the POSIMIR 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 POSIMIR 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 POSIMIR, 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 POSIMIR-related. The clinical history for serious adverse events has been reviewed and we do not believe POSIMIR was associated with any bupivacaine toxicity. The adverse event data was 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 POSIMIR had an instance of a severe central nervous system or cardiac adverse event traditionally associated with bupivacaine toxicity.

Plans for FDA Submission

After carefully reviewing the existing POSIMIR data and evaluating the feedback we have received from the FDA, including the CRL and other correspondence, we have made the decision to prepare and submit to FDA a response to the CRL. The submission will request FDA approval of POSIMIR based on what the Company and its advisors believe is adequate evidence of both safety and efficacy. As the submission is intended to be a response to a CRL, we expect a 6-month FDA review period.

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. Insufficient postoperative pain control remains a significant problem, with studies indicating that roughly 65% of patients experience moderate-to-extreme pain after surgery. The current standard of care for post-surgical pain includes a variety of opiate and non-opiate analgesics and muscle relaxants. While systemic opioids can effectively reduce 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.

PERSERIS™ (risperidone)

In September 2017, we entered into an agreement with Indivior, under which we assigned to Indivior certain patents that may provide further intellectual property protection for PERSERIS, Indivior's extended-release injectable suspension for the treatment of schizophrenia in adults. In consideration for such assignment, Indivior made an upfront non-refundable payment to DURECT of $12.5 million. Indivior also paid a $5.0 million milestone payment in August 2018 following the FDA approval of PERSERIS. Under the terms of the agreement with Indivior, DURECT will receive earn-out payments that are based on a single digit percentage of U.S. net sales of PERSERIS into 2026.

Through press releases on December 18, 2018, and February 14 and 27, 2019, Indivior has stated that: PERSERIS was made available in the U.S. in late November 2018; The PERSERIS commercial launch took place in February 2019 with an expected field force of 50 representatives; As of February 14, 2019, payor access was at 38% and Indivior is targeting quality of access comparable with peers; Indivior is targeting appropriate health care providers (HCPs) with high volume Long Acting Injectables (LAI) practices; Indivior plans to focus on key differentiating product specific attributes, including the first and only once-monthly risperidone LAI, supplemental oral risperidone or loading dose not recommended, initial peak plasma concentrations achieved in 4 to 6 hours, and just one subcutaneous injection monthly; and Indivior remained confident in its peak year net revenue goal for PERSERIS of $200 to $300 million.

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ORADUR-ADHD Program

Market Opportunity. Attention Deficit Hyperactivity Disorder (ADHD) is a neurobehavioral condition that is estimated to affect over 6 million (approximately 9%) of U.S. children ages 2-17, 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. 62% of children with ADHD are estimated to be under treatment with medication, utilizing stimulants such as amphetamine or methylphenidate as first-line treatments. U.S. sales of ADHD treatments were approximately $10.4 billion in 2016. The 2016 National Survey on Drug Use & Health estimates that 612,000 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- Methylphenidate ER) based on our 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, 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-Methylphenidate ER. We retain rights to North America, Europe, Japan and all other countries not specifically licensed to Orient Pharma.

Orient Pharma conducted a Phase 3, multi-center, randomized, double-blind, placebo-controlled, two-way cross-over study designed to demonstrate the efficacy and safety of ORADUR-Methylphenidate ER (referred to as Methydur Sustained Release Capsules or Methydur) in children and adolescents with ADHD between the ages of 6 and 18 years. According to Orient Pharma, the study was conducted in Taiwan and enrolled 110 subjects, of which 100 evaluable subjects completed the study. For the primary efficacy endpoint, Orient Pharma observed a statistically significant difference between Methydur and Placebo treatments in the mean change of total score for the Swanson, Nolan, and Pelham-IV (SNAP-IV) teacher form ($p=0.0044$ for the intent to treat population and $p=0.0104$ for the per protocol population). Orient Pharma's safety analysis indicates that the incidence of adverse events with Methydur was similar to other approved methylphenidate products.

In September 2018, Orient Pharma informed us that it had obtained marketing authorization for Methydur from the Ministry of Health and Welfare in Taiwan. Methydur is indicated for the treatment of ADHD and will be available in three strengths (22 mg, 33 mg and 44 mg) in Taiwan. Orient Pharma also has stated that it expects to make Methydur commercially available in Taiwan in 2019, while seeking a partner in China and pursuing regulatory approvals in selected other countries in Southeast Asia where it has commercialization rights and a commercialization presence. We are seeking potential development and commercialization partners for ORADUR-Methylphenidate ER Capsules for major markets not licensed to Orient Pharma.

REMOXY ER (ORADUR-Oxycodone)

In December 2002, we entered into an agreement with Pain Therapeutics, amended in December 2005, under which we granted Pain Therapeutics the exclusive, worldwide right to develop and commercialize selected long-acting oral opioid products using our ORADUR technology incorporating four specified opioid drugs. This agreement currently covers only REMOXY ER, a novel long-acting oral formulation of the opioid oxycodone under development with the goal of decreasing the potential for oxycodone abuse for patients who have pain serious enough to require daily, around-the-clock opioid treatment and for which alternative treatment options are inadequate. Even where abuse deterrent properties exist, opioid drugs such as oxycodone still expose users to the risks of addiction, abuse and misuse.

Following multiple CRLs and additional studies, on August 6, 2018, Pain Therapeutics stated that it had received another CRL from the FDA citing insufficient data to support the conclusion that the benefits of REMOXY ER

outweigh the risks. Pain Therapeutics further announced a strategic reorganization to align its resources on advancing its drug and diagnostic assets in Alzheimer's disease. Based on their interactions with the FDA, Pain Therapeutics has indicated that they and the FDA have disagreements around comments and conclusions made by the FDA during a regulatory review of the NDA for REMOXY ER. While Pain Therapeutics commenced an appeal

process in November 2018, there can be no assurance that they will continue to pursue an appeal or that any such appeal will be successful.

Drug Delivery Technologies and Programs

Our drug delivery technologies are designed to deliver the right drug to the right place, in the right amount and at the right time to treat a variety of chronic, acute and episodic diseases and conditions. We aim to improve 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 technologies can target the delivery of the drug to its intended site of action.

Our technologies are suitable for providing long-term drug therapy because they can often store highly concentrated, stabilized drugs in a small volume and protect the drug from degradation by the body. This, in combination with the ability to continuously deliver desired doses of a drug, can extend the therapeutic value of a wide variety of drugs, including, in some cases, 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 may 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 technology may thereby 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 drug delivery technology platforms:

The SABER and CLOUD 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 class of bioerodible injectable depot technology which generally does not contain SAIB but includes 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 tends to repel water and body enzymes 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 Onset and Release—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. In some cases, small injection volumes and

more liquid solutions can result in easier, less painful administration.

- 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, in some cases, our bioerodible injectable depot formulations are readily manufacturable at low cost.

The SABER technology is the basis of POSIMIR (described above). The SABER technology is also utilized in our ophthalmic program with Santen Pharmaceutical Co., Ltd. (Santen), as well as multiple feasibility programs. In our clinical studies thus far, our bioerodible injectable depot formulations have been observed to be generally safe and well-tolerated.

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 was the first FDA approved SABER injectable product when it was launched in 2011 by CreoSalus, Inc.

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 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). 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 our ORADUR-Methylphenidate ER and REMOXY ER programs (described above).

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. The ophthalmic program with Santen is a project which started as a depot injectable feasibility project and then matured into a development and license agreement.

DURECT Strategy

Our objective is to develop multiple pharmaceutical products 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 Areas with the Potential for Significant Value Creation. We view patients, physicians, the healthcare system, payers, and strategic partners, as all being important stakeholders in our company. We believe that developing the products in our pipeline, which may address significant unmet medical needs and may create value for our stakeholders, also has the potential to create value for our shareholders.

Apply our Drug Development Expertise to New Chemical Entities Derived from our Epigenetic Regulator Program. We have assembled a core team of employees with considerable experience in drug development, and it is our intent to leverage their capabilities by developing pharmaceuticals derived from our Epigenetic Regulator Program. We believe that these new chemical entities may have utility for several metabolic diseases such as NAFLD, NASH and other liver conditions, in acute organ injuries such as AH and AKI, in various orphan diseases, and in inflammatory skin conditions such as psoriasis and atopic dermatitis. We believe that these product candidates may be of interest to other pharmaceutical companies and that it may be possible to license the rights to certain products, formulations, indications or territories from this program while retaining the rights to other product candidates,

formulations, indications or territories for either our own development and commercialization or for licensing at a later stage of development.

Focus on Certain Acute Indications, Chronic Debilitating Medical Conditions and Certain Local Pain Conditions. Many of the diseases and disorders that present great challenges to medicine include pain management, CNS disorders, metabolic disorders, cardiovascular disease, acute organ injury, ophthalmic conditions

and other chronic diseases. In addition, we have identified certain local and acute pain and other medical 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 and on exploiting our Epigenetic Regulator Program through which we have identified new chemical entities that may have utility in conditions such as chronic metabolic/lipid disorders and acute organ injuries.

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 have multiple programs with the potential to generate significant value. 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 Agreements. We believe that entering into selective strategic collaborations and other arrangements with respect to our product development programs and technology can enhance the success of our product development and commercialization, the value of our intellectual property portfolio, mitigate our risk and enable us to better manage our operating costs. Additionally, such collaborations and arrangements enable us to leverage investment by third parties 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 product candidates, we may in the future enter into these alliances under circumstances that allow us to participate in the sales and marketing of these products.

Strategic Agreements

We have entered into the following strategic collaboration and other key agreements:

Virginia Commonwealth University Intellectual Property Foundation. We have entered into an exclusive in-license and research and development agreement with the Virginia Commonwealth University Intellectual Property Foundation regarding the new chemical entities under development through our Epigenetic Regulator Program, including DUR-928. Under this licensing arrangement, we have agreed to undertake certain efforts to bring licensed products to market, pay for prosecution of related patents and report on progress to VCU. In addition, we are obligated to pay low single-digit percentage patent royalties on net sales of licensed products, subject to annual minimum payments and additional milestone payments. This license includes rights to seven patent families. We may terminate this agreement at any time by written notice, and Virginia Commonwealth University may terminate this agreement by written notice if there is an uncured material breach.

Indivior UK Ltd. In September 2017, we entered into a patent purchase agreement (the “Indivior Agreement”) with Indivior. Pursuant to the Indivior Agreement, we assigned to Indivior certain patents that may provide further intellectual property protection for PERSERIS, Indivior’s once-monthly injectable risperidone product for the treatment of schizophrenia. In consideration for such assignment, Indivior made an upfront non-refundable payment to us of $12.5 million, and also agreed to make an additional $5 million payment to us contingent upon FDA approval of PERSERIS, as well as quarterly earn-out payments based on a single digit percentage of U.S. net sales for certain products covered by the assigned patent rights, including PERSERIS. The assigned patent rights include granted patents extending into at least 2026. We also receive a non-exclusive right under the assigned patents to develop and commercialize certain risperidone-containing products and products that do not contain risperidone or buprenorphine. The agreement contains customary representations, warranties and indemnities of the parties. We received the non-refundable payment of $12.5 million from Indivior in September 2017 and recognized this amount as revenue from sale of intellectual property rights in the year ended December 31, 2017 as we did not have any continuing

obligations under the purchase agreement. In July 2018, Indivior announced that the FDA had approved the NDA for PERSERIS thereby triggering the $5.0 million payment, which was received by DURECT in August 2018.

Santen Pharmaceutical Co., Ltd. In December 2014, we and Santen entered into a definitive agreement (the Santen Agreement). Pursuant to the Santen Agreement, we have granted Santen an exclusive worldwide license to our proprietary SABER formulation platform and other intellectual property to develop and commercialize a sustained release product utilizing our SABER technology to deliver an ophthalmology drug. Santen controls and funds the development and commercialization program, and the parties have established a joint management committee to oversee, review and coordinate the development activities of the parties under the Agreement.

In connection with the license agreement, Santen paid us a non-refundable upfront fee of $2.0 million in cash and agreed to make contingent cash payments to us of up to $76.0 million upon the achievement of certain milestones, of which $13.0 million are development-based milestones (none of which has been achieved as of December 31, 2018), and $63.0 million are commercialization-based milestones including milestones requiring the achievement of certain product sales targets (none of which has been achieved as of December 31, 2018). Santen will also pay for certain of our costs incurred in the development of the licensed product. If the product is commercialized, we would also receive a tiered royalty on annual net product sales ranging from single-digit to the low double digits, determined on a country-by-country basis. Santen may terminate the Agreement without cause at any time upon prior written notice, and either party may terminate the Agreement upon certain circumstances including a material uncured breach. As of December 31, 2018, the cumulative aggregate payments received by us under this agreement were $3.3 million. In January 2018, we were notified by Santen that due to a shift in near term priorities, Santen has elected to reallocate research and development resources and put our program on pause until further notice. While the main program is on pause, the parties are working together on a limited set of research and development activities funded by Santen.

Sandoz AG. In May 2017, the Company and Sandoz AG ("Sandoz") entered into a license agreement to develop and market POSIMIR in the United States. POSIMIR is the Company's investigational post-operative pain relief depot that utilizes the Company's patented SABER technology to deliver bupivacaine to provide up to three days of pain relief after surgery. Under terms of the agreement, Sandoz made an upfront payment of $20 million and the Company was eligible for additional milestone and royalty payments. In May 2018, the Company and Sandoz entered into an amendment (the "Amendment") to the license agreement, under which, among other things, both parties' termination provisions were modified. In January 2019, Sandoz AG provided notice that it was returning to DURECT all of its U.S. development and commercialization rights to POSIMIR. The parties are in dispute with regard to Sandoz's obligation to pay a termination fee to DURECT. DURECT has initiated a formal dispute resolution process related to the termination fee.

Pain Therapeutics, Inc. In December 2002, we entered into an agreement with Pain Therapeutics, amended in December 2005, under which we granted Pain Therapeutics the exclusive, worldwide right to develop and commercialize selected long-acting oral opioid products using our ORADUR technology incorporating four specified opioid drugs. Under the agreement with Pain Therapeutics, subject to and upon the achievement of predetermined development and regulatory milestones for REMOXY ER, we are entitled to receive milestone payments of up to $3.0 million in the aggregate. As of December 31, 2018, we had received $1.5 million in cumulative milestone payments. In addition, if commercialized, we will receive royalties of between 6.0% to 11.5% of net sales of REMOXY ER 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. This agreement currently covers only REMOXY ER, a novel long-acting oral formulation of the opioid oxycodone under development with the goal of decreasing the potential for oxycodone abuse. If approved, REMOXY ER would be intended for patients who have pain serious enough to require daily, around-the-clock opioid treatment and for which alternative treatment options are inadequate. Even where abuse deterrent properties exist, opioid drugs such as oxycodone still expose users to the risks of addiction, abuse and misuse. Following multiple CRLs and additional studies, in August 2018, Pain Therapeutics stated that it had received another CRL from the FDA citing insufficient data to support the conclusion that the benefits of REMOXY ER outweigh the risks. Pain Therapeutics further announced a strategic reorganization to align its resources on advancing its drug and diagnostic assets in Alzheimer's disease. Based on their interactions with the FDA, Pain Therapeutics has indicated that they and the FDA have disagreements around comments and conclusions made by the FDA during a regulatory review of the NDA for REMOXY ER. While Pain Therapeutics commenced an appeal process in November 2018, there can be no assurance that they will continue to pursue an appeal or that any such appeal will be successful.

As of December 31, 2018, the cumulative aggregate payments received by us from Pain Therapeutics under this agreement were $40.4 million. In addition, in 2018, 2017 and 2016, we recognized zero, zero and $653,000 of product revenue, respectively, related to key excipients for REMOXY ER and the associated cost of goods sold was zero, zero and $216,000, 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 16,000 scientific references that now exist.

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 our product candidates 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 product candidates, 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.

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 Methydur, POSIMIR, SucroMate, and REMOXY ER, from Eastman Chemical Company. We expect that we will continue to be able to obtain sufficient supply of these raw materials 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 product candidates, 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 sales 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 Methydur, SucroMate, REMOXY ER and other products. Until such time that we are able to bring our pharmaceutical product candidates 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 2018, Indivior and a pharmaceutical company with which we have a feasibility agreement accounted for 27% and 14% of our total revenues, respectively. In 2017, Sandoz and Indivior accounted for 41% and 25% of our total revenues, respectively. In 2016, Tolmar Inc. accounted for 15% of our total revenues.

Manufacturing

The process for manufacturing our pharmaceutical product candidates is technically complex, requires special skills, and must be performed in qualified facilities. We have entered into development and commercial manufacturing agreements with third parties for the manufacture of POSIMIR and DUR-928. 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 product candidates under GMP, including POSIMIR, DUR-928 and REMOXY ER. In the future, we may develop additional manufacturing capabilities for our pharmaceutical 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 current facilities in

California and/or Alabama. We manufacture our ALZET product line and certain key components for POSIMIR, Methydur, and REMOXY ER at one of our California facilities and our LACTEL product line at our Alabama facility.

Patents 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 molecules and technology, inventions and improvements that are important to the development of our business. As of March 4, 2019, we owned or exclusively in-licensed over 50 unexpired issued U.S. patents and over 285 unexpired issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have over 30 pending U.S. patent applications and over 145 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 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 products in development 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 products in development 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 products candidates in their intended uses; 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)). We expect that most of the Drug Delivery Program product candidates will be evaluated for approval after submission of a new drug application under section 505(b)(2) and that our drug candidates deriving from our Epigenetic Regulator Program will be evaluated for approval after submission of a new drug application under section 505(b)(1).

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 products candidates 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 product candidate. 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 FDA under 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 1: The drug is initially introduced into healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion.

- Phase 2: 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 3: When Phase 2 clinical trials demonstrate that a dosage range of the product is effective and has an acceptable safety profile, Phase 3 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 2 trials, and thus these trials are frequently referred to as Phase 1/2 clinical trials or Phase 1b trials. We cannot be certain that we will successfully complete Phase 1, Phase 2 or Phase 3 clinical trials of our pharmaceutical products in development 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 review; 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 may require 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, there can be no assurance 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 trials be conducted. 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 4 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 comparing a product to other dosage forms or competitive products typically need to be supported 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 products 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, any problems associated with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Any pharmaceutical products 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 products 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 products 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 product or the active pharmaceutical ingredient or other components of the product. 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 Federal Food, Drug, and Cosmetic Act strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples. 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 products are also subject to a variety of state laws and regulations in those states or localities where our products are or will be marketed. Any applicable state or local regulations may hinder our ability to market our products 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 product candidates. 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.For several years, the FDA has required companies engaged in manufacturing and sale of opioid drug products 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. All manufacturers of long-acting and extended-release opioids must ensure that training is provided to prescribers of these medications and develop information that prescribers can use when counseling patients about the risks and benefits of opioid use. More recently, in February 2016, the FDA announced a comprehensive action plan to take concrete steps towards reducing the impact of opioid abuse on American families and communities. As part of this plan, the agency will review product and labelling decisions and re-examine the risk-benefit paradigm for opioids.

Certain of our drug candidates, including REMOXY ER, are subject to the REMS requirement. These required REMS programs may cause 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 REMOXY and ORADUR-Methylphenidate 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.

Other Healthcare Laws. In addition to FDA and DEA restrictions on the marketing of pharmaceutical products, other foreign, federal and state healthcare regulatory laws restrict business practices in the pharmaceutical industry. These laws include, but are not limited to, federal and state anti kickback, false claims, data privacy and security, and

physician payment and drug pricing transparency laws.

The U.S. federal Anti Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or

other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti Kickback Statute has been interpreted to apply to arrangements between pharmaceutical and medical device manufacturers on the one hand and prescribers, purchasers, formulary managers and beneficiaries on the other hand. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not meet the requirements of a statutory or regulatory exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the U.S. federal Anti Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case by case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Moreover, a claim including items or services resulting from a violation of the U.S. federal Anti Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. The majority of states also have anti kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third party payor, including commercial insurers.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The Affordable Care Act imposed, among other things, new annual reporting requirements through the Physician Payments Sunshine Act for covered manufacturers for certain payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties. Covered manufacturers must submit reports by the 90th day of each subsequent calendar year and the reported information is publically made available on a searchable website. In addition, certain states require implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices and/or require the tracking and reporting of marketing expenditures and pricing information as well as gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities. Finally, the Physician Self-Referral (Stark) Law prohibits physicians from referring Medicare or Medicaid patients to providers of "designated health services" with whom the physician or a member of the physician's immediate family has an ownership interest or compensation arrangement, unless a statutory or regulatory exception applies.

Competition

We may face competition from other companies in numerous industries including pharmaceuticals, medical devices and drug delivery. POSIMIR and REMOXY ER, if approved, will compete with currently marketed oral opioids, transdermal opioids, local anesthetic patches, 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, AbbVie, Janssen, Medtronic, Endo, AstraZeneca, Pernix Therapeutics, Tricumed, Halyard Health, Cumberland Pharmaceuticals, Pacira, Acorda Therapeutics, Mallinckrodt, Johnson & Johnson, Eli Lilly, Pfizer, Novartis, Egalet, Collegium and others. Purdue Pharma, Sandoz, Actavis, Collegium, Pfizer, Elite Pharmaceuticals, Intellipharmaceutics, Egalet, Charleston Laboratories, Daiichi Sankyo, Teva Pharmaceuticals and others have also announced regulatory approval or development plans for abuse deterrent opioid products. Methydur Sustained Release Capsules and our ORADUR-ADHD product candidates, if approved, will compete with currently marketed or approved products by Shire, Johnson & Johnson, UCB, Novartis, Noven, Eli Lilly, Pfizer and others. PERSERIS will compete with currently marketed products by Johnson & Johnson, Eli Lilly, Astra Zeneca, Pfizer, Bristol-Myers Squibb, Otsuka, Sunovion Pharmaceuticals, Teva and others. Competition for DUR-928, if approved, will depend on the specific indications for which DUR-928 is approved. Intercept Pharmaceuticals, Gilead, Shire, Conatus Pharmaceuticals,

Allergan, Galectin Therapeutics, Genfit, Pfizer, Roche, Galmed Pharmaceuticals, Tobira Therapeutics, Madrigal Therapeutics, Gemphire, Enanta Pharmaceuticals, Novo Nordisk, Takeda, Vital Therapies, ChemomAb, Kowa, Boehringer Ingelheim, NGM, Lipocine, Enyo, Corcept, Second Genome, Nash Pharma, Pharmaxis, Merck, Pinnacle and others have development plans for products to treat NAFLD/NASH and other liver diseases. Ischemix, Thrasos Therapeutics, AM-Pharma, Complexa, AbbVie, AlloCure, Quark Pharmaceuticals and

others have development plans for products to treat acute kidney injury. Bristol Myers Squibb, Novartis, Eli Lilly, Almirall, LEO Pharma, Pfizer, Janssen, Abbvie, Boerhinger-Ingelheim, Amgen, Sandoz, Astra-Zeneca, Anacor, Valeant, Takeda, Merck, Idera Pharmaceuticals, Sanofi, Regeneron and others have development plans for products to treat psoriasis and atopic dermatitis. 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, Mallinckrodt, Pfizer, 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.

Competition for our ALZET product line primarily consists of customers choosing to utilize delivery methods for their research projects other than an osmotic pump. Competition for our LACTEL product line comes from companies including Evonik, Corbion, FUJIFILM Wako Pure Chemical Corporation, PCAS and others. 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. We may in the future face competition for our ALZET and LACTEL product lines from other companies including low cost foreign competitors.

Any pharmaceutical products we develop 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. 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 (SEC). The SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The SEC's website to access all of this information is www.sec.gov. Our Code of Ethics can be found on our website.

Employees

As of March 4, 2019, we had 88 employees, including 45 in research and development, 21 in manufacturing and 22 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 March 4, 2019 are as follows:

Name	Age	Position
James E. Brown, D.V.M.	62	President, Chief Executive Officer and Director
Michael H. Arenberg, M.B.A.	49	Chief Financial Officer
Judy R. Joice	62	Senior Vice President, Operations and Corporate Quality Assurance

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.

Michael H. Arenberg was appointed Chief Financial Officer effective October 2018. Mr. Arenberg has been with DURECT since 1999, most recently serving as Senior Vice President, Corporate and Business Development, where he negotiated and closed over 50 collaborations, including several important in-licensing transactions. Mr. Arenberg earned his undergraduate degree from the University of Colorado, his law degree from the University of Denver, and his MBA from the Leavy School of Business at Santa Clara University.

Judy R. Joice has served as our Senior Vice President, Operations and Corporate Quality Assurance since March 2014 and as our Vice President, Operations and Corporate Quality Assurance since April 2011. Previously, Ms. Joice served as our Vice President, Corporate Quality Assurance since July 2008 and as our Executive Director, Quality Assurance from July 2007 to July 2008. She has over 25 years' experience in the pharmaceutical industry with such companies as Nektar Therapeutics, Oread, Roche Pharmaceuticals, and Syntex Research. During her career, Ms. Joice has gained broad experience in CMC development activities including novel excipients, new chemical entities, devices, and combination products. She has developed, implemented and managed all aspects of company-wide quality systems and compliance functions, ranging from drug development through commercial manufacturing. Ms. Joice has a B.S. in Chemistry from California State University, Hayward.

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. If any of the following risks actually occur, our business, financial condition, results of operations and growth prospects may be materially and adversely affected.

Risks Related To Our Business

New chemical entities derived from our Epigenetic Regulator Program, which is in the early stages of development, may require more time and resources for development, testing and regulatory approval than our Drug Delivery Program product candidates, and may not result in any approval or viable commercial products

Our Epigenetic Regulator Program is in the early stages of development, involves a novel therapeutic approach and new chemical entities, requires significant further research and development and regulatory approvals and is subject to the risks of failure inherent in the development of products based on innovative approaches. New chemical entities derived from our Epigenetic Regulator Program are molecules that have not previously been approved and marketed as therapeutics, unlike product candidates in our Drug Delivery Programs, in which we apply our formulation expertise and technologies largely to active pharmaceutical ingredients whose safety and efficacy have previously been established but which we aim to improve in some manner through a new formulation. As a result, the product candidates from our Epigenetic Regulator Program may face greater risk of unanticipated safety issues or other side-effects, or may not demonstrate efficacy. Further, the regulatory pathway for our new chemical entities may be

more demanding than that for product candidates under our Drug Delivery Programs, for which we may be able to leverage existing data under Section 505(b)(2) of the Act to reduce development risk, time and cost. For example, we have yet to define the therapeutic dose or dosing regimen for DUR-928, the first drug candidate in our Epigenetic Regulator Program.

Also, because our Epigenetic Regulator Program is in early stages, we have not defined with precision those indications we wish to pursue, each of which may have unique challenges. If the first indications pursued do not show positive results, the credibility of any product candidate from this program may be tarnished, even if the molecule might be effective for other indications. Our decisions regarding which indications to pursue may cause us

to fail to capitalize on indications that could have given rise to viable commercial products and profitable market opportunities.

Early indications of activity from Phase 1 clinical trials of DUR-928 may not predict therapeutic efficacy

Although Phase 1 clinical trials of DUR-928 have demonstrated that DUR-928 can lead to the reduction of certain biomarkers, such as statistically significant reductions from baseline in the levels of both full-length and cleaved cytokeratin-18 (CK-18), bilirubin, high sensitivity C-Reactive Protein (hsCRP) and IL-18 in NASH patients, and non-statistically significant reductions in CK-18 and bilirubin in CKD patients, changes in such biomarkers may ultimately not be correlated with treatment or improvement in the associated disease, and there is a risk that DUR-928 may not demonstrate therapeutic efficacy, despite apparent improvements in biomarker levels. Additional controlled clinical trials will be required to evaluate the safety and efficacy of DUR-928 to treat any indication, including NASH, psoriasis and CKD. There can be no assurance that these studies will demonstrate the safety or efficacy of DUR-928 in a statistically significant manner. The failure of DUR-928 to show efficacy, or if safety signals emerge in ongoing and future clinical trials, would significantly harm our business.

Ongoing and planned clinical trials for DUR-928 may be delayed and may not demonstrate efficacy or safety in the indications tested.

We are planning to conduct a clinical trial of orally administered DUR-928 in NASH patients and a clinical trial of topically administered DUR-928 in patients with psoriasis beginning in the first quarter of 2019, with data expected in the second half of 2019. There can be no assurance that these trials will commence on time or enroll at a rate to generate data in the second half of 2019. We have also been conducting a Phase 2a trial of intravenously administered DUR-928 in patients with alcoholic hepatitis (AH). We have now completed dosing of the 30 mg cohort (n=4) of Part B, the enrollment of which was much more rapid than Part A. After reviewing the safety and PK data, the DEC has approved commencement of the 90 mg cohort in Part B. Based on the encouraging data from both the moderate and severe 30 mg cohorts, the relatively rapid enrollment of severe AH patients, and strong encouragement from several of our key expert advisors and clinical trial investigators, we have decided to continue our trial by conducting the next cohort of severe AH patients at the 90 mg dose. In parallel with our recruitment of patient for both of the 90 mg cohorts in our trial, we are supporting Dr. Craig McClain’s efforts to initiate his NIH-funded study at the University of Louisville. There can also be no assurance that biological activity demonstrated in previous animal disease models or earlier clinical trials will also be seen in these additional patients in ongoing trials or larger controlled trials, or that any clinically relevant biological activity will be observed, or that enrollment rates will be favorable or that these additional trials or additional patients in ongoing trials will not identify safety issues. Failure of these trials to achieve desired results in their anticipated timeframes would negatively impact our business and ability to raise additional capital.

The path to regulatory approval of DUR-928 is uncertain

We are currently developing DUR-928 in several indications, including AH, psoriasis and NASH. In several of these indications, there are no currently approved drugs. Accordingly, we will have to interact with the FDA and other regulatory agencies regarding important aspects of the clinical development program, including the size of clinical trials, the specific primary and secondary endpoints for the clinical trials, inclusion and exclusion criteria, stopping rules and other matters. This uncertainty may make it difficult to predict the timing or expense required to obtain regulatory approval for DUR-928. We also may need to revise our clinical development plans after trials have commenced or been completed, which could add to the time and expense associated with the clinical development of DUR-928. If we are unable to reach agreement with the FDA regarding clinical development plans for DUR-928, we may curtail or limit our development activities for this product candidate.

Prospects for POSIMIR are uncertain following the failure of the PERSIST trial to achieve its primary efficacy endpoint and the termination of our agreement with Sandoz

The failure of the PERSIST trial for POSIMIR to achieve its primary efficacy endpoint may reduce the prospects of obtaining FDA approval for POSIMIR. In January 2019, Sandoz elected to terminate our licensing agreement for POSIMIR, as a result of which we will not receive any milestone or royalty payments from Sandoz and will be responsible for commercialization of POSIMIR in the United States, if approved. We intend to seek a new collaboration partner for POSIMIR in the United States, but there is no assurance we will be successful in that effort or that any terms offered will be attractive to the Company. We may elect to terminate development of POSIMIR at any time. If we elect to continue to develop of POSIMIR, we may be required to make a larger

investment than previously planned, which would limit the funds available for other product development activities or require us to raise capital earlier than anticipated.

The FDA may not agree with our response to its Complete Response Letter (CRL) to the NDA submission for POSIMIR

After carefully reviewing the existing POSIMIR data and evaluating the feedback we have received from the FDA, including the CRL and other correspondence, we have made the decision to prepare and submit to FDA a response to the CRL. The submission will request FDA approval of POSIMIR based on what the Company and its advisors believe is adequate evidence of both safety and efficacy. As the submission is intended to be a response to a CRL, we expect a 6-month FDA review period. There can be no assurance that the FDA will complete their review in a timely manner or will agree with our response to the CRL and approve POSIMIR for marketing. The FDA may require additional studies or additional information regarding POSIMIR. We would need to review any such requests to determine whether we believe that a viable path for regulatory approval of POSIMIR remains available.

If we experience delays or difficulties in the enrollment of subjects in clinical trials, our product development expenses may increase, clinical trial data could be delayed and receipt of necessary regulatory approvals could be delayed or prevented

Successful and timely completion of clinical trials will require that we enroll a sufficient number of subjects. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population and the ability of clinical sites to successfully recruit subjects to participate in clinical trials. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible subjects to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. It is possible that the specific requirements by the FDA for our patients to be included in these trials may make the trials more difficult to conduct or may significantly extend the time required for enrollment of these trials.

We cannot predict how successful we will be at enrolling subjects in our clinical trials. Subject enrollment is affected by other factors including:

- the eligibility criteria for the trial in question;
- the prevalence and incidence of the conditions being studied in the clinical trials;
- the perceived risks and benefits of our product candidates;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs or therapeutic biologics that may be approved for the indications we are investigating;
- the efforts to facilitate timely enrollment in clinical trials;
- competition for patients from other clinical trials;
- the willingness of potential clinical trial subjects to provide informed consent to participate in the trial;
- the patient referral practices of physicians;
- the ability to monitor subjects adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective subjects.

Our inability to enroll a sufficient number of subjects for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our drug candidates or delays in regulatory filings and progression, which would cause the value of our company to decline and limit our ability to obtain additional financing.

The FDA may require more information or clinical studies for all of our product candidates, and our product candidates may never be approved

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 will result in delays to the regulatory approval or non-approvability of our product candidates, 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, or may require such significant numbers of patients or additional costs to make it impractical to satisfy the FDA's requirements, and thus our product candidates may not be approved for marketing. For example, the Phase 3 PERSIST trial for POSIMIR did not meet its primary efficacy endpoint of reduction in pain on movement over the first 48 hours after surgery as compared to standard bupivacaine HCl. In addition, 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 POSIMIR, 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 or to abuse deterrent properties of opioid product candidates, as they have in their Complete Response Letters for REMOXY ER, 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. Additionally, even if our product candidates receive FDA approval, the FDA may require that we conduct additional clinical studies after such approval, place limitations on our products in applicable labels, require marketing under a REMS program, delay approval to market our products or limit the use of our products, which may harm our business and results of operations.

We currently have a significant amount of debt. Compliance with repayment obligations and other covenants may be difficult, and failure by us to fulfill our obligations under the applicable loan agreements may cause the repayment obligations to accelerate

In July 2016, we entered into a Loan and Security Agreement (the Loan Agreement) with Oxford Finance LLC (Oxford Finance), pursuant to which Oxford Finance provided a $20 million secured single-draw term loan to us with an initial maturity date of August 1, 2020. The term loan was fully drawn at close and the proceeds may be used for working capital and general business requirements. The term loan repayment schedule provided initially for interest only payments for the first 18 months, followed by consecutive monthly payments of principal and interest in arrears starting on March 1, 2018 and continuing through the maturity date of August 1, 2020. Following two amendments, we make interest only payments under the amended Loan Agreement until December 1, 2020 and the final maturity date of the loan is November 1, 2022. The Loan Agreement provides for a floating interest rate (7.95% initially and 9.83% as of December 31, 2018) based on an index rate plus a spread and an additional payment equal to 10% of the principal amount of the term loan, which is due when the term loan becomes due or upon the prepayment of the facility. If we elect to prepay the loan, there is also a prepayment fee between 0.75% and 2.5% of the principal amount of the term loan depending on the timing of prepayment. Our debt repayment obligations under the Loan Agreement, as amended, may prove a burden to the Company as they become due, particularly following the expiration of the interest-only period.

The Loan Agreement contains customary events of default, including, among other things, our failure to fulfill certain of our obligations under the Loan Agreement and the occurrence of a material adverse change in our business, operations or condition (financial or otherwise), a material impairment of the prospect of repayment of any portion of the loan, the failure to deliver an unqualified audit report and board approved financial projections within time periods set forth in the Loan Agreement, or a material impairment in the perfection or priority of lender's lien in the collateral or in the value of such collateral. In the event of default by us under the Loan Agreement, the lender would be entitled to exercise its remedies thereunder, including the right to accelerate the debt, upon which we may be required to repay all amounts then outstanding under the Loan Agreement, which could harm our business, operations and financial condition.

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In addition, the term loan is secured by substantially all of our assets, except that the collateral does not include any equity interests in the Company, any intellectual property (including all licensing, collaboration and similar agreements relating thereto), and certain other excluded assets. The Loan Agreement contains customary representations, warranties and covenants by us, which covenants limit our ability to convey, sell, lease, transfer, assign or otherwise dispose of certain of our assets; engage in any business other than the businesses currently engaged in by us or reasonably related thereto; liquidate or dissolve; make certain management changes; undergo certain change of control events; create, incur, assume, or be liable with respect to certain indebtedness; grant certain liens; pay dividends and make certain other restricted payments; make certain investments; make payments on any subordinated debt; and enter into transactions with any of our affiliates outside of the ordinary course of business or permit our subsidiaries to do the same. Complying with these covenants may make it more difficult for us to successfully execute our business strategy.

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, and such availability will depend on a number of factors, some of which are outside of our control, including general capital markets conditions and investors' view of our prospects and valuation. 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 from the date the financial statements are filed. However, our actual capital requirements will depend on many factors, including:

- success in entering into collaboration agreements and achieving milestones under such agreements;
- the continuation of our collaborative agreements that provide financial funding for our activities;
- regulatory actions with respect to our and our collaborators' product candidates;
- continued progress and cost of our research and development programs;
- progress with preclinical studies and clinical trials;
- the time and costs involved in obtaining regulatory clearance;
- costs involved in preparing, filing, prosecuting, maintaining, defending 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;
- any failure to comply with the covenants in our debt instruments that results in acceleration of repayment obligations;
- 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 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 do not control the commercialization of PERSERIS or Methydur

We rely on Indivior for the commercialization of PERSERIS. Indivior has stated that it is moving ahead with the launch of PERSERIS in the U.S. with a sales force consisting of approximately 50 representatives and expects peak year net revenue goal for PERSERIS of $200 to $300 million. On February 27, 2019, Indivior announced the launch of PERSERIS. There can be no assurance that Indivior will obtain market acceptance and meaningful sales. If Indivior does not successfully commercialize PERSERIS, the earn-out payments we receive under our agreement with them may be limited. We rely on Orient Pharma for the commercialization of Methydur in the territories licensed to Orient Pharma. If Orient Pharma does not successfully commercialize Methydur, the royalty payments we receive under our agreement with them may be limited.

REMOXY ER may not be commercialized

We are dependent on Pain Therapeutics to obtain FDA approval of REMOXY ER. On August 6, 2018, following multiple Complete Response Letters, Pain Therapeutics stated that it had received a Complete Response Letter from the FDA, which concluded that “The data submitted in [the] NDA do not support the conclusion that the benefits of [REMOXY] Extended-Release Capsules outweigh the risks.” Pain Therapeutics further announced a strategic reorganization to align its resources on advancing its drug and diagnostic assets in Alzheimer’s disease. Based on their interactions with the FDA, Pain Therapeutics has indicated that they and the FDA have disagreements around comments and conclusions made by the FDA during a regulatory review of the NDA for REMOXY ER. While Pain Therapeutics has also indicated that they may pursue a formal dispute resolution process with the FDA, there can be no assurance that they will do so or that any such appeal will be successful. We cannot control whether Pain Therapeutics will continue to pursue regulatory approval, commercialization or licensing of REMOXY ER, or if they do so, whether REMOXY ER will ever be approved or commercially successful. If they do not, we would not realize any future income from our agreement with Pain Therapeutics.

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:

- with respect to each new chemical entity, determining appropriate indication(s);
- with respect to our Drug Delivery Program product candidates, selecting and developing a drug delivery technology to deliver the proper dose of drug over the desired period of time;
- determining the appropriate route of administration and 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 active pharmaceutical agent;
- demonstrating the drug formulation will be stable for commercially reasonable time periods;
-

demonstrating through clinical trials that the drug formulation is safe and effective in patients for the intended indication at an achievable dose and that the drug's benefits outweigh its risks;

- demonstrating abuse deterrent properties to the satisfaction of the FDA for certain products for which abuse-deterrence is considered an important feature by the FDA, 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. Except for marketing authorization for Orient Pharma's distribution of Methydur Sustained Release Capsules in Taiwan, development is incomplete for all product candidates in our development programs, including DUR-928. We may not be able to finalize the design or formulation of any of these product candidates. Further, although we believe our design and formulation of POSIMIR and ORADUR-Methylphenidate ER to be substantially complete, there can be no assurance that additional developments will not be required prior to any regulatory approval of these products. 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 DUR-928, POSIMIR, ORADUR-Methylphenidate ER (outside of the territories licensed to Orient Pharma) or other product candidates, we will not be able to earn revenue from them, which would materially harm our business.

Certain of our drug candidates that may be developed, including REMOXY ER, 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

For several years, FDA has required companies engaged in manufacturing and sales of opioid products 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. All manufacturers of long-acting and extended-release opioids must ensure that training is provided to prescribers of these medications and develop information that prescribers can use when counseling patients about the risks and benefits of opioid use. The FDA has also 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. More recently, in February 2016, the FDA announced a comprehensive action plan to take concrete steps towards reducing the impact of opioid abuse on American families and communities. As part of this plan, the agency will review product and labelling decisions and re-examine the risk-benefit paradigm for opioids.

Certain of our drug candidates that may be developed, including REMOXY ER, 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, and

until the results of the FDA's recently announced initiatives are known, 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 Indivior, Pain Therapeutics, Santen, Orient Pharma and others under which we granted such third parties the right to develop, apply for regulatory approval for, market, promote or distribute REMOXY ER and other product candidates, subject to payments to us in the form of product royalties, earn-out 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 collaborations regarding our product candidates may adversely affect potential economic benefits

Third-party collaboration agreements typically allow the third party to terminate the agreement (or a specific program within an agreement) by providing notice. For example in January 2019, Sandoz notified us that they were terminating our agreement with respect to POSIMIR. In this case, the product rights revert to us. If there have been payments under such agreements that are being recognized over time, termination of such agreements (or programs) can lead to a near-term increase in our reported revenues resulting from the immediate recognition of the balance of such payments. 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, Santen or Orient Pharma could have similar effects.

Our revenues depend on collaboration agreements with other companies. If we are unable to enter into new agreements or meet our obligations or manage our relationships with our collaborators under these agreements 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 have seen recent declines in revenues associated with our existing collaboration agreements, which reflect the current development stage of the product candidates subject to those agreements, and our collaborator’s decreased needs for our services. We do not expect our collaboration revenues to increase materially unless we enter into new collaboration agreements, and there can be no assurance that we will do so. Even if we enter into new collaboration 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 with respect to REMOXY ER, Orient Pharma with respect to Methydur, and Santen with respect to an ophthalmic product 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. Acquisitions of our collaborators or strategic changes or re-organizations or re-prioritizations of our collaborators 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 we do not enter into new collaboration agreements, and 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. As of December 31, 2018, we had $812,000 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 generally necessary to the achievement of development-based milestones, the performance of our third-party collaborators is also generally 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, including, but not limited to DUR-928, ORADUR-Methylphenidate ER in markets not already licensed to Orient Pharma, including the United States and Europe, and others. 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 as 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 and our third-party collaborators may not be able to manufacture sufficient quantities of our pharmaceutical product candidates and components to support the non-clinical, 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 non-clinical, 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 DUR-928, POSIMIR and REMOXY ER. 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 non-clinical, 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 quality and cost, then we and our third-party collaborators may not be able to develop or 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 POSIMIR and REMOXY ER. If we experience delays or technical difficulties in developing acceptable manufacturing processes or scaling up the manufacturing of our product candidates, it could result in delays or added cost in our development programs. 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 non-clinical and 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 non-clinical trials, clinical trials, chemistry, manufacturing and controls (CMC) and commercial launch of our product candidates and those of our third-party collaborators.

We have entered into a commercial manufacturing and packaging agreement with a third party manufacturer for future supply of POSIMIR. This third party is our sole source for the drug product required for development and commercialization of this drug candidate. There may be technical risks associated with establishing an alternative commercial manufacturer that could entail delays in supply, quality issues or delays in the possible regulatory approval of POSIMIR. Furthermore, we and our contract manufacturer may also need or choose to subcontract with additional third-party contractors to perform manufacturing steps of POSIMIR or supply required components for POSIMIR. 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 proceed with the development of POSIMIR, we expect to put in place in the future second source supply arrangements, which may be costly and time consuming.

We have entered into contract manufacturing agreements with multiple vendors for DUR-928. There can be no assurance that we will receive sufficient quantities of DUR-928 to commence and conduct the non-clinical trials, clinical trials and CMC activities we are planning, and delays in supply could delay development of DUR-928.

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

Developing, manufacturing, 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 meet GMP, GLP and/or other governmental requirements for drug development;
- 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 practice 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, put our or our partner's clinical trial on hold, withdraw or reject an investigational new drug (IND) application or require product recall, which may cause interruptions or delays in the development, 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, 2018, had an accumulated deficit of approximately $468.6 million. We expect to continue to incur significant operating losses over the next several years as we continue to incur significant costs for research and development, clinical trials, manufacturing, sales, and general and administrative functions. Our ability to achieve profitability depends upon our ability, alone or with others, to successfully complete the development of our proposed 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 and/or intellectual property rights 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 ALZET product line, from the LACTEL product line and from certain excipient sales, and from payments under collaborative research and development agreements with third parties. We do not expect our product revenues to increase significantly in the near future, and we do not expect that collaborative research and development revenues will exceed our actual operating expenses. We do not anticipate meaningful revenues to derive from the commercialization and marketing of our 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. Developing a sales force and commercial group would 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 our products in development, we may not be able to effectively launch these products. 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 collaborators 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, consultants, 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 and our collaborators' product candidates, including DUR-928, POSIMIR, Methydur, PERSERIS and REMOXY ER, 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 POSIMIR, REMOXY ER, ORADUR-Methylphenidate and certain other pharmaceutical product candidates we have under development, and a third party manufacturer is our sole supplier for future clinical and commercial supplies of POSIMIR. 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;

- delays associated with finding and contracting with a new supplier (if we can find one capable of replacing the old supplier and negotiate commercially reasonable terms) and then transferring the technology to the new supplier;
- 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 development 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.

Some of our pharmaceutical product candidates contain controlled substances, the making, use, sale, importation, exportation 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. REMOXY ER, and certain other product candidates we may develop 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 our goodwill, 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. 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, 2018. 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 2018 and determined that goodwill was not impaired as of December 31, 2018. 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, in part, include certain excipients that are sold to customers and included in products in development. These inventories are capitalized based on management's judgment of probable sale prior to their

expiration date which in turn is primarily based on 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 a product by the necessary regulatory bodies, changes in product development timelines, or other 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. For example, we recorded charges to cost of goods sold of approximately $926,000, of which approximately $426,000 related to the write-down of the cost basis of inventory and approximately $500,000 related to the prepaid inventory for the minimum purchase commitment for an excipient in the year ended December 31, 2016 as a result of a change in the forecasted demand for the excipients after Pain Therapeutics received a Complete Response Letter from the FDA on its resubmission of the NDA for REMOXY ER. In addition, during the year ended December 31, 2017, we recorded charges to cost of goods sold of approximately $2.0 million, of which approximately $503,000 related to the write-down of the cost basis of inventory on hand, $500,000 related to the prepaid inventory for the minimum purchase commitment for the excipient, and $1.0 million related to the recognition of our remaining minimum purchase commitment for the same excipient after we announced that PERSIST, the Phase 3 clinical trial for POSIMIR, did not meet its primary efficacy endpoint.

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, 2018, 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. In addition, our success will depend on our ability to attract and retain other highly skilled personnel, particularly as we develop and expand our Epigenetic Regulator Program. 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 involve 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.

Cyber-attacks or other failures in telecommunications or information technology systems could result in information theft, data corruption and significant disruption of our business operations

We utilize information technology, systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our systems and networks and the confidentiality, availability and integrity of our data, and may cause a disruption in our operations, harm our reputation and increase our stock trading risk. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our third-party collaborators, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems. Any cyber-attack or destruction or loss of data could have a material adverse effect on our business and prospects. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

Our corporate headquarters, certain manufacturing facilities and personnel are located in a geographical area that is seismically active and near wildfire zones.

Our corporate headquarters, certain manufacturing facilities and personnel are located in a geographical area that is known to be seismically active and prone to earthquakes, as well as wildfires. 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 Intellectual Property

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.

As of March 4, 2019, we owned or exclusively in-licensed over 50 unexpired issued U.S. patents and over 285 unexpired issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have over 30 pending U.S. patent applications and over 145 foreign applications pending in Europe, Australia, Japan, Canada and other countries.

The patent status of our most advanced drug candidates is as follows:

Our Epigenetic Regulator Program includes seven in-licensed patent families and one patent family solely owned by us. Two patent families each include granted patents expiring in at least 2026 and 2032, respectively. The other patent families include pending patent applications, which if granted, could result in patents expiring in 2033, 2034, 2035, 2037, 2037 and 2037, respectively, plus any eligible patent term adjustments and extensions. Of the eight patent families covering DUR-928 and/or other molecules in the Epigenetic Regulator Program, two were only filed in the United States, and the other six have been filed or likely will be filed both in the U.S. and

internationally. Since DUR-928 is an endogenous small molecule, patent claims directed to DUR-928 composition of matter may be more difficult to maintain or enforce in the United States under Myriad Genetics and other recent court decisions. One of the U.S. patents issued before Myriad Genetics, and four of the DUR-928 U.S. patents issued after Myriad Genetics. The granted claims in the U.S. include both composition of matter and method of treatment claims. There can be no assurance that the pending patent applications will be granted. Further, there can be no assurance that VCU will not attempt to terminate their license to us, which termination would result in the loss of our rights to these patent families.

In the United States, POSIMIR is covered by two patent families. One patent family includes granted patents expiring in at least 2025. Another patent family includes a pending patent application, which if granted, could result in a patent expiring in 2026, plus any eligible patent term adjustments and extensions. In Europe, POSIMIR is covered by five granted patents with three expiring in 2025 and two expiring in 2026, plus any eligible patent term extensions.

In the United States, our REMOXY ER patent portfolio includes four patent families. Three patent families include granted patents expiring in at least 2025, 2031, and 2034, respectively. The patent family providing protection until at least 2025 includes twelve granted patents. The patent family providing protection until at least 2031 includes three granted patents. The patent family providing protection until at least 2034 includes four granted patents. The fourth patent family includes a pending patent application, which if granted, could result in a patent expiring in 2026, plus any eligible patent term adjustments and extensions. We currently have pending U.S. applications for each of these four patent families. There can be no assurance that the pending patent applications will be granted. In Europe, REMOXY ER is covered by five granted patents with two expiring in 2023, two expiring in 2026, and one expiring in 2028, plus any eligible patent term extensions.

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 United States 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, constitutionality of inter partes reviews, enforceability, availability of injunctive relief and damages may make it more difficult for us to procure, maintain, defend 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, changed patent priority from “first to invent” to “first to file,” implemented a post-grant opposition system for patents and provided 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 or arbitration 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, Orient Pharma and Santen 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 and other case law 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.

Risks Related To Our Industry

The markets for our pharmaceutical product candidates and for our ALZET and LACTEL product lines are rapidly changing and competitive, and new products or technologies developed by others could impair our ability to maintain or 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, biotechnology, medical devices and drug delivery. Competition for DUR-928, if approved, will depend on the specific indications for which DUR-928 is approved. Intercept, Gilead, Shire, Conatus Pharmaceuticals, Galectin Therapeutics, Genfit, Pfizer, Roche, Bristol Myers Squibb, Novartis, Terns Pharmaceuticals, Galmed Pharmaceuticals, Enanta Pharmaceuticals, Novo Nordisk, Takeda, Vital Therapies, Allergan, Akarna Therapeutics,

Inventiva Pharma, Genkyotex, VBL Therapeutics, NGM Biopharmaceuticals, Gemphire Therapeutics, Albireo Pharma, CymaBay Therapeutics, Madrigal Pharmaceuticals, Viking Therapeutics, CohBar, FALK Pharma, Acorda, and others have development plans for products to treat NAFLD/NASH, PSC or other liver diseases. AbbVie, Ischemix, Thrasos Therapeutics, AM-Pharma, Complexa, Quark Pharmaceuticals and others have development plans for products to treat acute kidney injury. Bristol Myers Squibb, Novartis, Eli Lilly, Almirall, LEO Pharma, Pfizer, Janssen, AbbVie, Boerhinger-Ingelheim, Amgen, Sandoz, Astra-Zeneca, Valeant, Takeda, Merck, Idera Pharmaceuticals and others have development plans for products to treat psoriasis.

POSIMIR and REMOXY ER, if approved, will compete with currently marketed oral opioids, transdermal opioids, local anesthetic patches, 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, AbbVie, Janssen, Actavis, Medtronic, Endo, AstraZeneca, Pernix Therapeutics, Tricumed, Halyard Health, Cumberland Pharmaceuticals, Pacira, Acorda Therapeutics, Mallinckrodt, Inspirion Delivery Technologies, Mylan, Shire, Johnson & Johnson, Eli Lilly, Pfizer, Novartis, Egalet, Teva Pharmaceuticals, Collegium Pharmaceutical and others. Purdue Pharma, Sandoz, Actavis, Collegium Pharmaceutical, Pfizer, Elite Pharmaceuticals, Intellipharmaceutics, Egalet, Teva Pharmaceuticals and others have also announced regulatory approval or development plans for abuse deterrent opioid products. PERSERIS will compete with currently marketed or approved products by Johnson & Johnson, Eli Lilly, Otsuka, Alkermes, Merck, Allergan, 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, Eli Lilly, Pfizer 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, Mallinckrodt, Hospira, Pfizer, Cumberland Pharmaceuticals, Egalet, Acura, Elite Pharmaceuticals, Phosphagenics, Intellipharmaceutics, Collegium Pharmaceutical, Heron Therapeutics, Charleston Laboratories, Daiichi Sankyo 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.

Competition for our ALZET product line primarily consists of customers choosing to utilize delivery methods for their research projects other than an osmotic pump. Competition for our LACTEL product line comes from companies including Evonik, Corbion, FUJIFILM Wako Pure Chemical Corporation, PCAS and others. 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. We may in the future face competition for our ALZET and LACTEL product lines from other companies including low cost foreign competitors.

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 payers 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 payers 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 payers 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 pharmaceutical company, even though we do not and may not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payers, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. These regulations include:

- the Federal Healthcare Anti-Kickback Statute, which prohibits, 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, and which will constrain our marketing practices and the marketing practices of our licensees, educational programs, pricing policies, and relationships with healthcare providers or other entities;
- the federal physician self-referral prohibition, commonly known as the Stark Law, which prohibits physicians from referring Medicare or Medicaid patients to providers of "designated health services" with whom the physician or a member of the physician's immediate family has an ownership interest or compensation arrangement, unless a statutory or regulatory exception applies;
- federal false claims laws that prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other government reimbursement programs that are false or fraudulent, and which may expose entities that provide coding and billing advice to customers to potential criminal and civil penalties, including through civil whistleblower or qui tam actions, and including as a result of claims presented in violation of the Federal Healthcare Anti-Kickback Statute, the Stark Law or other healthcare-related laws, including laws enforced by the FDA;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which 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, and which 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;
- federal physician sunshine requirements under the Affordable Care Act, which 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;
- the Federal Food, Drug, and Cosmetic Act, which, among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples; and
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third-party payers, including private insurers, state laws requiring pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and which may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state and foreign laws governing 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 federal laws such as 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 and some non-U.S. jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post approval activities, affect our ability to profitably sell any product candidates for which we obtain marketing and otherwise affect our future revenue and profitability and the future revenue and profitability of our collaborators or potential collaborators.

For example, in March 2010, the Affordable Care Act was enacted in the United States to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The law has continued the downward pressure on the pricing of medical items and services, especially under the Medicare program, and increased the industry's regulatory burdens and operating costs. Among the provisions of the Affordable Care Act of importance to us are the following:

- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" and biologic agents;
- imposes an annual excise tax of 2.3% on any entity that manufactures or imports medical devices offered for sale in the United States;
- 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;
- extends manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- mandates a further shift in the burden of Medicaid payments to the states;
- expands the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- establishes a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- establishes a new Patient Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishes an independent payment advisory board that will submit recommendations to Congress to reduce Medicare spending if projected Medicare spending exceeds a specified growth rate.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future. The new Presidential Administration and U.S. Congress will likely continue to seek to modify, repeal, or otherwise

invalidate all, or certain provisions of, the Affordable Care Act. It is uncertain the extent to which any

such changes may impact our business or financial condition. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include the Budget Control Act of 2011, which, among other things, resulted in reductions to Medicare payments to providers of 2% per fiscal year and will remain in effect through 2025; the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years; and the Medicare Access and CHIP Reauthorization Act of 2015, which, among other things, ended the use of the sustainable growth rate formula and provides for a 0.5% update to physician payment rates for each calendar year through 2019, after which there will be a 0% annual update each year through 2025. More recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. For example, the current administration’s budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. The Department of Health and Human Services (HHS) has already started the process of soliciting feedback on some of these measures and is immediately implementing others under its existing authority. In addition, the marketing, pricing and sale of the Company’s products are subject to regulation, investigations and legal actions including under the Medicaid Drug Rebate Program under the Affordable Care Act, which has increased the statutory minimum rebates a manufacturer must pay under the program as well as a new methodology by which rebates are owed calculated for drugs that are inhaled, infused, instilled, implanted or injected. We are also subject to federal and state false claims acts, as well as federal and state antitrust and consumer protection laws. Increased scrutiny of health care industry business practices in recent years by government agencies and state attorneys general in the U.S., and any resulting investigations and prosecutions, carry risk of significant civil and criminal penalties including, but not limited to, debarment from participation in such government healthcare programs.

Individual states in the United States have also become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product and medical device pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, in October 2017, California passed a new law, to become effective in January 2019, which will require transparency from biopharmaceutical companies regarding price increases for prescription drugs. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and medical devices to purchase and which suppliers will be included in their prescription drug and other healthcare programs.

We expect that the Affordable Care Act, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved or cleared product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. We cannot

predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to new requirements or policies, or if we are not able to maintain regulatory compliance, our products and product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability, or be able to enter attractive collaboration agreements, which would adversely affect our business.

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, clinical development, 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 DUR-928, and POSIMIR, if approved, and including Indivior's PERSERIS. 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; 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.

In addition, market adoption of POSIMIR and other products in development may depend on what data from clinical studies is included in the product label, and there can be no assurance as to what the final product labels will contain. Physicians, patients, payers 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 payers, 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 payers 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 payers often limit 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 payers 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. Compliance with evolving corporate governance and public disclosure standards 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 actions on trade by the U.S. and foreign governments could adversely affect the Company's results of operations and financial condition

The U.S. government has indicated its intent to adopt a new approach to trade policy and in some cases to renegotiate, or potentially terminate, certain existing bilateral or multilateral trade agreements. It has also initiated or is considering the imposition of tariffs on certain foreign products. Changes in U.S. trade policy have resulted in, and could continue to result in, one or more U.S. trading partners adopting responsive trade policy making it more difficult or costly for us to export our products to those countries. These measures could also result in increased costs for goods imported into the United States. This in turn could require us to increase prices to our customers which may reduce demand, or, if we are unable to increase prices, result in lowering our margin on products sold.

There is also a concern that the imposition of additional tariffs by the United States could result in the adoption of tariffs by other countries. A potential resulting trade war could have a significant adverse effect on world trade and the world economy. We cannot predict future trade policy or the terms of any renegotiated trade agreements and their impact on our business. The adoption and expansion of trade restrictions, the occurrence of a trade war, or other governmental action related to tariffs or trade agreements or policies has the potential to adversely impact demand for our products, our costs, our customers, our suppliers, and the U.S. economy, which in turn could adversely impact our business, financial condition and results of operations.

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 Nasdaq. Our ability to continue operations or to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if we are delisted from Nasdaq

On December 24, 2018, 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).

The Company has until June 24, 2019 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. If the Company does not regain compliance within this 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) 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 if we were not in compliance, 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 would constitute an event of default under our loan facility with Oxford, entitling Oxford to accelerate our obligations under such facility, among other actions. Under such circumstances, we could be required to renegotiate the repayment terms of our loan facility, on terms which would not be favorable to the Company as our current terms, or we could be required to take other actions, such as discontinuing some or all of our operations, selling assets, or other action. Delisting could also 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

In order to raise capital and for other purposes, we may in the future offer and issue additional shares of our common stock or other securities convertible into or exchangeable for our common stock, and the price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share at which investors in our common stock bought their shares. In August 2018, we filed a shelf registration statement on Form S-3 with the SEC that allows us to offer up to $175 million of securities from time to time in one or more public offerings, inclusive of up to $75.0 million of additional shares of common stock which the Company may sell, subject to certain limitations, under the 2015 Sales Agreement through Cantor Fitzgerald, acting as agent. Any additional sales in the public market of our common stock, under our Controlled Equity Offering program with Cantor Fitzgerald, in other offerings under the shelf registration

statement or otherwise, could adversely affect prevailing market prices for our common stock. In addition, as of December 31, 2018, 30,317,615 shares of our common stock were issuable upon exercise of stock options outstanding under our stock option plans at a weighted average exercise price of $1.63 per share and 9,257,933 additional shares of common stock reserved for potential future issuance under our stock option plan, and an aggregate of 361,185 shares of common stock reserved for potential future issuance under our 2000 Employee Stock Purchase Plan. Investors will incur dilution from the sale of any additional shares or upon the issuance of any shares pursuant to such plans, or upon exercise of any outstanding options.

Our ability to use net operating losses and certain other tax attributes is uncertain and may be limited

Our ability to use our federal and state net operating losses to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income before the expiration dates of the net operating losses, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our net operating losses. In addition, utilization of net operating losses to offset potential future taxable income and related income taxes that would otherwise be due is subject to annual limitations under the "ownership change" provisions of Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (Internal Revenue Code) and similar state provisions, which may result in the expiration of net operating losses before future utilization. In general, under the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating losses and other pre-change tax attributes (such as research and development credit carryforwards) to offset its post-change taxable income or taxes may be limited. Our equity offerings and other changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change. If an ownership change limitation were to apply, utilization of our domestic net operating losses and tax credit carryforwards could be limited in future periods and a portion of the carryforwards could expire before being available to reduce future income tax liabilities.

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 third-party collaborators to continue development of 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 DUR-928 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;
- negative press coverage or online misinformation about the Company or its partners or their respective products or personnel;
- 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 us or 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.

Our bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees

Our bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on behalf of the Company, any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Company, any action asserting a claim arising pursuant to any provision of the General Corporation Law of Delaware or our Certificate of Incorporation or bylaws or any action asserting a claim governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees.

Alternatively, if a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

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	30,149 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2024 (with an option to renew for an additional five years)
Cupertino, CA	20,100 sq. ft.	Office and Laboratory	Lease expires 2024 (with an option to renew for an additional five years)
Vacaville, CA	24,634 sq. ft.	Manufacturing	Lease expires 2023 (with an option to renew for an additional five years)
Birmingham, AL	21,540 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2021 (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 Matters 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, 2017	Low	High
First Quarter	$0.91	$1.37
Second Quarter	0.74	1.59
Third Quarter	1.50	1.90
Fourth Quarter	0.75	2.17
Year ended December 31, 2018	Low	High
First Quarter	$0.88	$2.34
Second Quarter	1.30	2.55
Third Quarter	1.02	1.75
Fourth Quarter	0.46	1.15

The closing sale price of our common stock as reported on the NASDAQ Global Market on March 4, 2019 was $0.78 per share. As of that date there were approximately 108 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, 2013. The graph assumes that $100 was invested on December 31, 2013. The stock price performance on the following graph is not necessarily indicative of future stock price performance.

*$100 Invested on 12/31/13 in stock or index—including reinvestment of dividends. Fiscal year ending December 31.

DURECT CORPORATION

	Cumulative Total Return					
	12/31/13	12/31/14	12/31/15	12/31/16	12/31/17	12/31/18
DURECT CORPORATION	100.00	45.66	127.75	77.46	53.18	27.75
NASDAQ STOCK MARKET (U.S.)	100.00	113.40	119.89	128.89	165.29	158.87
NASDAQ BIOTECHNOLOGY	100.00	134.10	149.42	117.02	141.66	128.45

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, 2018, 2017 and 2016 and the balance sheet data at December 31, 2018 and 2017 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, 2015 and 2014, and the balance sheet data at December 31, 2016, 2015 and 2014 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,				
	2018	2017	2016	2015	2014
	(in thousands, except per share data)				
Statement of Operations Data:					
Collaborative research and development and other revenue (1)	$8,207	$23,577	$1,880	$7,832	$8,256
Product revenue, net	10,357	13,093	12,145	11,292	11,145
Revenue from sale of intellectual property rights	—	12,500	—	—	—
Total revenue	18,564	49,170	14,025	19,124	19,401
Operating expenses:					
Cost of revenue	4,263	6,633	5,290	3,905	5,686
Research and development	25,501	31,609	29,274	24,317	22,429
Selling, general and administrative	12,419	13,165	11,825	11,566	12,284
Total operating expenses	42,183	51,407	46,389	39,788	40,399
Loss from operations	(23,619)	(2,237)	(32,364)	(20,664)	(20,998)
Other income (expense):					
Interest and other income	870	967	143	237	39
Interest expense	(2,573)	(2,425)	(2,288)	(2,236)	(1,151)
Net other expense	(1,703)	(1,458)	(2,145)	(1,999)	(1,112)
Net loss	$(25,322)	$(3,695)	$(34,509)	$(22,663)	$(22,110)
Basic net loss per share	$(0.16)	$(0.03)	$(0.26)	$(0.19)	$(0.20)
Diluted net loss per share	$(0.16)	$(0.03)	$(0.26)	$(0.19)	$(0.20)
Shares used in computing basic net loss per share	159,834	145,273	133,163	118,523	111,666
Shares used in computing diluted net loss per share	159,834	145,273	133,163	118,523	111,666

	As of December 31,				
	2018	2017	2016	2015	2014
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and investments	$34,465	$36,909	$25,154	$29,290	$34,850
Working capital	34,078	29,530	3,676	30,874	32,526
Total assets	49,999	53,113	40,508	46,772	50,084

Term loan, net	20,533	20,859	20,137	20,511	20,113
Other long-term liabilities	992	1,126	1,541	1,664	1,747
Stockholders' equity	20,000	21,488	8,338	14,883	18,515

(1) The 2017 figure includes the recognition of $20.0 million in revenue associated with a nonrefundable upfront payment that we received in June 2017 under our license agreement with SANDOZ. The 2018 figure includes the recognition of $5.0 million in revenue associated with a nonrefundable milestone payment that we received in August 2018 under our agreement with Indivior.

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, 2018, 2017 and 2016 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. S forward-looking statements contained herein are based on current expectations.

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

- the clinical trial plans for DUR-928;
- potential regulatory filings for or approval of DUR-928, POSIMIR, REMOXY ER, or any of our or any third parties' other product candidates;
- the product launch of PERSERIS by Indivior and the associated earn-out payments we may receive from Indivior;
- the potential product launch of Methydur by Orient Pharma and the associated royalty payments we may receive from Orient Pharma;
- the progress of our third-party collaborations, including estimated milestones;
- our intention to seek, and ability to enter into and maintain strategic alliances and collaborations;
- the potential benefits and uses of our products;
- responsibilities of our third-party 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 and continued development of our products;
- our responsibilities to our third-party 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 and our evaluation of additional 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, including for DUR-928, the possible commencement of future clinical trials and announcements of the findings of our 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, asserting 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 products in development for at least the next twelve months, potential for future inventory write-offs and our expectations regarding our ability to achieve profitability;
- sufficiency of our cash resources, anticipated capital requirements and capital expenditures, our ability to comply with covenants of our term loan, and our need for additional financing, including potential sales under our shelf registration statement;
- 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 biopharmaceutical company with research and development programs broadly falling into two categories: (i) new chemical entities derived from our Epigenetic Regulator Program, in which we attempt to discover and develop molecules which have not previously been approved and marketed as therapeutics, and (ii) proprietary pharmaceutical programs, in which we apply our formulation expertise and technologies largely to active pharmaceutical ingredients whose safety and efficacy have previously been established but which we aim to improve in some manner through a new formulation. We also manufacture and sell osmotic pumps used in laboratory research and design, develop and manufacture 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, we conduct research and development of pharmaceutical products in collaboration with third party pharmaceutical and biotechnology companies.

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 royalties on product sales. At the same time, we have retained the rights to other programs, which are the basis of future potential collaborations and which over time may provide a pathway for us to develop our own biopharmaceutical 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 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 three years, we generated collaborative research and development revenues from collaborative agreements with Sandoz, Pain Therapeutics, Zogenix, Santen and others.

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Product Revenues

We also currently generate product revenue from the sale of three product lines:

- ALZET® osmotic pumps which are used for animal research;
- 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 Methydur and one excipient that is included in a currently marketed animal health product.

Because we consider our core business to be developing and commercializing pharmaceuticals, 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 revenues 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.

Revenues from Sale of Intellectual Property Rights

From time-to-time, we also enter into arrangements in which we sell intellectual property rights and, in return, may receive upfront payments, contingent milestone payments and earn-outs from third party collaborators. Our deliverable under these arrangements typically consists of the sale of intellectual property rights, and does not include any substantive continuing obligations subsequent to the transfer of the related rights, title, and interest to the buyer. We recognize the upfront payment as revenue because such arrangement is part of our revenue-earning activities and is in line with our ordinary course of ongoing business operations. In September 2017, we entered into a patent purchase agreement with Indivior and received a non-refundable payment of $12.5 million.

Operating Results

Since our inception in 1998, we have generally had a history of operating losses. At December 31, 2018, we had an accumulated deficit of $468.6 million. Our net losses were $25.3 million, $3.7 million and $34.5 million for the years ended December 31, 2018, 2017 and 2016, respectively. These losses have resulted primarily from costs incurred to research and develop our product candidates and to a lesser extent, from selling, general and administrative costs associated with our operations and product sales. We expect our research and development expenses to increase in 2019 compared to 2018 and our selling, general and administrative expenses to be comparable in 2019 to 2018. We do not anticipate meaningful revenues from our products in development, should they be approved, for at least the next twelve months. Therefore, we expect to incur continuing losses and negative cash flows 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 inventories and purchase commitments, revenue recognition, contract research liabilities, and stock-based compensation. Actual amounts could differ significantly from these estimates.

Inventories and Purchase Commitments

Our inventories, in part, include certain excipients that are sold to a customer for a currently marketed animal health product and included in several products in development, awaiting regulatory approval or commercial launch. These inventories are capitalized based on management’s judgment of probable sale prior to their expiration dates. The

valuation of inventory requires management 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 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 us to record a liability related to minimum purchase agreements that we have in

place for raw materials. In October 2017, we announced that PERSIST, the Phase 3 clinical trial for POSIMIR, did not meet its primary efficacy endpoint of reduction in pain on movement over the first 48 hours after surgery as compared to standard bupivacaine HCl. As a result, during the year ended December 31, 2017, we recorded charges to cost of goods sold of approximately $2.0 million, of which approximately $503,000 related to the write-down of the cost basis of inventory on hand, $500,000 related to the prepaid inventory for the minimum purchase commitment for the excipient, and $1.0 million related to the recognition of our remaining minimum purchase commitment for the same excipient. As of December 31, 2018, the remaining carrying value of the excipient residing within our inventory was $68,000. In the event that management determines that we will not utilize all of these materials, there could be a potential write-off related to this inventory. If we are able to subsequently sell products made with raw materials that were previously written down, we will report an unusually high gross profit as there will be no associated cost of goods for these materials.

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. Prior to January 1, 2018, we evaluated the accounting treatment under these agreements including whether multiple deliverables existed, 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 had concluded that the deliverables were 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 were 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 represented 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 determined that the expected timeline for a project and therefore our continuing involvement was materially different than we previously assumed, we adjusted the period over which we recognized the deferred revenue.

Effective January 1, 2018, we adopted FASB ASC Topic 606, Revenue from Contracts with Customers, or ASC 606. In accordance with ASC 606, we changed certain characteristics of our revenue recognition accounting policy as described below. ASC 606 was applied using the modified retrospective method, where the cumulative effect of the initial application was recognized as an adjustment to opening accumulated deficit at January 1, 2018. Therefore, comparative prior periods have not been adjusted and continue to be reported under FASB ASC Topic 605, Revenue Recognition, or ASC 605. We recorded a net decrease to opening accumulated deficit of $470,000 with an offset entry to a contra liability account as of January 1, 2018 due to the cumulative impact of adopting Topic 606, with the impact relating to our deferred collaborative research and development revenues. There was no impact to reported total assets, revenues and operating expenses for the twelve months ended December 31, 2018 as a result of applying Topic 606.

Product Revenues, Net

We sell osmotic pumps used in laboratory research, and design, develop and manufacture 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.

Revenues from product sales are recognized when the customer obtains control of our product, which occurs at a point in time, typically upon shipment to the customer. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less.

Trade Discounts and Allowances: We provide certain customers with discounts that are explicitly stated in our contracts and are recorded as a reduction of revenues in the period the related product revenues are recognized.

Product Returns: Consistent with industry practice, we generally offer customers a limited right of return for products that have been purchased from us. We estimate the amount of our product sales that may be returned by our customers and record this estimate as a reduction of revenues in the period the related product revenues is

recognized. We currently estimate product return liabilities using our own historical sales information. We expect product returns to be minimal.

Collaborative Research and Development Revenues

We enter into license agreements which are within the scope of Topic 606, under which we license certain rights to our product candidates to third parties. The terms of these arrangements typically include payment to us of one or more of the following: non-refundable, up-front license fees; reimbursement of development costs incurred by us under approved work plans; development, regulatory and commercial milestone payments; payments for manufacturing supply services we provide through our contract manufacturers; sales-based milestones and royalties on net sales of licensed products. Each of these payments results in collaborative research and development revenues, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of our agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. We use key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success. We expect to recognize revenue for the variable consideration currently being constrained when it is probable that a significant revenue reversal will not occur.

Licenses of intellectual property: If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments: At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of us or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaborative research and development revenues and net income (loss) in the period of adjustment.

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug product for either clinical development or commercial supply at the customer's discretion are generally considered options. We assess if these options provide a material right to the customer and if so, they are accounted for as separate performance obligations. If we are entitled to additional payments when the customer exercises these options, any additional payments are recorded in collaborative research and development revenues when the customer obtains control of the goods, which is upon delivery.

Royalties and Earn-outs: For arrangements that include sales-based royalties or earn-outs, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation

to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any significant royalty revenue resulting from our collaborative arrangements or any significant earn-out revenue from our patent purchase agreement with Indivior.

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. We amortize the fair value of options granted 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, 2018, 2017 and 2016

Collaborative research and development and other revenues

We recognize revenues from collaborative research and development activities and service contracts. Collaborative research and development and other revenues primarily represents reimbursement of qualified expenses related to the collaborative agreements with various third parties to research, develop and commercialize potential products using our drug delivery technologies, revenue recognized from recognition of non-refundable upfront fees, and milestone payments in connection with our collaborative agreements.

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

	Year ended December 31,		
	2018	2017	2016
Collaborator/Counterparty			
Indivior UK Limited (Indivior) (1)	$5,019	$—	$—
Santen Pharmaceutical Co. Ltd. (Santen) (2)	102	294	514
Sandoz AG (Sandoz) (3)	—	20,000	—
Zogenix, Inc. (Zogenix) (4)	—	835	555
Pain Therapeutics, Inc. (Pain Therapeutics)	—	109	670
Other (5)	3,086	2,339	141
Total collaborative research and development and other revenue	$8,207	$23,577	$1,880

(1) Amount consists of a $5.0 million milestone payment earned from Indivior upon NDA approval of PERSERIS in 2018 and earn-out revenue from PERSERIS net sales compared with zero in 2017 and 2016; we and Indivior signed a patent purchase agreement effective September 2017.

(2) Amounts related to ratable recognition of upfront fees were zero in 2018, $199,000 in 2017 and $228,000 in 2016, respectively; we and Santen signed a license agreement effective December 2014. In January 2018, we were notified by Santen that due to a shift in near term priorities, Santen has elected to reallocate research and development resources and put our program on pause until further notice. While the main program is on pause, the parties are working together on a limited set of research and development activities funded by Santen.

(3) Amounts related to recognition of upfront fees were zero in 2018, $20.0 million in 2017 and zero in 2016; we and Sandoz signed a license agreement effective June 2017. As of December 31, 2017, all of the $20.0 million upfront fee had been recognized as revenue as our contractual performance obligations had been fulfilled. In January 2019, the license agreement was terminated.

(4) Amounts related to ratable recognition of upfront fees were zero in 2018, $833,000 in 2017 and $208,000 in 2016; we and Zogenix signed a license agreement effective July 2011. In August 2017, we and Zogenix terminated the license agreement. As a result, we recognized as revenue all of the remaining upfront fees in the twelve months ended December 31, 2017 that had previously been deferred.

(5) Includes revenue recognized associated with our feasibility agreements for each of the years ended December 2018, 2017 and 2016.

The decrease in collaborative research and development revenues in 2018 compared with 2017 was primarily due to lower revenue recognized from our agreements with Sandoz, Zogenix and Pain Therapeutics, partially offset by higher revenue recognized from feasibility agreements with other companies. In addition, we earned a $5.0 million milestone payment from Indivior upon NDA approval of PERSERIS in the third quarter of 2018.

The increase in collaborative research and development revenue in 2017 compared with 2016 was primarily due to higher revenue recognized from our agreements with Sandoz and Zogenix and higher revenue recognized from feasibility agreements with other companies, partially offset by lower revenue recognized from our agreements with Pain Therapeutics and Santen.

We received a $20.0 million upfront fee in connection with the license agreement signed with Sandoz in June 2017. At December 31, 2017, all of the $20.0 million upfront fee had been recognized as revenue as our contractual performance obligations had been fulfilled. In January 2019, the license agreement with Sandoz was terminated.

We received a $2.0 million upfront fee in connection with the license agreement signed with Santen in December 2014. The $2.0 million upfront fee was recognized as collaborative research and development revenue over the term of our continuing involvement with Santen. At December 31, 2018, $1.2 million of the $2.0 million upfront fee had been recognized as revenue.

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 was being recognized as collaborative research and development revenue ratably over the term of our continuing involvement with Zogenix with respect to Relday. As a result of the termination of the Zogenix agreement in August 2017, we recognized revenue during the third quarter of 2017 for the remaining $750,000 of deferred revenue related to the upfront fee as we had no remaining performance obligations under the agreement; this recognition of revenue did not result in additional cash proceeds to us. At December 31, 2018, all of the $2.25 million upfront fee had been recognized as revenue.

As of March 4, 2019, we had potential milestones of up to $77.5 million that we may receive in the future under our collaborative arrangements, of which $14.5 million are development-based milestones and $63.0 million are sales-based milestones. Within the category of development-based milestones, $2.0 million are related to early stage clinical testing (defined as Phase 1 or 2 activities), $3.0 million are related to late stage clinical testing (defined as Phase 3 activities), $3.0 million are related to regulatory filings, and $6.5 million are related to regulatory approvals. No payments were received between December 31, 2018 and March 4, 2019.

Product revenues

A portion of our revenues is derived from product sales, which include our ALZET mini pump product line, our LACTEL biodegradable polymer product line and certain excipients that are included in Methydur, REMOXY ER and in a currently marketed animal health product. Net product revenues were $10.4 million, $13.1 million and $12.1 million in 2018, 2017 and 2016, respectively.

The decrease in product revenues in 2018 was primarily attributable to lower revenue from our LACTEL product line as a result of lower units sold, partially offset by slightly higher revenue from our ALZET mini pump product line as a result of higher units sold compared to 2017.

The increase in product revenues in 2017 was primarily attributable to higher revenue from our LACTEL product line as a result of higher units sold, partially offset by lower product revenue from the sale of certain excipients included in REMOXY ER and in a currently marketed animal health product as well as lower product revenue from our ALZET mini pump product line as a result of lower units sold compared to 2016.

Revenues in 2018, 2017 and 2016 included $1,000, $53,000 and $653,000 in product revenue related to the sale of excipients included in REMOXY ER and a currently marketed animal health product.

Revenue from sale of intellectual property rights

Revenue from the sale of intellectual property rights was zero in 2018, $12.5 million in 2017 and zero in 2016. We entered into a patent purchase agreement with Indivior and received a non-refundable payment of $12.5 million in September 2017. We recognized the $12.5 million as revenue from sale of intellectual property rights in 2017 as we did not have any substantive continuing obligations under the purchase agreement.

Cost of product revenues

Cost of product revenues was $4.3 million, $6.6 million and $5.3 million in 2018, 2017 and 2016, respectively. Cost of product revenues includes the cost of product revenue from our ALZET product line, our LACTEL product line and certain excipients that are included in several products in development, or awaiting regulatory approval or commercial launch by partners and a currently marketed animal health product.

The decrease in the cost of product revenue in 2018 were primarily the result of charges of approximately $2.0 million in 2017 associated with write-down of an excipient in light of the failure of PERSIST, the Phase 3 clinical trial of POSIMIR. Excluding the charges associated with the write-down of the excipient included in 2017, the decrease in the

cost of product revenue in 2018 was primarily the result of lower cost of goods sold related to our LACTEL product line arising from lower units sold, partially offset by higher cost of goods sold related to our ALZET product line arising from higher units sold compared to 2017.

The increase in the cost of product revenue in 2017 was primarily the result of charges of approximately $2.0 million associated with the write-down of an excipient in light of the failure to achieve the primary efficacy endpoint in the PERSIST clinical trial, compared with $926,000 associated with the write-down of the excipient included in REMOXY ER in light of the Complete Response Letter received by Pain Therapeutics for REMOXY ER in 2016. Excluding the charges associated with the write-down of certain excipients included in 2017 and 2016, respectively, the increase in the cost of product revenue in 2017 was primarily the result of higher cost of goods sold related to our LACTEL product line arising from higher units sold, partially offset by lower cost of goods sold related to our ALZET product line arising from lower units sold and from lower cost of goods sold related to the sale of certain excipients included in REMOXY ER and another product compared to 2016.

Stock-based compensation expense related to cost of product revenues was $94,000, $109,000 and $106,000 in 2018, 2017 and 2016, respectively.

As of December 31, 2018, 2017 and 2016, we had 21, 21 and 20 manufacturing employees, respectively.

Research and development. Research and development expenses are primarily comprised of salaries, benefits, stock-based compensation and other compensation cost associated with research and development personnel, overhead and facility costs, preclinical and non-clinical development costs, clinical trial and related clinical manufacturing costs, contract services, and other outside costs. Research and development expenses were $25.5 million, $31.6 million and $29.3 million in 2018, 2017 and 2016, respectively. Stock-based compensation expense recognized related to research and development personnel was $1.5 million in 2018 and $1.4 million in each of 2017 and 2016.

Research and development expenses decreased by $6.1 million in 2018 compared to 2017. The decrease in 2018 was primarily attributable to lower research and development costs associated with POSIMIR, REMOXY ER, Relday, ORADUR-ADHD and other research programs, partially offset by higher research and development costs associated with DUR-928, depot injectable programs and the Santen ophthalmic program compared to 2017, as more fully discussed below.

Research and development expenses increased by $2.3 million in 2017 compared to 2016. The increase in 2017 was primarily attributable to higher research and development costs associated with POSIMIR and depot injectable programs, partially offset by lower research and development costs associated with DUR-928, Relday, REMOXY ER, the Santen ophthalmic program, ORADUR-ADHD and other research programs compared to 2016, as more fully discussed below.

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

	Year Ended December 31,		
	2018	2017	2016
DUR-928	$15,106	$13,279	$13,739
POSIMIR (1)	6,757	15,075	11,680
Depot injectable programs	2,994	2,437	1,407
Santen ophthalmic program (1)	118	99	366
ORADUR-ADHD	100	104	177
REMOXY ER (1)	15	115	525
Relday (1)	—	39	463
Other	411	461	917
Total research and development expenses	$25,501	$31,609	$29,274

(1)

See Note 2 Strategic Agreements in the financial statements for more details about our agreements with Sandoz, Pain Therapeutics, Zogenix and Santen.

DUR-928

Our research and development expenses for DUR-928 increased to $15.1 million in 2018 from $13.3 million in 2017, primarily due to higher contract manufacturing expenses and higher clinical trial and non-clinical study expenses incurred.

Our research and development expenses for DUR-928 decreased to $13.3 million in 2017 from $13.7 million in 2016, primarily due to lower contract manufacturing expenses, partially offset by higher clinical trial expenses and higher employee-related costs incurred.

POSIMIR

Our research and development expenses for POSIMIR decreased to $6.8 million in 2018 from $15.1 million in 2017, primarily due to lower clinical trial expenses, lower contract manufacturing expenses and lower employee-related expenses.

Our research and development expenses for POSIMIR increased to $15.1 million in 2017 from $11.7 million in 2016, primarily due to higher clinical trial expenses and other outside expenses.

Depot injectable programs

Our research and development expenses for depot injectable programs increased to $3.0 million in 2018 from $2.4 million in 2017 primarily due to higher employee-related costs and higher research supplies expenses for these programs.

Our research and development expenses for depot injectable programs increased to $2.4 million in 2017 from $1.4 million in 2016 primarily due to higher employee-related costs for these programs.

Santen ophthalmic program

Our research and development expenses for the Santen ophthalmic program increased to $118,000 in 2018 from $99,000 in 2017, primarily due to increased development activities and higher employee-related costs.

Our research and development expenses for the Santen ophthalmic program decreased to $99,000 in 2017 from $366,000 in 2016, primarily due to decreased formulation development activities and lower employee-related costs.

ORADUR-ADHD

Our research and development expenses for ORADUR-ADHD decreased to $100,000 in 2018 from $104,000 in 2017, primarily due lower employee-related costs.

Our research and development expenses for ORADUR-ADHD decreased to $104,000 in 2017 from $177,000 in 2016, primarily due lower employee-related costs.

REMOXY ER

Our research and development expenses for REMOXY ER decreased to $15,000 in 2018 from $115,000 in 2017, primarily due to lower employee-related costs.

Our research and development expenses for REMOXY ER decreased to $115,000 in 2017 from $525,000 in 2016, primarily due to lower employee-related costs.

Relday

Our research and development expenses for Relday decreased to zero in 2018 from $39,000 in 2017 primarily due to decreased development activities and lower employee-related costs incurred for this drug candidate.

Our research and development expenses for Relday decreased to $39,000 in 2017 from $463,000 in 2016 primarily due to decreased development activities and lower employee-related costs.

Other DURECT research programs

Our research and development expenses for all other research activities decreased to $411,000 in 2018 from $461,000 in 2017, primarily due to lower employee-related costs incurred for these programs.

Our research and development expenses for all other research activities decreased to $461,000 in 2017 from $917,000 in 2016, primarily due to lower employee-related costs incurred for these programs.

As of December 31, 2018, 2017 and 2016, we had 47, 49 and 52 research and development employees, respectively.

We cannot reasonably estimate the timing and costs of our research and development programs due to the risks and uncertainties associated with developing pharmaceuticals 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 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 (including sales and marketing expenses for our ALZET and LACTEL product lines) and other administrative personnel, overhead and facility costs, and other general and administrative costs. Selling, general and administrative expenses were $12.4 million, $13.2 million and $11.8 million in 2018, 2017 and 2016, respectively. Stock-based compensation expense recognized related to selling, general and administrative personnel was $1.4 million in 2018, $1.1 million in each of 2017 and 2016, respectively.

Selling, general and administrative expenses decreased by approximately $746,000 in 2018 compared to 2017, primarily due to an advisory fee related to the execution of the Sandoz agreement which occurred in 2017. Selling, general and administrative expenses increased by approximately $1.4 million in 2017 compared to 2016, primarily due to an advisory fee related to the execution of the Sandoz agreement which occurred in 2017 and higher general legal expenses.

As of December 31, 2018, 2017 and 2016, we had 22, 24 and 24 selling, general and administrative personnel, respectively.

Other income (expense). Interest and other income was $870,000, $967,000 and $143,000 in 2018, 2017, and 2016, respectively. The decrease in interest and other income in 2018 compared to 2017 was primarily the result of a gain of $500,000 from selling certain intellectual property rights in 2017 which were not part of our ordinary course of business, partially offset by higher interest income generated from our investments as a result of higher yields and higher average investment balances in 2018 compared with 2017. The increase in interest and other income in 2017 compared to 2016 was primarily the result of a gain of $500,000 from selling certain intellectual property rights in 2017 which were not part of our ordinary course of business. In addition, we recorded a deferred tax benefit of $153,000 in 2017 as a result of the Tax Cuts and Jobs Act compared to zero in 2016. The increase in interest and other income in 2017 was also due to higher interest income generated from our investments as a result of higher yields and higher average investments balances in 2017 compared to 2016.

Interest expense was $2.6 million, $2.4 million and $2.3 million in 2018, 2017 and 2016, respectively. The increase in interest expense in 2018 compared to 2017 was primarily due to higher interest rates associated with the term loan in 2018 compared to 2017. The increase in interest expense in 2017 compared to 2016 was primarily due to higher interest rates recorded for the term loan refinanced in July 2016 compared to 2016.

Income taxes. On December 22, 2017, the 2017 Tax Cut and Jobs Act (the Act) was enacted into law and the new legislation contains several key tax provisions, with a primary impact to us being a reduction of the corporate income tax rate to 21% effective January 1, 2018. We are required to recognize the effect of the tax law changes in the period

of enactment, such as re-measuring our U.S. deferred tax assets and liabilities at a 21% rate as well as reassessing the net realizability of our deferred tax assets and liabilities. The provisional amount related to the re-measurement of our deferred tax balance was estimated to be a reduction of approximately $42.5 million at December 31, 2017. Due to the corresponding valuation allowance fully offsetting deferred taxes, there was no income statement impact.

As of December 31, 2018, we had net operating loss (NOL) carryforwards for federal income tax purposes of approximately $347.9 million, of which $327.2 million will expire in the years 2019 through 2037, and $20.7 million will not expire. As of December 31, 2018, we had federal research and development tax credits of approximately $13.5 million, which expire at various dates beginning in 2019 through 2038, if not utilized. As of December 31, 2018, we had NOL carryforwards for state income tax purposes of approximately $211.8 million, which expire in the years 2019 through 2038, and state research and development tax credits of approximately $14.6 million, which do not expire. Utilization of the net operating losses may be subject to a substantial annual limitation due to federal and state ownership change limitations. The annual limitation may result in the expiration of net operating losses and credits before utilization.

As of December 31, 2018 and 2017, we had net deferred tax assets of $112.7 million and $106.4 million, respectively. Deferred tax assets reflect the net tax effects of net operating loss and credit carryforwards and the temporary differences between the carrying amounts of assets and liabilities for financial reporting and the 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, 2018 and 2017. 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 is defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating losses and other pre-change tax attributes (such as research and development credit carryforwards) to offset its post-change taxable income or taxes may be limited. 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. 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, November 2013 and April 2016, we completed underwritten public offerings in which we sold an aggregate of approximately 14.0 million, 8.2 million and 13.8 million shares, respectively, of our common stock pursuant to effective registration statements. In 2016, 2017 and 2018, we issued approximately 5.2 million, 8.9 million and 9.6 million shares, respectively, of our common stock in the open market through Controlled Equity Offering sales agreements with Cantor Fitzgerald pursuant to effective registration statements. 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 2018 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 $34.5 million and $36.9 million at December 31, 2018 and 2017, respectively. This includes $150,000 of interest-bearing marketable securities classified as restricted investments on our balance sheet as of December 31, 2018 and 2017, which primarily serve as collateral for a letter of credit securing our leased facility in California. The letter of credit for our leased facility in California will expire in February 2024.

We used $19.8 million, $1.3 million and $27.3 million of cash in operating activities in the years ended December 31, 2018, 2017 and 2016, respectively. The cash used for operations was primarily to fund operations as well as working capital requirements. Our cash used in operating activities differs from our net loss in part 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 increase in cash used in operating activities in 2018 compared to 2017 was primarily due to decreased payments received from collaboration partners and customers as we received the $20.0 million upfront fee from Sandoz in 2017, partially offset by changes in accounts receivable, prepaid expenses and other assets, and accrued and other liabilities in 2018. The decrease in cash used in operations in 2017 compared with 2016 was primarily due to the receipt of the $20.0 million non-refundable upfront fee from Sandoz and the $12.5 million non-refundable upfront fee from Indivior in 2017, partially offset by cash used to fund operations as well as working capital requirements and reflected a net loss of $3.7 million as well as changes in accrued and other liabilities.

We received $4.5 million, $12.7 million and $6.0 million of cash from investing activities in the years ended December 31, 2018, 2017 and 2016, respectively. The decrease in cash received from investing activities was primarily due to a decrease in proceeds from maturities of available-for-sale securities in 2018 compared to 2017. The increase in cash provided by investing activities in 2017 compared to 2016 was primarily due to a decrease in purchase of available-for-sale securities offset by a decrease in net maturities of available-for-sale securities. We anticipate incurring capital expenditures of approximately $100,000 over the next 12 months. The amount and timing of these capital expenditures will depend on, among other things, our research and development activities and needs, and the need for equipment replacements.

We generated $17.5 million, $12.6 million and $23.1 million of cash from financing activities in the years ended December 31, 2018, 2017 and 2016, respectively. The increase in cash received from financing activities was primarily due to higher net proceeds received from issuances of common stock in 2018 compared to 2017. In 2018, we raised net proceeds (net of commission) of approximately $16.8 million from the sale of 9.6 million shares of common stock at a weighted average price of $1.80 per share in the open market through our Controlled Equity Offering sales agreement with Cantor Fitzgerald. The decrease in cash provided by financing activities in 2017 compared to 2016 was primarily due to lower net proceeds received from issuances of common stock.

In November 2015, we entered into the 2015 Sales Agreement with Cantor Fitzgerald, acting as agent. As of December 31, 2018, approximately 24.6 million registered shares of common stock were sold through the 2015 Sales Agreement for total net proceeds (net of commissions) of approximately $38.3 million. In August 2018, we filed a shelf registration statement on Form S-3 with the SEC, which upon being declared effective in October 2018 and allowed us to offer up to $175.0 million of securities from time to time in one or more public offerings, inclusive of up to $75.0 million of additional shares of common stock which we may sell, subject to certain limitations, under the 2015 Sales Agreement through Cantor Fitzgerald, acting as agent. As of each of December 31, 2018 and March 4, 2019, no sales had been made pursuant to the October 2018 registration statement. Any additional sales in the public market of our common stock, under the Controlled Equity Offering program with Cantor Fitzgerald or otherwise under the October 2018 shelf registration statement, could adversely affect prevailing market prices for our common stock.

In July 2016, we renegotiated the terms of our $20.0 million secured single-draw term loan with Oxford Finance with such renegotiated terms being formalized in a new Loan and Security Agreement (the 2016 Loan Agreement). The 2016 Loan Agreement provided for interest only payments for the first 18 months, followed by consecutive monthly payments of principal and interest in arrears starting on March 1, 2018 and continuing through the maturity date of the term loan of August 1, 2020. The 2016 Loan Agreement also provided for a floating interest rate (7.95% initially and 9.83% as of December 31, 2018) based on an index rate plus a spread, a $150,000 facility fee that was paid at closing and an additional payment equal to 9.25% of the principal amount of the term loan, which was due when the term loan becomes due or upon the prepayment of the facility. If we elect to prepay the loan, there was also a prepayment fee

between 1% and 3% of the principal amount of the term loan depending on the timing of prepayment. The facility fee and other debt offering/issuance costs have been recorded as debt discount on our balance sheet and together with the final $1.9 million payment and interest rate payments were being amortized to interest expense throughout the life of the term loan using the effective interest rate method. In connection with this renegotiation, we also paid Oxford Finance $886,000, which was previously accrued for as a

portion of the final payment under a previous term loan agreement executed in 2014 which would have been payable to Oxford Finance when that loan became due on August 1, 2020.

The term loan is secured by substantially all of our assets, except that the collateral does not include any intellectual property (including licensing, collaboration and similar agreements relating thereto), and certain other excluded assets. The 2016 Loan Agreement contains customary representations, warranties and covenants by us, which covenants limit our ability to convey, sell, lease, transfer, assign or otherwise dispose of certain assets; engage in any business other than the businesses currently engaged in by us or reasonably related thereto; liquidate or dissolve; make certain management changes; undergo certain change of control events; create, incur, assume, or be liable with respect to certain indebtedness; grant certain liens; pay dividends and make certain other restricted payments; make certain investments; and make payments on any subordinated debt.

The 2016 Loan Agreement also contains customary indemnification obligations and customary events of default, including, among other things, our failure to fulfill certain obligations under the 2016 Loan Agreement and the occurrence of a material adverse change which is defined as a material adverse change in our business, operations, or condition (financial or otherwise), a material impairment of the prospect of repayment of any portion of the loan, or a material impairment in the perfection or priority of lender's lien in the collateral or in the value of such collateral. In the event of default by us under the 2016 Loan Agreement, the lender would be entitled to exercise its remedies thereunder, including the right to accelerate the debt, upon which we may be required to repay all amounts then outstanding under the 2016 Loan Agreement. As a result, that portion of the term loan that was due more than 12 months after December 31, 2017 has been classified within non-current liabilities.

In February 2018, the Company and Oxford Finance entered into a First Amendment of the Loan Agreement, which modified the terms of the Loan Agreement to change the first principal payment date from March 1, 2018 to December 1, 2018 and to increase the additional payment due when the term loan becomes due or upon the prepayment of the facility from 9.25% of the principal amount of the term loan to 10% of such amount. The interest rate and the maturity date remained unchanged, and the Company paid Oxford Finance a loan modification fee of $100,000.

In November 2018, the Company and Oxford Finance entered into a Second Amendment of the Loan Agreement, which modified the terms of the Loan Agreement to change the first principal payment date from December 1, 2018 to June 1, 2020 and the final maturity date from August 1, 2020 to November 1, 2022. If the Company elects to prepay the loan, there is also a prepayment fee of between 0.75% and 2.5% of the principal amount of the term loan depending on the timing of prepayment. The interest rate and the final payment remain unchanged, and the Company paid Oxford Finance a Second Amendment fee of $900,000.

Cash used in our operating activities is heavily influenced by the timing and structure of new corporate collaborations. While one feature of our business strategy is seeking new corporate collaborations, assuming no new collaborations and no milestone payments, we anticipate that cash used in operating activities will increase in the near term as we received a non-refundable milestone payment of $5.0 million from Indivior in 2018.

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 from the date the financial statements are filed. 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 products 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 that additional capital will be available on favorable terms, if at all. If adequate funds are not available, we may be required to significantly reduce or refocus our operations or to obtain funds through

arrangements that may require us to relinquish rights to certain of our products, technologies or potential markets, either of which could have a material adverse effect on our business, financial condition and results of operations. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of such securities would result in ownership dilution to our existing stockholders (assuming convertible debt securities were converted into shares).

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.

In 2018, there were significant changes in our commercial commitments and contractual obligations due to the extension of our three building facility leases (see Note 6 of the financial statements). In aggregate, we are required to make future payments pursuant to our existing contractual obligations as follows (in thousands):

Contractual Obligations	2019	2020	2021	2022	2023	Total
Term loan (1)	1,612	6,824	8,885	8,912	—	26,233
Operating lease obligations	2,122	2,200	2,126	1,991	2,245	10,684
Total contractual cash obligations	$3,734	$9,024	$11,011	$10,903	$2,245	$36,917

(1) Includes principal, interest payments and final payments and assumes no acceleration of obligations.

Recent Accounting Pronouncements

In August 2018, the FASB issued Accounting Standards Update (“ASU”) No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement, which eliminates certain disclosure requirements for fair value measurements for all entities, requires public entities to disclose certain new information and modifies some disclosure requirements. This standard is effective for fiscal years beginning after December 15, 2019, including interim reporting periods within those years, with early adoption permitted. We do not expect the adoption of this standard to have a material effect on our financial statements.

In June 2018, the FASB issued Accounting Standards Update (“ASU”) No. 2018-07, Compensation – Stock Compensation (Topic 718), which expands the scope of ASC 718 to include all share-based payment arrangements related to the acquisition of goods and services from both nonemployees and employees. Under the new standard, most of the guidance on stock compensation payments to nonemployees would be aligned with the requirements for share-based payments granted to employees. This standard is effective for fiscal years beginning after December 15, 2018, including interim reporting periods within those years, with early adoption permitted. We do not expect the adoption of this standard to have a material effect on our financial statements.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842). This ASU will require the recognition of lease assets and liabilities for operating leases with terms of more than 12 months, in addition to the capital lease assets and liabilities currently recorded on our consolidated balance sheets. Presentation of leases within the consolidated statements of operations and cash flows will be substantially consistent with current accounting guidance. The ASU, which is effective for annual reporting periods beginning after December 15, 2018, and interim periods within those annual periods, will have a material impact on our consolidated balance sheets. We plan to adopt the ASU effective January 1, 2019 using the modified retrospective transition method and will not restate comparative periods. The modified retrospective transition method requires the cumulative effect, if any, of initially applying the guidance to be recognized as an adjustment to our accumulated deficit as of that adoption date. We plan to elect the package of

practical expedients permitted under the transition guidance within the ASU, which allows us to carry forward prior conclusions about lease identification, classification and initial direct costs for leases entered into prior to adoption of Topic 842. Additionally, we plan to not separate lease and non-lease components for all of our leases. For leases with a term of 12 months or less, we plan to elect the short-term lease exemption, which allows us to not recognize right-of-use assets or lease liabilities for qualifying leases existing at transition and new leases we may enter into in the future. While we continue to assess all impacts of adoption, we currently expect to recognize additional lease liabilities of approximately $7.7 million representing the present value of the remaining

minimum lease payments at January 1, 2019 and corresponding right-of-use assets of approximately $7.3 million. See Note 6, Commitments, for information about our lease commitments.

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 and to our term loan. 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 interest expense on the term loan may rise if the interest rates increase.

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, certificates of deposit, commercial paper, corporate debt, and U.S. government agencies. The diversity of our portfolio helps us to achieve our investment objectives. As of December 31, 2018, all of our investment portfolio was composed of investments with original maturities of one year or less and approximately 78.7% 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, 2018 by year of maturity (dollars in thousands):

	2019	
Cash equivalents:		
Fixed rate	$502	
Average fixed rate	2.27	%
Variable rate	$29,553	
Average variable rate	2.82	%
Short-term investments:		
Fixed rate	$2,671	
Average fixed rate	2.80	%
Long-term investments:		
Fixed rate	$—	
Average fixed rate	—	
Restricted investments:		
Fixed rate	$150	
Average fixed rate	2.09	%
Total investment securities	$32,876	
Average rate	2.77	%

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, 2017 by year of maturity (dollars in thousands):

	2018	
Cash equivalents:		
Fixed rate	$568	
Average fixed rate	1.16	%
Variable rate	$27,220	
Average variable rate	1.58	%
Short-term investments:		
Fixed rate	$7,384	
Average fixed rate	1.39	%
Long-term investments:		
Fixed rate	$—	
Average fixed rate	—	
Restricted investments:		
Fixed rate	$150	
Average fixed rate	1.00	%
Total investment securities	$35,322	
Average rate	1.51	%

As of December 31, 2018, the fair value of our term loan was estimated to be $20.5 million. The term loan repayment schedule provides for interest only payments until August 1, 2020, followed by consecutive monthly payments of principal and interest in arrears and continuing through the maturity date of the term loan of November 1, 2022. The term loan also provides for a floating interest rate (9.83% as of December 31, 2018) based on an index rate plus a spread and an additional payment equal to 9.25% of the principal amount of the term loan, which has been accrued over the life of the term loan and is due when the term loan becomes due or upon the prepayment of the facility. If the Company elects to prepay the loan, there is also a prepayment fee between 0.75% and 2.5% of the principal amount of the term loan depending on the timing of prepayment. The obligation under the term loan is subject to interest rate risk because the interest rates under the obligation may exceed current interest rates.

Item 8. Financial Statements and Supplementary Data.
DURECT CORPORATION

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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of DURECT Corporation

Opinion on the Financial Statements

We have audited the accompanying balance sheets of DURECT Corporation (the Company) as of December 31, 2018 and 2017, and the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes and the financial statement schedule listed in the Index at Item 15(a)(2) (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) and our report dated March 8, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 1998.

San Francisco, California

March 8, 2019

DURECT CORPORATION

BALANCE SHEETS

(in thousands, except per share amounts)

	December 31,	
	2018	2017
ASSETS		
Current assets:		
Cash and cash equivalents	$31,644	$29,375
Short-term investments	2,671	7,384
Accounts receivable (net of allowances of $102 at December 31, 2018 and $155 at December 31, 2017)	1,757	2,376
Inventories, net	3,421	3,163
Prepaid expenses and other current assets	2,247	3,060
Total current assets	41,740	45,358
Property and equipment, net	605	929
Goodwill	6,399	6,399
Long-term restricted investments	150	150
Other long-term assets	1,105	277
Total assets	$49,999	$53,113
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$1,589	$1,520
Accrued liabilities	4,668	5,511
Contract research liabilities	1,405	834
Deferred revenue, current portion	—	682
Term loan, current portion, net	—	7,281
Total current liabilities	7,662	15,828
Deferred revenue, non-current portion	812	1,093
Term loan, non-current portion, net	20,533	13,578
Other long-term liabilities	992	1,126
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: 350,000 shares authorized; 162,060 and 150,837 shares issued and outstanding at December 31, 2018 and 2017, respectively	16	15
Additional paid-in capital	488,608	465,246
Accumulated other comprehensive loss	—	(1)
Accumulated deficit	(468,624)	(443,772)
Stockholders' equity	20,000	21,488
Total liabilities and stockholders' equity	$49,999	$53,113

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

DURECT CORPORATION

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except per share amounts)

	Year ended December 31,		
	2018	2017	2016
Collaborative research and development and other revenue	$8,207	$23,577	$1,880
Product revenue, net	10,357	13,093	12,145
Revenue from sale of intellectual property rights	—	12,500	—
Total revenues	18,564	49,170	14,025
Operating expenses:			
Cost of product revenues	4,263	6,633	5,290
Research and development	25,501	31,609	29,274
Selling, general and administrative	12,419	13,165	11,825
Total operating expenses	42,183	51,407	46,389
Loss from operations	(23,619)	(2,237)	(32,364)
Other income (expense):			
Interest and other income	870	967	143
Interest expense	(2,573)	(2,425)	(2,288)
Net other expense	(1,703)	(1,458)	(2,145)
Net loss	(25,322)	(3,695)	(34,509)
Net change in unrealized gain on available-for-sale securities, net of tax	1	2	11
Total comprehensive loss	$(25,321)	$(3,693)	$(34,498)
Net loss per share			
Basic	$(0.16)	$(0.03)	$(0.26)
Diluted	$(0.16)	$(0.03)	$(0.26)
Weighted-average shares used in computing net loss per share			
Basic	159,834	145,273	133,163
Diluted	159,834	145,273	133,163

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

DURECT CORPORATION

STATEMENT OF STOCKHOLDERS' EQUITY

(in thousands)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (loss)	Deficit	Equity
Balance at December 31, 2015	121,839	$ 12	$ 420,453	$ (14)	$ (405,568)	$ 14,883
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	413	—	410	—	—	410
Issuance of common stock upon equity financings, net of issuance costs of $1,364	19,045	2	23,743	—	—	23,745
Issuance of fully vested options to settle accrued liabilities	—	—	1,143	—	—	1,143
Stock-based compensation expense from stock options and ESPP shares	—	—	2,655	—	—	2,655
Net loss	—	—	—	—	(34,509)	(34,509)
Change in unrealized gain on available-for-sale securities, net of tax	—	—	—	11	—	11
Balance at December 31, 2016	141,297	$ 14	$ 448,404	$ (3)	$ (440,077)	$ 8,338
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	667	—	649	—	—	649
Issuance of common stock upon equity financings, net of issuance costs of $374	8,873	1	11,988	—	—	11,989
Issuance of fully vested options to settle accrued liabilities	—	—	1,600	—	—	1,600
Stock-based compensation expense from stock options and ESPP shares	—	—	2,605	—	—	2,605
Net loss	—	—	—	—	(3,695)	(3,695)
Change in unrealized gain on available-for-sale securities, net of tax	—	—	—	2	—	2
Balance at December 31, 2017	150,837	$ 15	$ 465,246	$ (1)	$ (443,772)	$ 21,488
Issuance of common stock upon exercise of stock options and purchases of ESPP shares	1,594	—	1,725	—	—	1,725
Issuance of common stock upon equity financings, net of issuance costs of $566	9,629	1	16,779	—	—	16,780
Issuance of fully vested options to settle accrued liabilities	—	—	1,860	—	—	1,860
Stock-based compensation expense from stock options and ESPP shares	—	—	2,998	—	—	2,998
Net loss	—	—	—	—	(25,322)	(25,322)
Change in unrealized gain on available-for-sale securities, net of tax	—	—	—	1	—	1

Adjustment due to changes in accounting policies					470	470
Balance at December 31, 2018	162,060	$ 16	$488,608	$ —	$ (468,624)	$ 20,000

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

DURECT CORPORATION

STATEMENTS OF CASH FLOWS

(in thousands)

	Year ended December 31,		
	2018	2017	2016
Cash flows from operating activities			
Net loss	$(25,322)	$(3,695)	$(34,509)
Adjustments to reconcile net loss to net cash used in operating activities:			
Sale of intellectual property rights for non-operating purposes	—	(500)	—
Depreciation and amortization	254	437	416
Stock-based compensation	2,998	2,605	2,655
Inventory write-down	291	2,259	687
Amortization of debt issuance cost	149	62	104
Loss on debt extinguishment	—	—	9
Net accretion/amortization on investments	84	(41)	(216)
Changes in assets and liabilities:			
Accounts receivable	619	(1,222)	1,068
Inventories	(549)	(140)	(552)
Prepaid expenses and other assets	(15)	(1,115)	656
Accounts payable	69	(566)	800
Accrued liabilities	1,594	1,594	1,419
Contract research liability	571	51	208
Deferred revenue	(493)	(1,072)	(38)
Total adjustments	5,572	2,352	7,216
Net cash used in operating activities	(19,750)	(1,343)	(27,293)
Cash flows from investing activities			
Sale of intellectual property rights for non-operating purposes	—	500	—
Purchases of property and equipment	(93)	(69)	(147)
Purchases of available-for-sale securities	(9,588)	(8,373)	(24,400)
Proceeds from maturities of available-for-sale securities	14,218	20,632	30,584
Net cash provided by investing activities	4,537	12,690	6,037
Cash flows from financing activities			
Payments on equipment financing obligations	(9)	(14)	(19)
Net proceeds from issuances of common stock upon exercise of stock options, and purchases of ESPP shares	1,725	649	410
Net proceeds from issuances of common stock in connection with equity financings	16,780	11,989	23,745
Term loan amendment cost	(1,014)	—	(173)
Payment of final payment for term loan	—	—	(886)
Net cash provided by financing activities	17,482	12,624	23,077
Net increase in cash and cash equivalents	2,269	23,971	1,821
Cash, cash equivalents, and restricted cash, beginning of the period (1)	29,525	5,554	3,733

Cash, cash equivalents, and restricted cash, end of the period (1)	$31,794	$29,525	$5,554
Supplemental disclosure of cash flow information			
Cash paid for interest	$1,886	$1,703	$1,611
Supplementary disclosure of non-cash financing information			
Fully vested options issued to settle accrued liabilities	$1,860	$1,600	$1,143
(1) Includes restricted cash of $150,000 (presented as long term restricted investments) on the balance sheets at both December 31, 2018 and 2017, respectively, and $250,000 at December 31, 2016.			

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 biopharmaceutical company with research and development programs broadly falling into two categories: (i) new chemical entities derived from our Epigenetics Regulator Program, in which the Company attempts to discover and develop molecules which have not previously been approved and marketed as therapeutics, and (ii) Proprietary Pharmaceutical Programs, in which the Company applies its formulation expertise and technologies largely to active pharmaceutical ingredients whose safety and efficacy have previously been established but which the Company aims to improve in some manner through a new formulation. 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). The preparation of the accompanying Financial Statements conforms to accounting principles generally accepted in the U.S. which requires management to make judgments, estimates and assumptions that affect the reported amounts of assets, liabilities, equity, revenues and expenses, and related disclosures. On an ongoing basis, management evaluates its estimates including, but not limited to, those related to revenue recognition, the period of performance, identification of deliverables and evaluation of milestones with respect to our collaborations, the amounts of revenues, recoverability of inventory, certain accrued liabilities including accrued clinical trial liability, and stock-based compensation. The Company bases its estimates on historical experience and on various other market-specific and other relevant assumptions that the Company believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ materially from those estimates.

Reclassifications

Certain prior period amounts on the accompanying Balance Sheets have been reclassified to conform to current period presentation.

The Company has reclassified the accretion of final payment of the term loan from other long-term liabilities to net non-current portion of the term loan on the balance sheets as of December 31, 2018 and 2017.

Liquidity and Need to Raise Additional Capital

As of December 31, 2018, the Company has an accumulated deficit of $468.6 million as well as negative cash flows from operating activities.

The Company historically has had negative cash flows from operating activities and expects its negative cash flows to continue. The Company will continue to require substantial funds to continue research and development, including

clinical trials of its product candidates. Management's plans in order to meet its operating cash flow requirements include seeking additional collaborative agreements for certain of its programs and achieving milestone and other payments under its collaboration and licensing agreements as well as financing activities such as public offerings and private placements of its common stock, preferred stock offerings, issuances of debt and convertible debt instruments.

There are no assurances that such additional funding will be obtained and that the Company will succeed in its future operations. If the Company cannot successfully raise additional capital and implement its strategic development plan, its liquidity, financial condition and business prospects will be materially and adversely affected.

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 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, 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. 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 to a certain extent 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 immaterial in all periods presented.

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 Methydur and one excipient that is included in a currently marketed animal health product.

In 2018, revenue from the sale of products from the ALZET product line and the LACTEL product line accounted for 38% and 18% of total revenue, respectively. In 2017, revenue from the ALZET product line and the LACTEL product line accounted for 14% and 12% of total revenue, respectively. In 2016, revenue from the ALZET product line and the LACTEL product line accounted for 51% and 31% of total revenue, respectively.

In 2018, Indivior and a pharmaceutical company with which the Company has a feasibility agreement accounted for 27% and 14% of the Company's total revenues, respectively. In 2017, Sandoz and Indivior accounted for 41% and 25% of the Company's total revenues, respectively. In 2016, Tolmar accounted for 15% of the Company's total revenues.

Total revenue by geographic region for the years 2018, 2017 and 2016 are as follows (in thousands):

	Year ended December 31,		
	2018	2017	2016
Europe	$8,118	$34,261	$1,945
United States	7,990	11,323	9,082
Japan	978	1,395	1,413
Others	1,478	2,191	1,585
Total	$18,564	$49,170	$14,025

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

Inventories

Inventories are stated at the lower of cost or net realizable value, with cost determined on a first-in, first-out basis. Inventories, in part, include certain excipients that are sold to a customer for a currently marketed animal health product and included in several products in development, or awaiting regulatory approval or commercial launch. In October 2017, the Company announced that PERSIST, the Phase 3 clinical trial for POSIMIR, did not meet its primary efficacy endpoint. As a result, the Company wrote down certain lots of inventory which are no longer considered to be probable for use prior to expiration and prepaid inventory related to a minimum purchase agreement for an excipient. In addition, the Company recorded a liability related to a minimum purchase agreement for the same excipient. In 2017, the Company recorded charges to cost of goods sold of approximately $2.0 million, of which approximately $503,000 related to the write-down of the cost basis of inventory on hand, $500,000 related to the prepaid inventory for the minimum purchase commitment for this excipient, and $1.0 million related to the accrual of a liability for the remaining minimum purchase commitment for the same excipient. As of December 31, 2018, the remaining carrying value of the excipient in the Company’s inventory was $68,000. 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. If the Company is able to subsequently sell products made with raw materials that were previously written down, the Company will report an unusually high gross profit as there will be no associated cost of goods for these materials.

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

	December 31,	
	2018	2017
Raw materials	$223	$282
Work in-process	1,486	1,182
Finished goods	1,712	1,699
Total inventories	$3,421	$3,163

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.

Goodwill

Goodwill is periodically assessed and evaluated for impairment at the reporting unit level. The Company operates in one operating segment and also has only one reporting unit, which is the research, development and manufacturing of pharmaceutical products. The Company assesses the impairment of goodwill at least annually and

whenever events or changes in circumstances indicate that the carrying value may not be recoverable. Factors the Company considers important which could trigger an impairment review include the following:

- significant decline in our stock price for a prolonged 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 the Company's overall business; and
- significant negative industry or economic trends.

As of December 31, 2018, the carrying value of goodwill was approximately $6.4 million and no impairment of goodwill has been recorded for any of the periods presented. The Company evaluates goodwill for impairment at least annually. In 2018, 2017 and 2016, goodwill was evaluated and no indicators of impairment were identified. To date, the Company has not recorded any impairment charge related to goodwill.

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, 2018, 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

The Company enters into license and collaboration agreements under which the Company may receive upfront license fees, research funding and contingent milestone payments and royalties. Prior to January 1, 2018, the Company evaluated the accounting treatment under these agreements including whether multiple deliverables existed, how the deliverables should be separated and how the consideration should be allocated to one or more units of accounting. For the Company's collaborations with multiple deliverables, the Company had concluded that the deliverables were not separable and the arrangements should be accounted for as a combined unit of accounting. As a combined unit of accounting, 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 were 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 represented 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. If the Company determined that the expected timeline for a project and therefore the Company's continuing involvement was materially different than we previously assumed, the Company adjusted the period over which it recognized the deferred revenue.

Effective January 1, 2018, the Company adopted FASB ASC Topic 606, Revenue from Contracts with Customers, or ASC 606. In accordance with ASC 606, the Company changed certain characteristics of its revenue recognition accounting policy as described below. ASC 606 was applied using the modified retrospective method,

where the cumulative effect of the initial application was recognized as an adjustment to opening retained earnings at January 1, 2018. Therefore, comparative prior periods have not been adjusted and continue to be reported under FASB ASC Topic 605, Revenue Recognition, or ASC 605. The Company recorded a net increase to opening accumulated deficit of $470,000 with a corresponding entry to deferred revenue as of January 1, 2018 due to the cumulative impact of adopting Topic 606, with the impact relating to a reduction in the Company's deferred collaborative research and development revenues. There was no impact to reported total assets, revenues and operating expenses for the twelve months ended December 31, 2018 as a result of applying Topic 606.

Product Revenue, Net

The Company 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.

Revenues from product sales are recognized when the customer obtains control of the Company's product, which occurs at a point in time, typically upon shipment to the customer. The Company expenses incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that the Company would have recognized is one year or less.

Trade Discounts and Allowances: The Company provides certain customers with discounts that are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized.

Product Returns: Consistent with industry practice, the Company generally offers customers a limited right of return for products that have been purchased from the Company. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized. The Company currently estimates product return liabilities using its historical sales information. The Company expects product returns to be minimal.

Collaborative Research and Development Revenues

The Company enters into license agreements which are within the scope of Topic 606, under which it licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees; reimbursement of development costs incurred by the Company under approved work plans; development, regulatory and commercial milestone payments; payments for manufacturing supply services the Company provides through its contract manufacturers; and royalties on net sales of licensed products. Each of these payments results in collaborative research and development revenues, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company uses key assumptions to determine the standalone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success. The Company expects to recognize revenue for the variable consideration currently being constrained when it is probable that a significant revenue reversal will not occur.

Licenses of intellectual property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company

evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. Milestone Payments: At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaborative research and development revenues and net income (loss) in the period of adjustment.

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug product for either clinical development or commercial supply at the customer's discretion are generally considered as options. The Company assesses if these options provide a material right to the customer and if so, they are accounted for as separate performance obligations. If the Company is entitled to additional payments when the customer exercises these options, any additional payments are recorded in collaborative research and development revenue when the customer obtains control of the goods, which is upon delivery.

Royalties and Earn-outs: For arrangements that include sales-based royalties or earn-outs, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any significant royalty revenue resulting from the Company's collaborative arrangements or any earn-out revenue from the Company's patent purchase agreement with Indivior.

The cumulative effect of the changes made to the Company's January 1, 2018 balance sheet for the adoption of ASC 606 Revenue – Revenue from Contract with Customers was as follows (in thousands):

	Balance at December 31, 2017	Adjustments Due to ASC 606	Balance at January 1, 2018
Balance Sheet			
Liabilities			
Deferred revenue, non-current portion	$1,093	$ 470	$623
Equity			
Accumulated deficit	$(443,772)	$ 470	$(443,302)

During the twelve months ended December 31, 2018, the Company did not recognize any revenue as a result of changes in the contract asset and the contract liability balances associated with the Company's deferred research and development revenues for the Company's collaboration agreements as a result of adoption of ASC 606.

In accordance with the new revenue standard requirements, the disclosure of the impact of adoption on balance sheet, statement of operations and comprehensive loss, and statement of cash flows for the twelve months ended December 31, 2018 was as follows (in thousands):

	As of December 31, 2018		
	As reported	Balances without adoption of ASC 606	Effect of change Higher/(Lower)
Balance Sheet			
Liabilities			
Deferred revenue, non-current portion	$812	$1,282	$ (470)

	For the year ended December 31, 2018		
	As reported	Balances without adoption of ASC 606	Effect of change Higher/(Lower)
Statement of Operations and Comprehensive Loss			
Collaborative research and development and other revenue	$8,207	$8,207	$ -
Product revenue, net	10,357	10,357	-
Total revenues	$18,564	$18,564	$ -

	For the year ended December 31, 2018		
	As reported	Balances without adoption of ASC 606	Effect of change Higher/(Lower)
Statement of Cash Flows			
Cash flow from Operating Activities			
Deferred revenue, non-current portion	$(493)	$(23)	$ (470)

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, reimbursements of research and development expenses incurred by the Company’s partners are recorded as collaborative research and development revenue.

Comprehensive Loss

Components of other comprehensive loss are comprised entirely of unrealized gains and losses on the Company’s available-for-sale securities for all periods presented. Total comprehensive loss has been disclosed in the Company’s Statements of Comprehensive Loss.

Segment Reporting

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

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of common shares outstanding. Diluted net loss per share is computed using the weighted-average number of common shares outstanding and common stock equivalents (i.e., options to purchase common stock) outstanding during the period, if dilutive, using the treasury stock method for options.

The numerators and denominators in the calculation of basic and diluted net loss per share were as follows (in thousands except per share amounts):

	Year Ended December 31,		
	2018	2017	2016
Numerators:			
Net loss	$(25,322)	$(3,695)	$(34,509)
Denominators:			
Weighted average shares used to compute basic net loss per share	159,834	145,273	133,163
Effect of dilutive securities:			
Dilution from stock options	—	—	—
Dilution from ESPP	—	—	—
Dilutive common shares	—	—	—
Weighted average shares used to compute diluted net loss per share	159,834	145,273	133,163
Net loss per share:			
Basic	$(0.16)	$(0.03)	$(0.26)
Diluted	$(0.16)	$(0.03)	$(0.26)

The computation of diluted net loss per share for the years ended 2018, 2017 and 2016 excludes the impact of options to purchase 16.6 million, 20.1 million and 18.7 million shares of common stock outstanding, respectively, at December 31, 2018, 2017 and 2016, 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 and comprehensive loss.

Recent Accounting Pronouncements

In August 2018, the FASB issued Accounting Standards Update ("ASU") No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement, which eliminates certain disclosure requirements for fair value measurements for all entities, requires public entities to disclose certain new information and modifies some disclosure requirements. This standard is effective for fiscal years beginning after December 15, 2019, including interim reporting periods within those years, with early adoption permitted. The Company does not expect the adoption of this standard to have a material effect on its financial statements.

In June 2018, the FASB issued Accounting Standards Update ("ASU") No. 2018-07, Compensation – Stock Compensation (Topic 718), which expands the scope of ASC 718 to include all share-based payment arrangements related to the acquisition of goods and services from both nonemployees and employees. Under the new standard,

most of the guidance on stock compensation payments to nonemployees would be aligned with the requirements for share-based payments granted to employees. This standard is effective for fiscal years beginning after December 15, 2018, including interim reporting periods within those years, with early adoption permitted. The Company does not expect the adoption of this standard to have a material effect on its financial statements.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842). This ASU will require the recognition of lease assets and liabilities for operating leases with terms of more than 12 months, in addition to the capital lease assets and liabilities currently recorded on our consolidated balance sheets. Presentation of leases within the consolidated statements of operations and cash flows will be substantially consistent with current accounting guidance. The ASU, which is effective for annual reporting periods beginning after December 15, 2018, and interim periods within those annual periods, will have a material impact on our consolidated balance sheets. The Company plans to adopt the ASU effective January 1, 2019 using the modified retrospective transition method and will not restate comparative periods. The modified retrospective transition method requires the cumulative effect, if any, of initially applying the guidance to be recognized as an adjustment to the Company's accumulated deficit as of that adoption date. The Company plans to elect the package of practical expedients permitted under the transition guidance within the ASU, which allows it to carry forward prior conclusions about lease identification, classification and initial direct costs for leases entered into prior to adoption of Topic 842. Additionally, the Company plans to not separate lease and non-lease components for all of our leases. For leases with a term of 12 months or less, the Company plans to elect the short-term lease exemption, which allows it to not recognize right-of-use assets or lease liabilities for qualifying leases existing at transition and new leases we may enter into in the future. While the Company continues to assess all impacts of adoption, it currently expects to recognize additional lease liabilities of approximately $7.7 million representing the present value of the remaining minimum lease payments at January 1, 2019 and corresponding right-of-use assets of approximately $7.3 million. See Note 6, Commitments, for information about the Company's lease commitments.

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,		
	2018	2017	2016
Collaborator/Counterparty			
Indivior UK Limited (Indivior) (1)	$5,019	$—	$—
Santen Pharmaceutical Co. Ltd. (Santen) (2)	102	294	514
Sandoz AG (Sandoz) (3)	—	20,000	—
Zogenix, Inc. (Zogenix) (4)	—	835	555
Pain Therapeutics, Inc. (Pain Therapeutics)	—	109	670
Other (5)	3,086	2,339	141
Total collaborative research and development and other revenue	$8,207	$23,577	$1,880

(1) Amount consists of a $5.0 million milestone payment earned from Indivior upon NDA approval of PERSERIS in 2018 and earn-out revenue from PERSERIS net sales compared with zero in 2017 and 2016; we and Indivior signed a license agreement effective July 2017.

(2) Amounts related to recognition of upfront fees were zero in 2018, $199,000 in 2017, and $228,000 in 2016. The Company and Santen signed a license agreement effective December 2014. In January 2018, the Company was

notified by Santen that due to a shift in near term priorities, Santen has elected to reallocate research and development resources and put the Company's program on pause until further notice. While the main program is on pause, the parties are working together on a limited set of research and development activities funded by Santen.

(3) Amounts related to recognition of upfront fees were zero in 2018, $20.0 million in 2017 and zero in 2016; the Company and Sandoz signed a license agreement effective June 2017. As of December 31, 2017, all of the

$20.0 million upfront fee had been recognized as revenue as the Company's contractual performance obligations had been fulfilled. In January 2019, the license agreement was terminated.

(4) Amounts related to ratable recognition of upfront fees were zero in 2018, $833,000 in 2017, and $208,000 in 2016. The Company and Zogenix signed a license agreement effective July 2011. In August 2017, the Company and Zogenix terminated their Development and License Agreement dated July 11, 2011 relating to the development and commercialization of Relday.

(5) Includes revenue recognized associated with the Company's feasibility agreements for years ended December 31, 2018, 2017 and 2016.

As of March 4, 2019, the Company had potential milestones of up to $77.5 million that the Company may receive in the future under its collaborative arrangements, of which $14.5 million are development-based milestones and $63.0 million are sales-based milestones. Within the category of development-based milestones, $2.0 million are related to early stage clinical testing (defined as Phase 1 or 2 activities), $3.0 million are related to late stage clinical testing (defined as Phase 3 activities), $3.0 million are related to regulatory filings, and $6.5 million are related to regulatory approvals. No payments were received between December 31, 2018 and March 4, 2019.

Patent Purchase Agreement with Indivior

On September 26, 2017, the Company entered into a Patent Purchase Agreement (the "Agreement") with Indivior. Pursuant to the Agreement, the Company assigned to Indivior certain patents that may provide further intellectual property protection for PERSERIS™ (risperidone), Indivior's extended-release injectable suspension for the treatment of schizophrenia in adults. In consideration for such assignment, Indivior made an upfront non-refundable payment to the Company of $12.5 million. Indivior also agreed to make an additional $5.0 million payment to the Company contingent upon NDA approval of PERSERIS, as well as quarterly earn-out payments that are based on a single digit percentage of U.S. net sales for certain products covered by the assigned patent rights, including PERSERIS. The assigned patent rights include granted patents extending through at least 2026. The Company also receives a non-exclusive right under the assigned patents to develop and commercialize certain risperidone-containing products and products that do not contain risperidone or buprenorphine. The agreement contains customary representations, warranties and indemnities of the parties. The Company received the payment of $12.5 million from Indivior in September 2017 and recognized the $12.5 million as revenue from sale of intellectual property rights in 2017 as the Company did not have any continuing obligations under the purchase agreement. On July 27, 2018, Indivior announced that the FDA had approved the NDA for PERSERIS thereby triggering the $5.0 million payment to the Company; this payment was received by the Company in August 2018. The Company recognized the $5.0 million as milestone revenue during the twelve months ended December 31, 2018 as there is no further performance obligation associated with this milestone payment. The Company recognized earn-out revenue of approximately $19,000 from PERSERIS net sales in 2018.

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 ER and other oral sustained release, abuse deterrent opioid products incorporating four specified opioid drugs, using the ORADUR technology. This agreement currently covers only REMOXY ER.

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 $3.0 million in performance milestone payments based on the successful development and approval of REMOXY ER. Of these potential milestones, all $3.0 million are development-based milestones. There are no sales-based milestones under the agreement. As of December 31, 2018, the Company had received $1.5 million in cumulative milestone payments.

Total collaborative research and development revenue recognized for REMOXY-related work performed by the Company for Pain Therapeutics was zero in 2018, $109,000 in 2017, and $670,000 in 2016. The cumulative aggregate payments received by the Company from Pain Therapeutics as of December 31, 2018 were $40.4 million under this agreement.

In 2018, 2017 and 2016, the Company recognized zero, zero and $653,000 of product revenue related to key excipients for REMOXY ER and the associated cost of goods sold was zero, zero and $216,000, respectively.

Agreement with Santen Pharmaceutical Co., Ltd.

On December 11, 2014, the Company and Santen Pharmaceutical Co., Ltd. (Santen) entered into a definitive agreement (the Santen Agreement). Pursuant to the Santen Agreement, the Company granted Santen an exclusive worldwide license to the Company's proprietary SABER formulation platform and other intellectual property to develop and commercialize a sustained release product utilizing the Company's SABER technology to deliver an ophthalmology drug. Santen controls and funds the development and commercialization program, and the parties established a joint management committee to oversee, review and coordinate the development activities of the parties under the Santen Agreement.

In connection with the Santen agreement, Santen 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 $76.0 million upon the achievement of certain milestones, of which $13.0 million are development-based milestones and $63.0 million are commercialization-based milestones including milestones requiring the achievement of certain product sales targets (none of which has been achieved as of December 31, 2018). Santen will also pay for certain Company costs incurred in the development of the licensed product. If the product is commercialized, the Company would also receive a tiered royalty on annual net product sales ranging from single-digit to the low double digits, determined on a country-by-country basis. As of December 31, 2018, the cumulative aggregate payments received by the Company under this agreement were $3.3 million. In January 2018, the Company was notified by Santen that due to a shift in near term priorities, Santen elected to reallocate research and development resources and put the Company's program on pause until further notice.

The following table provides a summary of collaborative research and development revenue recognized under the Santen Agreement (in thousands).

	Year Ended December 31,		
	2018	2017	2016
Ratable recognition of upfront payment	$—	$199	$228
Research and development expenses reimbursable by Santen	102	95	286
Total collaborative research and development revenue	$102	$294	$514

Agreement with Sandoz AG.

In May 2017, the Company and Sandoz AG ("Sandoz") entered into a license agreement to develop and market POSIMIR (bupivacaine extended release solution) in the United States. Following expiration of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (HSR), the agreement became effective in June 2017. The Company retained commercialization rights in the rest of the world. Under terms of the agreement, Sandoz made an upfront payment of $20 million, and the Company remained eligible for up to an additional $30 million in milestone payments based on successful development and regulatory milestones, up to an additional $230 million in sales-based milestones, and a tiered double-digit royalty on product sales for a defined period. DURECT was responsible for the completion of the ongoing PERSIST Phase 3 clinical trial for POSIMIR as well as FDA interactions through potential approval. If approved, DURECT also has certain manufacturing obligations under this agreement. Sandoz will have exclusive commercialization rights in the United States upon regulatory approval with sole funding responsibility for commercialization activities. Sandoz will pay the Company a tiered double-digit royalty on product sales for a defined period, after which the license granted to Sandoz shall convert to a non-exclusive, fully paid, royalty-free, irrevocable and perpetual license. The term of the agreement shall be for the duration of Sandoz's obligation to pay royalties for product sales under the Agreement. The agreement provides each party with specified termination rights, including the right of Sandoz to terminate at will after a specified period and

each party to terminate the agreement upon material breach of the agreement by the other party. The failure of the PERSIST trial for POSIMIR to achieve its primary endpoint gives Sandoz a right to terminate the Company's agreement with them on thirty days' notice, in addition to the rights they have to terminate for convenience on six months' notice. In May 2018, the Company and Sandoz entered into an amendment (the "Amendment") to the license agreement. Pursuant to the Amendment, the Company is eligible for up to $30 million in milestone payments based on NDA approval, and remains eligible for up to an additional $230 million in sales-based milestones and a tiered double-digit royalty on product sales for a defined period. Pursuant to the Amendment, each party is also permitted to develop or commercialize competing products. The Amendment also includes modifications to the Company's development obligations and to both parties' termination provisions,

including a right for the Company to terminate for convenience prior to NDA approval, and a new termination fee payable to the Company in the event that Sandoz terminates the agreement for convenience.

The Company evaluated the agreement under the accounting guidance for multiple element arrangements and identified three deliverables: the license to develop and market POSIMIR, the research and development services and the manufacturing services. Given that the delivery of the manufacturing services by the Company is dependent upon approval of POSIMIR by the FDA, and that the fee to be received by the Company for these services, should they be delivered, is consistent with their estimated selling price, the Company considers the manufacturing services to be a contingent deliverable and has excluded them from the initial measurement and allocation of the arrangement consideration. The Company evaluated the license deliverable and concluded that it did not have stand alone value separate from the research and development services and accordingly combined these deliverables into a single unit of accounting. The Company allocated the arrangement consideration, which consists of the $20.0 million upfront payment, to this single unit of accounting. As of December 31, 2017, all of the $20.0 million upfront fee had been recognized as revenue as the Company's contractual performance obligations had been fulfilled.

Total collaborative research and development revenue recognized by the Company for Sandoz was zero for 2018 and 2016, respectively, compared with $20.0 million for 2017. The cumulative aggregate payments received by the Company from Sandoz as of December 31, 2018 were $20.0 million under this agreement.

On January 2, 2019, the Company received written notice from Sandoz AG that effective January 27, 2019, Sandoz AG is terminating the Development and Commercialization Agreement, dated May 5, 2017, as amended (the "Sandoz Agreement"). As a result of this termination, Sandoz AG will be returning its exclusive commercialization rights to develop and market POSIMIR® (bupivacaine extended release solution) in the United States. POSIMIR is the Company's investigational post-operative pain relief depot that utilizes the Company's patented SABER® technology and is designed to deliver bupivacaine to provide up to three days of pain relief after surgery.

The parties are in dispute with regard to Sandoz AG's obligation to pay a termination fee to the Company. The Company has initiated a formal dispute resolution process related to the termination fee.

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 was 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 potentially in combination with Zogenix's DosePro® needle-free, subcutaneous drug delivery system. DURECT was responsible for non-clinical, formulation and CMC development activities. The Company was to 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 were considered integral to utilizing the licensed intellectual property and, accordingly, the deliverable were accounted for as a single unit of accounting. The $2.25 million upfront fee had been recognized as collaborative research and development revenue ratably over the term of the Company's research and development involvement with Zogenix with respect to this product candidate.

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 retained the right to supply Zogenix's Phase 3 clinical trial and commercial product requirements on the terms set forth in the Zogenix Agreement. Zogenix was permitted to

terminate the Zogenix Agreement without cause at any time upon prior written notice, and either party was permitted to terminate the Zogenix Agreement upon certain circumstances including written notice of a material uncured breach.

In August 2017, the Company and Zogenix terminated the Zogenix Agreement. Under the mutual termination agreement, Zogenix's development and commercialization rights were returned to the Company, and Zogenix

transferred to the Company all regulatory filings and development information related to Relday. As a result of the termination of the Zogenix agreement, the Company recognized revenue during the third quarter of 2017 for the remaining $750,000 of deferred revenue related to the upfront fee 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 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, 2018 were $20.1 million under these agreements.

	Year Ended December 31,		
	2018	2017	2016
Ratable recognition of upfront payment	$—	$833	$208
Research and development expenses reimbursable by Zogenix	—	2	347
Total collaborative research and development revenue	$—	$835	$555

3. 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, 2018 (in thousands):

	Level 1	Level 2	Level 3	Total
Money market funds	$502	$—	$—	$502
Certificates of deposit	—	150	—	150
Commercial paper	—	32,224	—	32,224
Total	$502	$32,374	$—	$32,876

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, 2017 (in thousands):

	Level 1	Level 2	Level 3	Total
Money market funds	$568	$—	$ —	$568
Certificates of deposit	—	150	—	150
Commercial paper	—	33,307	—	33,307
Corporate debt	—	1,297	—	1,297
Total	$568	$34,754	$ —	$35,322

The Company's financial instruments are valued using quoted prices in active markets or based upon other observable inputs. 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 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, 2018 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, 2018 and 2017 (in thousands):

	December 31, 2018			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value
Money market funds	$502	$ —	$ —	$502
Certificates of deposit	150	—	—	150
Commercial paper	32,224	—	—	32,224
	$32,876	$ —	$ —	$32,876
Reported as:				
Cash and cash equivalents	$30,055	$ —	$ —	$30,055
Short-term investments	2,671	—	—	2,671
Long-term restricted investments	150	—	—	150
	$32,876	$ —	$ —	$32,876

	December 31, 2017			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value
Money market funds	$568	$ —	$ —	$568
Certificates of deposit	150	—	—	150
Commercial paper	33,307	—	—	33,307
Corporate debt	1,298	—	(1)	1,297
	$35,323	$ —	$ (1)	$35,322
Reported as:				
Cash and cash equivalents	$27,788	$ —	$ —	$27,788
Short-term investments	7,385	—	(1)	7,384
Long-term restricted investments	150	—	—	150
	$35,323	$ —	$ (1)	$35,322

The following is a summary of the cost and estimated fair value of available-for-sale securities at December 31, 2018, by contractual maturity (in thousands):

	December 31, 2018	
	Amortized Cost	Estimated Fair Value
Mature in one year or less	$32,374	$ 32,374
	$32,374	$ 32,374

There were no securities that have had an unrealized loss for more than 12 months as of December 31, 2018.

As of December 31, 2018, 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.

4. Property and Equipment

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

	December 31,	
	2018	2017
Equipment	$12,785	$12,688
Leasehold improvement	9,828	9,929
Construction-in-progress	33	119
	22,646	22,736
Less accumulated depreciation and amortization	(22,041)	(21,807)
Property and equipment, net	$605	$929

Depreciation expense was $254,000, $437,000 and $416,000 in 2018, 2017 and 2016, respectively. Amortization expense was zero in 2018, 2017 and 2016 for assets held under capital leases.

As of December 31, 2018, the Company has recorded $470,000 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.

5. Restricted Investments

As of December 31, 2018 and 2017, the Company had $150,000 recorded as restricted investments, which primarily served as collateral for letters of credit securing a leased facility in California.

6. Commitments

Operating Leases

In April 2018, the Company entered into a lease amendment on a 24,634 square foot facility in Vacaville, California.

In August 2018 and September 2018, the Company entered into lease amendments on a 30,149 square foot facility and a 20,100 square foot facility in Cupertino, California.

Location	Approximate Square Feet	Operation	Expiration
Cupertino, CA	30,149 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2024 (with an option to renew for an additional five years)

Cupertino, CA	20,100 sq. ft.	Office and Laboratory	Lease expires 2024 (with an option to renew for an additional five years)
Vacaville, CA	24,634 sq. ft.	Manufacturing	Lease expires 2023 (with an option to renew for an additional five years)
Birmingham, AL	21,540 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2021 (with two options to renew the lease term for an additional five years each after the current lease expires)

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 $1.9 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Future minimum payments under these noncancelable leases are as follows (in thousands):

	Operating Leases
Year ending December 31,	
2019	$ 2,122
2020	2,200
2021	2,126
2022	1,991
2023 and thereafter	2,245
	$ 10,684

Other Purchase Commitments

In 2005, the Company entered into a supply agreement with a vendor. The remaining minimum purchase commitment under this agreement was $500,000 in 2018, which had been recorded as an accrued liability on the Company's Balance Sheet at December 31, 2018, and which was charged to cost of goods sold in the Company's Statements of Operations and Comprehensive Loss in 2017.

7. Term Loan

In July 2016, the Company entered a $20.0 million secured single-draw term loan with Oxford Finance LLC (Oxford Finance). The Loan Agreement provides for interest only payments for the first 18 months, followed by consecutive monthly payments of principal and interest in arrears starting on March 1, 2018 and continuing through the maturity date of the term loan of August 1, 2020. The Loan Agreement also provides for a floating interest rate (7.95% initially and 9.83% as of December 31, 2018) based on an index rate plus a spread, a $150,000 facility fee that was paid at closing and an additional payment equal to 9.25% of the principal amount of the term loan, which is due when the term loan becomes due or upon the prepayment of the facility. If the Company elects to prepay the loan, there is also a prepayment fee between 1% and 3% of the principal amount of the term loan depending on the timing of prepayment. The facility fee and other debt offering/issuance costs have been recorded as debt discount on the Company's balance sheet and together with the final $1.9 million payment are being amortized to interest expense during the life of the term loan using the effective interest rate method.

The term loan is secured by substantially all of the assets of the Company, except that the collateral does not include any intellectual property (including licensing, collaboration and similar agreements relating thereto), and certain other excluded assets. The Loan Agreement contains customary representations, warranties and covenants by the Company, which covenants limit the Company's ability to convey, sell, lease, transfer, assign or otherwise dispose of certain assets of the Company; engage in any business other than the businesses currently engaged in by the Company or reasonably related thereto; liquidate or dissolve; make certain management changes; undergo certain change of control events; create, incur, assume, or be liable with respect to certain indebtedness; grant certain liens; pay dividends and make certain other restricted payments; make certain investments; and make payments on any subordinated debt.

The Loan Agreement also contains customary indemnification obligations and customary events of default, including, among other things, the Company's failure to fulfill certain obligations of the Company under the Loan Agreement and

the occurrence of a material adverse change which is defined as a material adverse change in the Company's business, operations, or condition (financial or otherwise), a material impairment of the prospect of repayment of any portion of the loan, or a material impairment in the perfection or priority of lender's lien in the collateral or in the value of such collateral. In the event of default by the Company under the Loan Agreement, the lender would be entitled to exercise its remedies thereunder, including the right to accelerate the debt, upon which the Company may be required to repay all amounts then outstanding under the Loan Agreement, which could harm the Company's financial condition. The conditionally exercisable call option related to the event of default is considered to be an embedded derivative which is required to be bifurcated and accounted for as a separate financial instrument. In the periods presented, the value of the embedded derivative is not material, but could become material in future periods if an event of default became more probable than is currently estimated.

In February 2018, the Company and Oxford Finance entered into a First Amendment of the Loan Agreement, which modified the terms of the Loan Agreement to change the first principal payment date from March 1, 2018 to December 1, 2018 and to increase the additional payment due when the term loan becomes due or upon the prepayment of the facility from 9.25% of the principal amount of the term loan to 10% of such amount. The interest rate and the maturity date remain unchanged, and the Company paid Oxford Finance a loan modification fee of $100,000.

On November 1, 2018, the Company and Oxford Finance entered into a Second Amendment of the Loan Agreement, which modified the terms of the Loan Agreement to change the first principal payment date from December 1, 2018 to June 1, 2020 and the final maturity date from August 1, 2020 to November 1, 2022. If the Company elects to prepay the loan, there is also a prepayment fee of between 0.75% and 2.5% of the principal amount of the term loan depending on the timing of prepayment. The interest rate and the final payment remained unchanged, however the Company paid Oxford Finance a Second Amendment fee of $900,000. This amount was recorded as additional debt discount and presented within net non-current portion of term loan on the Company's balance sheet as of December 31, 2018 and will be amortized as interest expense using the effective interest method over the revised term of the loan.

The fair value of the term loan approximates the carrying value. Future maturities and interest payments under the term loan as of December 31, 2018, are as follows (in thousands):

2019	$1,612
2020	6,824
2021	8,885
2022	8,912
Total minimum payments	26,233
Less amount representing interest	(4,750)
Gross balance of term loan	21,483
Less unamortized debt discount	(950)
Carrying value of term loan	20,533
Less term loan, current portion, net	—
Term loan, non-current portion, net	$20,533

8. Stockholders' Equity

Common Stock

In November 2015, the Company filed a shelf registration statement on Form S-3 with the SEC, which upon being declared effective in November 2015, terminated the December 2013 registration statement and allowed the Company to offer up to $125.0 million of securities from time to time in one or more public offerings of its common stock. In addition, the Company entered into a Controlled Equity Offering sales agreement with Cantor Fitzgerald, under which the Company may sell, subject to certain limitations, up to $40 million of common stock through Cantor Fitzgerald, acting as agent.

In 2016, the Company raised net proceeds of approximately $16.1 million (after deducting underwriting discounts and commissions and offering expense) through the sale of approximately 13.8 million shares of its common stock in an underwritten public offering at a price to the public of $1.25 per share and raised net proceeds (net of commissions) of approximately $7.6 million from the sale of approximately 5.2 million shares of its common stock in the open market through the Controlled Equity Offering program with Cantor Fitzgerald at a weighted average price of $1.50 per

share. In 2017, the Company raised net proceeds (net of commissions) of approximately $12.0 million from the sale of approximately 8.9 million shares of common stock in the open market through the Controlled Equity Offering program with Cantor Fitzgerald at a weighted average price of $1.39 per share. In 2018, the Company raised net proceeds (net of commissions) of approximately $16.8 million from the sale of approximately 9.6 million shares of common stock in the open market through the Controlled Equity Offering program with Cantor Fitzgerald at a weighted average price of $1.80 per share.

In August 2018, the Company filed a new shelf registration statement on Form S-3 with the SEC, which upon being declared effective in October 2018, terminated the November 2015 registration statement and allowed the Company to offer up to $175.0 million of securities from time to time in one or more public offerings, inclusive of up to $75.0 million of additional shares of common stock which the Company may sell, subject to certain limitations, under the 2015 Sales Agreement 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.

At the Company's annual stockholders meeting in June 2010, the stockholders approved 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.

At the Company's annual stockholders meeting in June 2011, June 2014 and June 2016, the stockholders approved amendments 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, 4,000,000 shares and 5,000,000 shares, respectively, each of which had previously been approved by the Board of Directors. A total of 33,449,989 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, 2018, 9,257,933 shares of common stock were available for future grant and options to purchase 30,217,615 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, which provided for the issuance of stock options to non-employee directors of the Company. As of December 31, 2018, options to purchase 100,000 shares of common stock were outstanding under this plan, all of which were vested. The 2000 Directors' Stock Option Plan expired in September 2000. Grants of stock options to our non-employee directors are made through the 2000 Stock Plan since September 2000.

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 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.

In March 2015, the Board of Directors approved certain amendments to the 2000 Employee Stock Purchase Plan. At the Company's annual stockholders meeting in June 2015, 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 350,000 shares; and (ii) extend the term of the ESPP to the date that is ten (10) years following the stockholders meeting.

The plan expires in June 2025. A total of 2,900,000 shares of common stock have been reserved for issuance under this plan. As of December 31, 2018, 361,185 shares of common stock were available for future grant and 2,538,815 shares of common stock have been issued under the 2000 Employee Stock Purchase Plan.

As of December 31, 2018, shares of common stock reserved for future issuance consisted of the following:

	December 31, 2018
Stock options outstanding	30,317,615
Stock options available for grant	9,257,933
Employee Stock Purchase Plan	361,185
	39,936,733

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, 2017	30,301,405	$ 1.87	5.18	$ 0.4
Options granted	4,267,360	$ 1.31		
Options exercised	(1,474,441)	$ 1.11		
Options forfeited	(672,015)	$ 1.33		
Options expired	(2,104,694)	$ 4.86		
Outstanding at December 31, 2018	30,317,615	$ 1.63	5.02	$ —
Exercisable at December 31, 2018	27,130,089	$ 1.67	4.65	$ —
Vested and expected to vest at December 31, 2018	30,317,615	$ 1.63	5.02	$ —

The aggregate intrinsic value in the table above represents the total intrinsic value (i.e., the difference between the Company's closing stock price on the last trading day of 2018 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 in-the-money options on December 31, 2018. This amount changes based on the fair market value of the Company's common stock. The total intrinsic value of options exercised was $1.6 million, $328,000 and $158,000 for the years ended December 31, 2018, 2017 and 2016, respectively.

In lieu of providing cash bonuses to certain employees, in January 2018, 2017 and 2016, the Company granted its employees stock options to purchase 1.9 million, 1.7 million and 1.4 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 $0.94 in 2018, $0.92 in 2017 and $0.81 in 2016 determined by the Black-Scholes option valuation method. There were no options granted with exercise prices lower than fair market value in 2018, 2017 and 2016.

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

As of December 31, 2018, 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 loss is shown as below (in thousands):

	Year ended December 31,		
	2018	2017	2016
Cost of product revenues	$94	$109	$106
Research and development	1,549	1,415	1,433
Selling, general and administrative	1,355	1,081	1,116

$2,998 $2,605 $2,655

Because the Company had a net operating loss carryforward as of December 31, 2018, 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 2018, 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. 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. The Company determines 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 January 2018, 2017 and 2016) and shares purchased under its stock plans and employee stock purchase plan for the years ended December 31, 2018, 2017 and 2016:

	Year ended December 31,		
	2018	2017	2016
Stock Options			
Risk-free rate	2.7-3.1%	2.0-2.5%	1.3-2.4%
Expected dividend yield	—	—	—
Expected term (in years)	7.0-10.0	6.8-10.0	6.5-10.0
Volatility	78-86%	75-86%	76-83%
Forfeiture rate (1)	0.0%	0.0%	4.2%

(1) Effective January 1, 2017, the Company elected to account for forfeitures as they occur.

	Year ended December 31,		
	2018	2017	2016
Employee Stock Purchase Plan			
Risk-free rate	1.3-2.5%	0.5-1.3%	0.3-0.6%
Expected dividend yield	—	—	—
Expected term (in years)	0.5	0.5	0.5
Volatility	60-146%	44-146%	65-81%

There were 119,097, 122,033 and 114,025 shares purchased under the Company's employee stock purchase plan during the years ended December 31, 2018, 2017 and 2016, respectively. Included in the statement of operations and comprehensive loss for the year ended December 31, 2018, 2017 and 2016 was $24,000, $34,000 and $45,000, 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, 2018, $2.5 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 2022. The weighted average term of the unrecognized stock-based compensation expense is 2.1 years.

The following table summarizes information about stock options outstanding at December 31, 2018:

	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 - $0.88	4,574,794	4.80	$0.84	4,482,934	$ 0.84
$0.93 - $1.19	3,164,866	6.80	$1.15	2,666,690	$ 1.15
$1.20 - $1.20	114,293	5.55	$1.20	114,293	$ 1.20
$1.21 - $1.21	3,151,604	4.11	$1.21	3,140,354	$ 1.21
$1.24 - $1.24	3,345,280	8.86	$1.24	2,101,191	$ 1.24
$1.26 - $1.26	140,000	4.16	$1.26	140,000	$ 1.26
$1.31 - $1.31	3,239,274	7.63	$1.31	2,275,895	$ 1.31
$1.33 - $2.04	2,171,924	6.79	$1.48	2,113,048	$ 1.47
$2.09 - $2.09	3,691,859	3.69	$2.09	3,684,734	$ 2.09
$2.10 - $3.61	6,723,721	1.75	$2.76	6,410,950	$ 2.79
$0.73 - $3.61	30,317,615	5.02	$1.63	27,130,089	$ 1.67

The Company received $1.6 million, $562,000 and $290,000 in cash from option exercises under all stock-based compensation plans for the years ended December 31, 2018, 2017 and 2016, 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 $244,000 and $244,000 on its balance sheet at both December 31, 2018 and 2017, that arose from tax amortization of an indefinite-lived intangible asset. The Company also recorded a deferred tax expense of zero, a benefit of $153,000, and a deferred tax expense of zero related to the deferred tax liability in the years ended December 31, 2018, 2017 and 2016, respectively. The Company recorded no tax expense in 2018, and tax expenses of $3,000 in 2017.

The reconciliation of income tax expenses (benefit) at the statutory federal income tax rate of 21% for 2018, and 34% for 2017 and 2016, to net income tax benefit included in the statements of operations and comprehensive loss for the

years ended December 31, 2018, 2017 and 2016 is as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
U.S. federal taxes benefit at statutory rate	$(5,318)	$(1,307)	$(11,733)
State taxes	—	3	—
Change in valuation allowance	5,143	(41,865)	10,847
Stock-based compensation	999	1,832	2,045
Change in deferred	175	12	(3)
Deferred Tax Remeasurement	0	42,528	—
Other	(999)	(1,353)	(1,156)
Total income tax provision (benefit)	$—	$(150)	$—

In 2018, 2017 and 2016, total income tax provision (benefit) expense was zero, $(150,000) and zero, respectively. The Company has presented these amounts within interest and other income, net in the Statements of Operations and Comprehensive Loss. 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,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$87,275	$82,369
Research and other credits	17,524	16,303
Deferred revenue	277	395
Stock-based compensation	4,755	5,053
Other	2,823	2,261
Total deferred tax assets	112,654	106,381
Valuation allowance for deferred tax assets	(112,654)	(106,381)
Deferred tax liabilities—Intangibles	(244)	(244)
Net deferred tax assets and liabilities	$(244)	$(244)

The Company recognizes deferred tax assets to the extent that the Company believes that these assets are more likely than not to be realized. In making such a determination, all available positive and negative evidence is considered, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If it is determined that the Company would be able to realize deferred tax assets in the future in excess of their net recorded amount, the Company would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of tax benefit might change as new information becomes available. Given the Company's history of operating losses, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $6.3 million and $11.4 million during 2018 and 2016, respectively, and decreased by $43.1 million during 2017.

As of December 31, 2018, the Company had net operating loss carryforwards for federal income tax purposes of approximately $347.9 million, of which $327.1 million will expire in the years 2019 through 2037, and 20.8 million which do not expire, and federal research and development tax credits of approximately $13.5 million, which expire at various dates beginning in 2019 through 2038, if not utilized.

As of December 31, 2018, the Company had net operating loss carryforwards for state income tax purposes of approximately $211.8 million, which expire in the years 2019 through 2038, if not utilized, and state research and development tax credits of approximately $14.6 million, which do not expire.

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

At December 31, 2018 and December 31, 2017, the Company had unrecognized tax benefits of approximately $8.4 million and $7.8 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.

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

	December 31,	
	2018	2017
Balance at beginning of the year	$7,849	$6,982
Decreased related to prior year tax positions	(7)	—
Increased related to current year tax positions	590	867
Balance at end of the year	$8,432	$7,849

Interest and penalty costs related to unrecognized tax benefits, if any, are classified as a component of interest and other income, net in the Statements of Operations and Comprehensive Loss. The Company did not recognize any interest and penalties expenses related to unrecognized tax benefits for the years ended December 31, 2018, 2017 and 2016.

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 2018 due to unutilized net operating losses and research credits.

On December 22, 2017, the 2017 Tax Cut and Jobs Act (the Act) was enacted into law and the new legislation contains several key tax provisions, with a primary impact to the Company being a reduction of the corporate income tax rate to 21% effective January 1, 2018. We are required to recognize the effect of the tax law changes in the period of enactment, such as re-measuring our U.S. deferred tax assets and liabilities at a 21% rate as well as reassessing the net realizability of our deferred tax assets and liabilities. The provisional amount related to the re-measurement of our deferred tax balance was estimated to be a reduction of approximately $42.5 million at December 31, 2017. Due to the corresponding valuation allowance fully offsetting deferred taxes, there was no income statement impact.

In December 2017, the SEC staff issued Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act (SAB 118) which allows companies to record provisional amounts during a measurement period not to extend beyond one year of the enactment date. Since the Act was passed late in the fourth quarter of 2017, and ongoing guidance and accounting interpretation was yet to be issued, our accounting of the deferred tax re-measurements was incomplete as of December 31, 2017. The 2017 federal corporate income tax return was filed in the fourth quarter of 2018. The final analysis and impact of the Act is reflected in the tax provision and related tax disclosures for the year ended December 31, 2018. There were no material differences to the originally estimated $42.5 million remeasurement of deferred tax assets.

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

	First Quarter		Second Quarter		Third Quarter		Fourth Quarter	
	2018	2017	2018	2017	2018	2017	2018	2017

Revenue (1)	$3,488	$4,567	$3,413	$4,319	$8,036	$20,746	$3,627	$19,538
Net income (loss)	$(8,297)	$(8,114)	$(7,011)	$(9,927)	$(2,715)	$6,111	$(7,299)	$8,235
Basic net income (loss) per share	$(0.05)	$(0.06)	$(0.04)	$(0.07)	$(0.02)	$0.04	$(0.05)	$0.06
Diluted net income (loss) per share	$(0.05)	$(0.06)	$(0.04)	$(0.07)	$(0.02)	$0.04	$(0.05)	$0.05

(1) The figures for the second, third and fourth quarters of 2017 include $0.8 million, $3.8 million and $15.4 million, respectively, related to the recognition of $20.0 million in revenue associated with a nonrefundable upfront payment that the Company received in June 2017 under its license agreement with SANDOZ. In addition, the third quarter of 2017 figure also includes the recognition of a non-refundable payment of $12.5 million received in September 2017 under the Company's patent purchase agreement with Indivior. The third quarter of 2018 figure includes the recognition of $5.0 million in revenue associated with a

nonrefundable milestone payment that the Company received in August 2018 under its agreement with Indivior.

11. Subsequent Events

On January 2, 2019, the Company received written notice from Sandoz AG that effective January 27, 2019, Sandoz AG is terminating the Development and Commercialization Agreement, dated May 5, 2017, as amended (the "Sandoz Agreement"). As a result of this termination, Sandoz AG will be returning its exclusive commercialization rights to develop and market POSIMIR® (bupivacaine extended release solution) in the United States. POSIMIR is the Company's investigational post-operative pain relief depot that utilizes the Company's patented SABER® technology and is designed to deliver bupivacaine to provide up to three days of pain relief after surgery.

The parties are in dispute with regard to Sandoz AG's obligation to pay a termination fee to the Company. The Company has initiated a formal dispute resolution process related to the termination fee.

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, 2018 based on the framework in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework). Based on that evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2018.

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 Stockholders and the Board of Directors of DURECT Corporation

Opinion on Internal Control over Financial Reporting

We have audited DURECT Corporation's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, DURECT Corporation (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the balance sheets as of December 31, 2018 and 2017, and the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes and the financial statement schedule listed in the Index at Item 15(a)(2) and our report dated March 8, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company'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 Financing Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. 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.

Definition and Limitations of Internal Control over Financial Reporting

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.

/s/ Ernst & Young LLP

San Francisco, California

March 8, 2019

Item 9B. Other Information.
None

PART III

Item 10. Directors, Executive Officers and Corporate Governance
The names of the executive officers of the Company and their ages, titles and biographies as of the date hereof are incorporated by reference from Part I, Item 1, above,

Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2019 Annual Meeting of Stockholders (the Proxy Statement), which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2018, under the headings "Election of Directors," "The Board, Board Committees and Meetings," "Code of Ethics," and "Section 16(a) Beneficial Ownership Reporting Compliance," and is incorporated herein by reference.

Item 11. Executive Compensation
Information required by this item will be contained in the Proxy Statement under the headings "Executive Compensation," "Director Compensation," and "Compensation Committee Report" and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters
Information required by this item will be contained in the Proxy Statement under the headings "Common Stock Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information," and is incorporated herein by reference.

Item 13. Certain Relationships, Related Transactions and Director Independence
Information required by this item will be contained in the Proxy Statement under the headings "Certain Relationships," "Other Transactions," and "The Board, Board Committees and Meetings," and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services
Information required by this item will be contained in the Proxy Statement under the heading "Fees Billed for Services Rendered by Principal Accountant," and is incorporated herein by reference.

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
See Schedule II—Valuation and Qualifying Accounts, immediately following Item 16 of this Form 10-K

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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) The list of exhibits filed as part of this report is set forth on the Exhibit Index immediately preceding the signature page of this report and is incorporated herein by reference in this Item 5(a)(3) or is filed in accordance with Item 601 of Regulation S–K.

Item 16. Form 10-K Summary.

The Company has elected not to include summary information.

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).
3.1	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).
3.2	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.
3.3	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of DURECT Corporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, as filed with the SEC on June 20, 2018).
3.4	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).
3.5	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).
3.6	Amended and Restated Bylaws of the Company (incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K (File No. 000-31615), filed on December 17, 2014).
4.1	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).
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+	2000 Stock Plan, as amended (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K (File No. 000-31615) filed on June 16, 2015).

10.3+	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).
10.4+	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).
10.5	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).
10.6	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).

Number	Description
10.7**	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).
10.8**	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).
10.9	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).
10.10**	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).
10.11**	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).
10.12	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).
10.13	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).
10.14	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).
10.15	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).
10.16	Fourth Amendment to Lease between De Anza Enterprises and the Company dated as of August 20, 2013 (incorporated by reference to Exhibit 10.71 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on November 5, 2013).
10.17	Addendum II to Lease between the Company and Northwest Asset Management Company dated as of August 27, 2013 (incorporated by reference to Exhibit 10.72 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on November 5, 2013).

10.18	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 (incorporated by reference to Exhibit 10.73 to our Annual Report on Form 10-K (File No. 000-31615) filed with the SEC on February 27, 2014).
10.19	Executive Change of Control Policy, as amended December 12, 2013 (incorporated by reference to Exhibit 10.74 to our Annual Report on Form 10-K (File No. 000-31615) filed with the SEC on February 27, 2014).
10.20	Loan and Security Agreement between the Company and Oxford Finance, LLC dated June 26, 2014 (incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on August 8, 2014).

Number	Description
10.21**	License Agreement between the Company and Santen Pharmaceutical Co., Ltd. dated December 11, 2014 (incorporated by reference to Exhibit 10.28 to our Annual Report on Form 10-K (File No. 000-31615) filed with the SEC on March 3, 2015).
10.22**	Exclusive License Agreement between the Company and Virginia Commonwealth University Intellectual Property Foundation dated December 5, 2012 (incorporated by reference to Exhibit 10.29 to our Annual Report on Form 10-K (File No. 000-31615) filed with the SEC on March 3, 2015).
10.23	First Amendment to Loan and Security Agreement and First Amendment to Disbursement Letter between the Company and Oxford Finance, LLC dated July 31, 2015 (incorporated by reference to Exhibit 10.2 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on November 3, 2015).
10.24	Loan and Security Agreement between the Company and Oxford Finance LLC dated July 28, 2016. (incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on November 1, 2016).
10.25**	Development and Commercialization Agreement between the Company and SANDOZ AG dated May 5, 2017. (incorporated by reference to Exhibit 10.2 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on August 9, 2017).
10.26**	Patent purchase agreement between the Company and Indivior UK Limited dated as of September 26, 2017. (incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on November 2, 2017).
10.27	First Amendment to Loan and Security Agreement between the Company and Oxford Finance LLC dated February 28, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed March 5, 2018).
10.28	Second Amendment to Loan and Security Agreement between the Company and Oxford Finance LLC dated November 1, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 5, 2018).
10.29	Addendum III to Lease between the Company and Northwest Asset Management Company dated as of April 10, 2018 (incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on August 2, 2018).
10.30**	First Amendment to the Development and Commercialization Agreement between the Company and SANDOZ AG effective as of May 4, 2018 (incorporated by reference to Exhibit 10.2 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on August 2, 2018).
10.31	Fifth Amendment to Lease between De Anza Enterprises and the Company dated as of August 15, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on August 17, 2018).

10.32	Third Amendment to Lease between Handley Management Corporation, as successor-by-merger to Renault & Handley Employee Investments Co. and the Company dated September 17, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on September 21, 2018).
10.33	Amendment No. 1 to Exclusive License Agreement between the Company and Virginia Commonwealth University Intellectual Property Foundation dated July 2, 2015 (incorporated by reference to Exhibit 10.4 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on November 8, 2018).

Number	Description
10.34	Amendment No. 2 to Exclusive License Agreement between the Company and Virginia Commonwealth University Intellectual Property Foundation dated March 6, 2018 (incorporated by reference to Exhibit 10.5 to our Quarterly Report on Form 10-Q (File No. 000-31615) filed with the SEC on November 8, 2018).
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.
+Indicates a management contract or compensatory plan or arrangement.

SCHEDULE II—VALUATION AND QUALIFYING ACCOUNTS

Year Ended December 31, 2018, 2017 and 2016

(in thousands)

	Balance at beginning of the year	Additions (Reductions) to allowances	Deductions	Balance at end of the year
Allowance for doubtful accounts				
Year ended December 31, 2018	$ 155	$ (52)	$ (1)	$ 102
Year ended December 31, 2017	$ 73	$ 165	$ (83)	$ 155
Year ended December 31, 2016	$ 161	$ (70)	$ (18)	$ 73

EXHIBIT INDEX

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*Filed herewith.

SIGNATURES

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

DURECT CORPORATION

By: /s/ james e. brown
James E. Brown

President and Chief Executive Officer

Date: March 8, 2019

POWER OF ATTORNEY

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

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

Signature	Title	Date
/s/ james e. brown James E. Brown	President, Chief Executive Officer and Director (Principal Executive Officer)	March 8, 2019
/s/ michael h. arenberg Michael H. Arenberg	Chief Financial Officer (Principal Accounting Officer)	March 8, 2019
/s/ simon x. benito Simon X. Benito	Director	March 8, 2019
/s/ terrence f. blaschke Terrence F. Blaschke	Director	March 8, 2019

/s/ david r. hoffmann David R. Hoffmann	Director, Chairman of the Board	March 8, 2019
/s/ armand p. neukermans Armand P. Neukermans	Director	March 8, 2019
/s/ jon s. saxe Jon S. Saxe	Director	March 8, 2019