UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

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

For the fiscal year ended December 31, 2019

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: 001-35068

ACELRX PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**41-2193603**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**

351 Galveston Drive
Redwood City, CA 94063
(650) 216-3500
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on Which Registered**
Common Stock, $0.001 par value	ACRX	The Nasdaq Stock Market LLC

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(d) 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 that 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 whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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 a shell company (as defined in Exchange Act Rule 12b-2) Yes ☐ No ☑

The aggregate market value of the voting stock held by non-affiliates of the registrant on June 28, 2019 (the last business day of the registrant's most recently completed second fiscal quarter), based upon the last sale price reported on the Nasdaq Global Market on that date, was approximately $197,006,167. The calculation excludes 1,046,120 shares of the registrant's common stock held by current executive officers and directors that the registrant has concluded are affiliates of the registrant. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of March 5, 2020, the number of outstanding shares of the registrant's common stock was 80,411,856.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's notice of annual meeting of stockholders and proxy statement to be filed pursuant to Regulation 14A within 120 days after Registrant's fiscal year end of December 31, 2019, are incorporated by reference into Part III of this report.

ACELRX PHARMACEUTICALS, INC.

2019 ANNUAL REPORT ON FORM 10-K

TABLE OF CONTENTS

Unless the context indicates otherwise, the terms "AcelRx," "AcelRx Pharmaceuticals," "we," "us" and "our" refer to AcelRx Pharmaceuticals, Inc. "DSUVIA", "ACELRX" and "Zalviso" are registered trademarks, all owned by AcelRx Pharmaceuticals, Inc. This report also contains trademarks and trade names that are the property of their respective owners.

Forward-Looking Statements

This Annual Report on Form 10-K, or Form 10-K, contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by that section. The forward-looking statements in this Form 10-K are contained principally under "Item 1. Business," "Item 1A. Risk Factors" and "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations." In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Form 10-K, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Many important factors affect our ability to achieve our objectives, including:

- failure to satisfy the required conditions and otherwise complete our planned acquisition of Tetraphase Pharmaceuticals, Inc., or Tetraphase, pursuant to the Agreement and Plan of Merger, or merger agreement, on a timely basis or at all;
- the expected benefits and potential value created by the proposed merger and co-promotion agreement with Tetraphase for our stockholders, including the ownership percentage of our stockholders in the combined organization immediately following the consummation of the proposed merger;
- potential legal proceedings relating to the proposed merger with Tetraphase and the outcome of any such legal proceeding;
- the inherent risks, costs and uncertainties associated with integrating the businesses in the proposed merger with Tetraphase successfully and risks of not achieving all or any of the anticipated benefits of the proposed merger with Tetraphase, or the risk that the anticipated benefits of the proposed acquisition may not be fully realized or take longer to realize than expected;
- our estimates regarding the sufficiency of our cash resources, expenses, including those related to the consummation of the proposed acquisition, capital requirements and needs for additional financing, and our ability to obtain additional financing if the merger is not completed.
- our success in commercializing DSUVIA® (sufentanil sublingual tablet, 30 mcg) in the United States, including the marketing, sales, and distribution of the product;
- our ability to maintain regulatory approval of DSUVIA in the United States, including effective management of and compliance with the DSUVIA Risk Evaluation and Mitigation Strategies, or REMS, program;
- acceptance of DSUVIA by physicians, patients and the healthcare community, including the acceptance of pricing and placement of DSUVIA on payers' formularies;
- the integration and performance of any businesses we acquire;
- our ability to develop sales and marketing capabilities in a timely fashion, whether alone through recruiting qualified employees, by engaging a contract sales organization, or with potential future collaborators;
- successfully establishing and maintaining commercial manufacturing with third parties;
- our ability to manage effectively, and the impact of any costs associated with, potential governmental investigations, inquiries, regulatory actions or lawsuits that may be brought against us;
- continued demonstration of an acceptable safety profile of DSUVIA;
- effectively competing with other medications for the treatment of moderate-to-severe acute pain in medically supervised settings, including IV-opioids and any subsequently approved products;
- our ability to maintain regulatory approval of DZUVEO™ in the European Union or EU, and enter into a collaboration agreement with a strategic partner for the commercialization of DZUVEO in Europe;
- our ability to manufacture and supply DZUVEO in Europe to any future strategic partner;
- our ability to successfully execute the pathway towards a resubmission of the Zalviso® (sufentanil sublingual tablet system) New Drug Application, or NDA, and subsequently obtain and maintain regulatory approval of Zalviso in the United States and comply with any related restrictions, limitations, and/or warnings in the label of Zalviso, if approved;
- the outcome of any potential FDA Advisory Committee meeting held for Zalviso;
- our ability to manufacture and supply Zalviso to Grünenthal GmbH, or Grünenthal, in accordance with their forecast and the Manufacture and Supply Agreement with Grünenthal;
- the status of the Collaboration and License Agreement with Grünenthal or any other future potential collaborations, including potential milestones and royalty payments under the Grünenthal agreement and obligations under the Purchase and Sale Agreement with PDL BioPharma, Inc., or PDL;

- our ability to attract additional collaborators with development, regulatory and commercialization expertise;
- our ability to successfully retain our key commercial, scientific, engineering, medical or management personnel and hire new personnel as needed;
- the size and growth potential of the markets for DSUVIA, and Zalviso, if approved in the United States, and our ability to serve those markets;
- our ability to successfully commercialize Zalviso, if approved in the United States;
- the rate and degree of market acceptance of Zalviso, if approved in the United States;
- our ability to obtain adequate government or third-party payer reimbursement;
- regulatory developments in the United States and foreign countries;

- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- our liquidity and capital resources; and
- our ability to obtain and maintain intellectual property protection for DSUVIA/DZUVEO and Zalviso.

In addition, you should refer to "Item 1A. Risk Factors" in this Form 10-K for a discussion of these and other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Form 10-K will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Also, forward-looking statements represent our estimates and assumptions only as of the date of this Form 10-K. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I

Item 1. Business

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings.

Our Portfolio

The following table summarizes our portfolio.

United States

Product	Description	Target Use	Status
DSUVIA®	Sufentanil sublingual tablet, 30 mcg	Moderate-to-severe acute pain in a medically supervised setting, administered by a healthcare professional	Received FDA approval in November 2018, commercial launch began Q1 2019.

Europe

Product	Description	Target Use	Status
DZUVEO	Sufentanil sublingual tablet, 30 mcg	Moderate-to-severe acute pain in a medically supervised setting, administered by a healthcare professional	Received European Commission, or EC, approval in June 2018.
Zalviso®	Sufentanil sublingual tablet system, 15 mcg	Moderate-to-severe acute pain in the hospital setting, administered by the patient as needed	Positive results from Phase 3 trial, IAP312, announced in August 2017. Currently evaluating the timing of the resubmission of the NDA, which is dependent on the finalization of the FDA's new opioid approval guidelines and process. Approved in the European Union and marketed commercially by Grünenthal.

We have created a proprietary sublingual (under the tongue) formulation of sufentanil intended for the treatment of moderate-to-severe acute pain. We believe our non-invasive, proprietary sublingual sufentanil tablet potentially overcomes many of the limitations of current treatment options available for moderate-to-severe acute pain. The sufentanil pharmacokinetic profile when delivered sublingually avoids the high peak plasma levels and short duration of action observed with IV administration. The sublingual formulation retains the therapeutic value of sufentanil, and novel delivery devices provide a non-invasive route of administration. Sufentanil is highly lipophilic which provides for rapid absorption in the mucosal tissue, or fatty cells, found under the tongue, and for rapid transit across the blood-brain barrier to reach the mu-opioid receptors in the brain. The sublingual route of delivery used by DSUVIA and Zalviso provides a predictable onset of analgesia. The sublingual delivery system also eliminates the risk of intravenous, or IV, complications, such as catheter-related infections. In addition, because patients do not require direct connection to an IV infusion pump, or IV line, DSUVIA and Zalviso may allow for ease of patient mobility.

We have chosen sufentanil as the therapeutic ingredient for DSUVIA and Zalviso. Opioids have been utilized for pain relief for centuries and are the standard-of-care for the treatment of moderate-to-severe acute pain. Sufentanil, a high-therapeutic index opioid, which has no active metabolites, is available as an injectable in several markets around the world and is used by anesthesiologists for induction of sedation or as an epidural; however, the injectable formulation is not suitable for the treatment of acute pain. Sufentanil has many pharmacological advantages over other opioids. Published studies demonstrate that sufentanil produces significantly less respiratory depressive effects relative to its analgesic effects compared to other opioids, including morphine and fentanyl. These third-party clinical results correlate well with preclinical trials demonstrating sufentanil's high therapeutic index, or the ratio of the toxic dose to the therapeutic dose of a drug, used as a measure of the relative safety of the drug for a particular treatment. Accordingly, we believe that sufentanil can provide an effective and well-tolerated treatment for acute pain. The following table illustrates the difference between the therapeutic index of different opioids.

Opioid	**Therapeutic Index**
Meperidine	5
Methadone	12
Morphine	71
Hydromorphone	250
Fentanyl	277
Sufentanil	26,716

In addition, the pharmaceutical attributes of sufentanil, including lipid solubility and ionization, result in rapid cell membrane penetration and onset of action, which we believe make sufentanil an optimal opioid for the treatment of acute pain.

Although the analgesic efficacy and safety of sufentanil have been well established, the product's use has been historically limited due to its short duration of action when delivered intravenously. Sublingual delivery of sufentanil avoids the high peak plasma levels and short duration of action of intravenous, or IV, administration.

DSUVIA® (sufentanil sublingual tablet, 30 mcg)

DSUVIA, known as DZUVEO in Europe, approved by the United States Food and Drug Administration, or FDA, in November 2018 (and by the European Medicines Agency, or EMA, in June 2018), is indicated for use in adults in certified medically supervised healthcare settings, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. DSUVIA was designed to provide rapid analgesia via a non-invasive route and to eliminate dosing errors associated with intravenous, or IV, administration. DSUVIA is a single-strength solid dosage form administered sublingually via a single-dose applicator, or SDA, by healthcare professionals. Sufentanil is an opioid analgesic currently marketed for IV and epidural anesthesia and analgesia. The sufentanil pharmacokinetic profile when delivered sublingually avoids the high peak plasma levels and short duration of action observed with IV administration.

Examples of potential patient populations and settings in which DSUVIA could be used include: emergency room patients; patients who are recovering from short-stay or ambulatory surgery and do not require more long-term analgesia; post-operative patients who are transitioning from the operating room to the recovery floor; certain types of office-based or hospital-based procedures; patients being treated and transported by paramedics; and for battlefield casualties. In the emergency room and in ambulatory care environments, patients often do not have immediate IV access available, or maintaining IV access may provide an impediment to rapid discharge. Moreover, IV dosing results in high peak plasma levels, thereby limiting the opioid dose and requiring frequent redosing intervals to titrate to satisfactory analgesia. Oral pills and liquids generally have slow and erratic onset of analgesia. Based on internal market research conducted to date, we believe that additional treatment options are needed that can safely and effectively treat acute trauma pain, in both civilian and military settings, and that can provide an alternative to currently marketed oral pills and liquids, as well as IV-administered opioids, for moderate-to-severe acute pain.

DSUVIA was approved with a Risk Evaluation and Mitigation Strategy, or REMS, which restricts distribution to certified medically supervised healthcare settings in order to prevent respiratory depression resulting from accidental exposure. DSUVIA is only distributed to facilities certified in the DSUVIA REMS program following attestation by an authorized representative to comply with appropriate dispensing and use restrictions of DSUVIA. To become certified, a healthcare setting is required to train their healthcare professionals on the proper use of DSUVIA and have the ability to manage respiratory depression. DSUVIA is not available in retail pharmacies or for outpatient use. As part of the REMS program, we monitor distribution and audit wholesalers' data, evaluate proper usage within the healthcare settings and monitor for any diversion and abuse. We will de-certify healthcare settings that are non-compliant with the REMS program.

Zalviso® (sufentanil sublingual tablet system, 15 mcg)

While still under development in the United States, as discussed further below, Zalviso is approved and marketed in the European Union, or EU. Zalviso is intended for the management of moderate-to-severe acute pain in hospitalized adult patients. Zalviso consists of a pre-filled cartridge of 40 sufentanil sublingual tablets, 15 mcg, delivered by the Zalviso System, a needle-free, handheld, patient-administered, pain management system. Zalviso is a pre-programmed non-invasive system that allows hospital patients with moderate-to-severe acute pain to self-dose with sufentanil sublingual tablets, 15 mcg, to manage their pain. Zalviso is designed to help address certain problems associated with post-operative IV patient-controlled analgesia, or PCA. Zalviso allows patients to self-administer sufentanil sublingual tablets via a pre-programmed, secure system designed in part to eliminate the risk of healthcare provider programming errors.

The Zalviso System consists of the following components: a disposable dispenser tip, a disposable dispenser cap, an adhesive thumb tag, a cartridge of 40 sufentanil sublingual 15 mcg tablets (approximately a two-day supply) in a disposable radio frequency identification and bar-coded cartridge, a reusable, rechargeable handheld controller, a tether, and an authorized access card.

The potential benefits of Zalviso are the result of combining the following three elements:

- sufentanil, a high therapeutic index opioid;
- sufentanil sublingual tablets, our proprietary, non-invasive sublingual dosage form; and
- our novel, pre-programmed, handheld PCA device that enables simple patient-controlled delivery of sufentanil sublingual tablets in the hospital setting and eliminates the risk of programming errors.

Drugs are classified or scheduled by the Drug Enforcement Agency, or DEA, according to their potential for abuse and addiction. Sufentanil is classified as a Schedule II controlled substance. Scheduled drugs, when they are under patient control in a hospital setting, must be secured and have adequate dose access control and tracking mechanisms. Our novel handheld PCA device has the following safety features:

- an authorized access card, which is a wireless system access key for the healthcare professional;
- a wireless, electronic, adhesive thumb tag that acts as a single-patient identification key;
- pre-programmed 20-minute lock-out to avoid overdosing;
- tablet singulation, or dispensing, motion that eliminates runaway motor delivery risk;
- a security tether that is designed to prevent theft and misuse; and
- fully automated inventory record of sufentanil sublingual tablet usage.

On December 16, 2013, AcelRx and Grünenthal entered into a Collaboration and License Agreement, or the License Agreement, or, as amended, the Amended License Agreement, which grants Grünenthal the European rights to commercialize Zalviso in the 28 European Union, or EU, member states, at the time of the agreement, plus Switzerland, Liechtenstein, Iceland, Norway and Australia, or the Territory, for human use in pain treatment in medically supervised settings. Also on December 16, 2013, AcelRx and Grünenthal, entered into a related Manufacture and Supply Agreement, or the MSA, or as amended, the Amended MSA, under which AcelRx will exclusively manufacture and supply Zalviso to Grünenthal for commercial sales in the Territory. The Amended MSA, together with the Amended License Agreement, are referred to as the Amended Agreements. For additional information on the Amended Agreements, see Note 5 "Revenue from Contracts with Customers" in the accompanying notes to the Consolidated Financial Statements.

Zalviso was approved for commercial sale in the European Community, or EC, in September 2015 and Grünenthal began its commercial launch of Zalviso in the European Union in April 2016. On September 18, 2015, we sold a majority of the expected royalty stream and commercial milestones from the sales of Zalviso in Europe by Grünenthal to PDL, which we refer to in this Annual Report as the Royalty Monetization. For additional information on the Royalty Monetization, see Note 8 “Liability Related to Sale of Future Royalties” in the accompanying notes to the Consolidated Financial Statements.

We submitted an NDA for Zalviso in September 2013, or the Zalviso NDA, and on July 25, 2014, the Division of Anesthesia, Analgesia, and Addiction Products of the FDA issued a Complete Response Letter, or CRL, for the Zalviso NDA. The CRL contained requests for additional information on the Zalviso System to ensure proper use of the device. The requests include submission of data demonstrating a reduction in the incidence of device errors, changes to address inadvertent dosing, among other items, and submission of additional data to support the shelf life of the product. In March 2015, we received correspondence from the FDA stating that, in addition to the work we had performed to address the items in the CRL, a clinical study would be required to test the modifications to the Zalviso device and mitigations put in place to reduce the risk of inadvertent dosing/misplaced tablets.

Our IAP312 study was designed to evaluate the effectiveness of changes made to the functionality and usability of the Zalviso device and to take into account comments from the FDA on the study protocol. In the IAP312 study, 320 hospitalized, post-operative patients used Zalviso to self-administer 15 mcg sublingual sufentanil tablets as often as once every 20 minutes for 24-to-72 hours to manage their moderate-to-severe acute pain. Throughout the study, for which top-line results were announced in August 2017, 2.2% of patients experienced a Zalviso device error, which was statistically less than the 5% limit specified in the study objectives. None of these device errors resulted in an over-dosing event. This 2.2% rate was lower ($p < 0.001$) than the 7.9% rate of device errors during patient use previously reported for the earlier version of the Zalviso device in the Phase 3 IAP311 study. In addition, results of this study supported earlier clinical findings, with favorable tolerability and a significant majority of “good” or “excellent” ratings provided by both patients and healthcare providers when assessing the method of pain control. These results will supplement those of our earlier Phase 3 studies (IAP309, IAP310 and IAP311), all of which met safety and efficacy endpoints, in the Zalviso NDA resubmission. The timing of the resubmission of the Zalviso NDA is dependent upon the finalization of the FDA’s new opioid approval guidelines and process.

Clinical Trials

Active comparator trial (IAP309)

In November 2012, we reported top-line data showing that Zalviso had met its primary endpoint of non-inferiority in the Phase 3 open-label active comparator trial designed to compare the efficacy and safety of Zalviso (15 mcg/dose) to IV PCA with morphine (1mg/dose) for the treatment of moderate-to-severe acute post-operative pain. Utilizing a randomized, open-label, parallel group design, this trial enrolled 359 adult patients at 26 U.S. sites for the treatment of pain immediately following open-abdominal or major orthopedic surgery (hip and knee replacement). Patients were randomized 1:1 to treatment with Zalviso or IV PCA morphine and were treated for a minimum of 48 hours and up to 72 hours.

Double-blind, placebo-controlled, abdominal surgery trial (IAP310)

In March 2013, we reported top-line data results demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major open abdominal surgery. Adverse events reported in the trial were generally mild or moderate in nature and similar in both placebo and treatment groups. Utilizing a randomized, double-blind, placebo-controlled design, this Phase 3 trial enrolled 178 adult patients at 13 U.S. sites. Patients were treated for post-operative pain for a minimum of 48 hours, and up to 72 hours. Patients were randomized 2:1, with 119 patients randomized to sufentanil sublingual tablet treatment and 59 to placebo treatment. Both treatments were delivered by the patient, as needed, using Zalviso with a 20-minute lock-out period. Patients in both groups could receive up to 2 mg morphine intravenously per hour as a rescue medication, the primary purpose of this rescue medication being to provide placebo-treated patients access to pain medication to enable them to stay in the trial as long as possible. Pre-rescue pain scores were imputed to minimize the impact of this rescue opioid on efficacy evaluations.

The primary endpoint evaluated pain intensity over the 48-hour study period compared to baseline, or Summed Pain Intensity Difference, or SPID-48, in patients following major open abdominal surgery. Patients receiving sufentanil sublingual tablets demonstrated a significantly greater SPID-48 compared to placebo-treated patients during the study period (105.6 and 55.6, respectively; p=0.001).

Double-blind, placebo-controlled, orthopedic surgery trial (IAP311)

In May 2013, we reported top-line data results demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major orthopedic surgery. Adverse events reported in the study were generally mild or moderate in nature and were similar in both placebo and treatment groups for the majority of adverse events. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 study enrolled 426 adult patients at 34 U.S. sites for treatment of moderate-to-severe acute pain immediately following major orthopedic surgery. Seven patients did not receive study drug, resulting in 419 patients being included in the ITT population. Patients were treated for a minimum of 48 hours, and up to 72 hours. Patients were randomized 3:1, with 321 patients randomized to sufentanil sublingual tablet treatment and 105 to placebo treatment. Both treatments were delivered by the patient, as needed, using the Zalviso System with a 20-minute lock-out period. Patients in both groups could receive up to 2 mg morphine intravenously per hour as a rescue medication, the primary purpose of this rescue medication being to enable placebo-treated patients to stay in the study. Pain scores recorded just prior to the delivery of rescue medication were gathered and imputed forward to minimize the impact of this rescue opioid on efficacy evaluations.

The primary endpoint evaluated SPID-48 in patients following major orthopedic surgery. Patients receiving Zalviso demonstrated a significantly greater SPID-48 compared to placebo-treated patients during the study period (+76.2 and -11.4, respectively; $p < 0.001$). Two hundred fifteen (68.3%) sufentanil sublingual tablet-treated patients completed the 48-hour study period, compared to 43 (41.3%) placebo-treated patients. Primary reasons for drop-out in the sufentanil sublingual tablet- and placebo-treated groups were adverse events (7.0% and 6.7%, respectively) and lack of efficacy (14.3% and 48.1%, respectively).

Four patients (three in the sufentanil sublingual tablet group and one in the placebo group) experienced a serious adverse event, or SAE, considered possibly or probably related to the study drug by the investigator. The SAEs observed in the patients in the sufentanil sublingual tablet group included severe oxygen saturation decrease, sinus tachycardia, and confusional state.

Combined related adverse events for the two placebo-controlled pivotal studies (IAP310 and IAP311) compared to placebo are shown below. Only pruritus (itching) was statistically different for Zalviso compared to placebo ($p = 0.002$).

Adverse Events Occurring in $\geq$ 2% in Either Group

Possibly or Probably Related Adverse Events At least 2% in either group	Zalviso n=429 Two Placebo-Controlled Phase 3 Studies	Placebo n=162
Nausea	29.4%	22.2%
Vomiting	8.9%	4.9%
Oxygen Saturation Decreased	6.1%	2.5%
Pruritus	4.7%	0%
Dizziness	4.4%	1.2%
Constipation	3.7%	0.6%
Headache	3.3%	3.7%
Insomnia	3.3%	1.9%
Hypotension	3.0%	1.2%
Confusional state	2.1%	0.6%

3 patients (0.7%) in the Zalviso group had treatment-emergent respiratory events that required naloxone reversal.

Multi-center, single-arm, open-label study (IAP312)

IAP312 was a Phase 3 study designed to evaluate the overall performance of the Zalviso System, in response to the CRL received from the FDA for Zalviso. Throughout the study in 320 enrolled patients, 2.2% of patients experienced a Zalviso device error, which was statistically less than the 5% limit specified in the study objectives. Importantly, none of these device errors resulted in an over-dosing event. This 2.2% rate was lower ($p < 0.001$) than the 7.9% rate of device errors during patient use previously reported for the earlier version of the Zalviso device in the Phase 3 IAP311 study.

In addition, as requested by FDA, the IAP312 study prospectively evaluated the number of inadvertently misplaced tablets which occurred during patient dosing. A small number of inadvertently misplaced tablets (less than 0.1% of total dispensed tablets) was observed in the original Phase 3 studies. However, the presence of inadvertently misplaced tablets had not been routinely assessed as part of the previous protocols. Throughout the IAP312 study, patients self-administered a total of 7,293 sufentanil tablets. Per the updated Zalviso training instructions electronically displayed on the hand-held device, 6 patients called the nurse when they failed to properly self-administer a single tablet to allow for proper retrieval and disposal of the tablet. Also, during inspection by the nurse, which occurred every two hours per protocol, a total of 7 misplaced tablets (<0.1% of total dispensed tablets) were discovered with 6 additional patients. No patient had a repeat incidence of an inadvertently misplaced tablet following re-training on the device. This combination of patient training and nurse inspection, along with the tracking features of the Zalviso device, could potentially address the FDA's concerns regarding drug accountability.

Finally, in this study, 86%, 89% and 100% of patients at the 24, 48 and 72-hour time points, respectively, recorded "good" or "excellent" ratings on the patient global assessment, or PGA, of the method of pain control, which measures a patient's satisfaction with their quality of analgesia. Healthcare professional global assessment, or HPGA, of the method of pain control was similarly strong, with 91%, 95% and 100% of nurses rating Zalviso as "good" or "excellent" over each respective 24-hour period. Zalviso was shown to be well tolerated by study participants, with nausea, hypotension and vomiting representing the most commonly reported adverse events. A total of 5 patients experienced serious adverse events, but all were considered unrelated to study drug by investigators.

The Market Opportunity for DSUVIA and Zalviso

Unmet Medical Need

Settings in which patients might require the short-term management of moderate-to-severe acute pain include emergency room patients; patients who are recovering from short-stay or ambulatory surgery and do not require more long-term patient-controlled analgesia; post-operative patients who are transitioning from the operating room to the recovery floor; certain types of office-based procedures; patients being treated and transported by paramedics; and for battlefield casualties.

While IV opioids are currently employed to control moderate-to-severe acute pain in many of these settings, the use of IV opioids suffers from the following:

- potential high peaks and troughs of plasma concentrations
- infection risk associated with the invasive nature of IV delivery;
- consumption of hospital resources including an IV pump, a bed where the patient can be monitored, and nurse time; and
- possible impairment of a patient’s cognitive abilities, which can make it difficult to provide accurate medical history to physicians during evaluation.

We believe healthcare providers and hospital administrators caring for patients in moderate-to-severe acute pain in the aforementioned medically supervised settings could significantly benefit from the following items:

- a pharmacokinetic profile that avoids the high peak plasma levels and short duration of action observed with IV administration
- non-invasively delivered analgesic that utilizes fewer hospital resources, thereby incurring less cost;
- effective and rapid-acting pain relief with sufficient duration of effect allowing efficient treatment while assuring patient satisfaction;
- pain relief that does not sacrifice cognitive function; and/or
- infection risks due to invasive routes of delivery, such as IV.

In our phase 1 through phase 3 clinical studies, sublingual sufentanil has demonstrated the following attributes:

- a pharmacokinetic profile that blunts peak plasma levels compared to IV administration
- ease of administration;
- pain reduction (as much as 3-points on a validated 10-point scale) beginning as early as 15-to-30 minutes after administration;
- maintenance of cognitive function;
- adverse event types similar to IV opioids, such as nausea, headache, vomiting and dizziness; and
- lower percentage of patients with decreased oxygen saturation events compared to IV-PCA morphine.

We believe that sublingual sufentanil provides a safety, efficacy and tolerability profile enabling our products to potentially replace IV opioid use in patients with moderate-to-severe acute pain in the proposed medically supervised settings. This may be especially true for DSUVIA in the post-operative settings where, because of the unique pharmacokinetic profile, the healthcare practitioner may be able to more efficiently manage patient-flow in the recovery room after surgery, and in emergency medical settings. The number of emergency departments is decreasing in the United States, resulting in an increased focus on resource management to treat a growing number of patients in an efficient manner.

United States Market

Based on commissioned research conducted in 2016, we estimate that there are over 90 million patients who are treated in various medically supervised settings for their moderate-to-severe acute pain which is significant enough to warrant the use of an opioid. We believe these patients may be eligible for treatment with DSUVIA, and in some cases Zalviso, if approved in the United States. The target patient population for DSUVIA are those patients in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for less than 24 hours. The target patient population for Zalviso are patients in a hospital setting for greater than 24 hours. Our current estimate of patients in moderate-to-severe acute pain in medically supervised settings, by setting, is as follows:

Emergency services (includes pre-hospital and Emergency Department treatment)	52 million
Outpatient surgery	11 million
Hospital/surgery center/office-based procedures	20 million
Inpatient surgery/inpatient conditions	10 million

The market for Zalviso, given the target patients in a hospital setting for greater than 24 hours, is the approximately 10 million inpatient surgeries and inpatient conditions above. There can be no assurance that our estimates regarding the number of patients treated in the various settings will be accurate.

European Market

Based on commissioned research conducted in 2016, there are an estimated 142 million patients in the EU5 (France, Germany, Italy, Spain, and the United Kingdom) represented across DZUVEO target care settings annually. Each year, there are an estimated 110 million emergency attendances and 32 million surgical procedures performed each year. It is anticipated that there are 51 million patients in emergency medicine with moderate-to-severe acute pain and 16 million with moderate-to-severe acute pain following surgery each year.

Our Strategy

Our strategy remains focused upon the commercial launch of DSUVIA into the medically supervised healthcare settings market, such as hospitals, surgical centers and emergency departments. The process of selling into these settings and obtaining approval for a product to be used within these types of institutions is complex and takes time. Our initial focus was to build a foundation of different institutions approving DSUVIA for use in their facility, and our certifying these institutions to purchase DSUVIA under our REMS program.

The number or pharmaceutical companies developing or commercializing one single product for selling into the medically supervised settings continues to grow. We believe having a single product to market and sell into this setting is inherently inefficient and building a portfolio of products is important to mitigate such inefficiency. Accordingly, we will focus on business development activities to increase the number of products in our portfolio.

DSUVIA

Our specific strategy with respect to DSUVIA is to:

- continue the launch of DSUVIA in the United States focused on the emergency room, hospitals and surgical centers to promote DSUVIA;
- identify potential commercial partners to support the launch for use in specialties outside our initial core focus area, for example, oral surgeries;
- complete our transition to automated packaging equipment with our contract manufacturing organization to leverage improved technology to lower production cost;
- support the finalization of the Milestone C meeting with the DoD, and finalize broader use within the DoD and other military organizations as requested and appropriate; and
- seek commercial partnerships for DSUVIA/DZUVEO in countries outside of the United States.

Zalviso

Our specific strategy with respect to Zalviso is to:

- continue to collaborate with Grünenthal to support commercial sales of Zalviso in their licensed territories;
- complete our transition of the Zalviso contract manufacturing to one device supplier; and
- resubmit the Zalviso NDA to seek regulatory approval in the United States and, if successful, promote Zalviso as a follow-on product to DSUVIA or potentially seek a commercial partnership.

The timing of the resubmission of the Zalviso NDA is dependent upon the finalization of the FDA's new opioid approval guidelines and process.

Sales and Marketing

We have established and will continue developing our distribution capability and commercial organization in the United States to market and sell DSUVIA in the United States. In geographies where we decide not to commercialize ourselves, we will seek to out-license commercialization rights. In specialty areas that are not core to the hospital, ambulatory surgery centers, or ASCs, or emergency room settings, (e.g. oral surgeries), we will seek commercialization partners that will support accessing these markets.

We are building commercial capability in the United States progressively to support the launch of DSUVIA in the United States market. We foresee two stages of commercial execution to support successful introduction of DSUVIA in the United States:

To date, we have:

- created and deployed a focused scientific support team to gather a detailed understanding of individual emergency room and hospital needs in order to present DSUVIA effectively;
- increased awareness of the clinical profile of sublingual administration of sufentanil through publication of our clinical data;
- engaged appropriate Advisory Boards that include representative emergency room physicians, anesthesiologists, surgeons, nurses, pharmacy and therapeutics, or P&T, committee members and other related experts to provide us with input on appropriate commercial positioning for DSUVIA for each of these key audiences;
- built a sales and marketing organization that can define appropriate segmentation and positioning strategies and tactics for DSUVIA;
- established DSUVIA on hospital and ambulatory surgery center formularies through deployment of an experienced team to explain the clinical and health economic attributes of DSUVIA; and
- gathered relevant clinical and health economic data identifying the limitations of IV opioids and other relevant treatments for moderate-to-severe acute pain in use today.

Next, we may adjust our commercialization plan through:

- as needed, continuing to build and progressively deploy a high-quality, customer-focused and experienced sales organization in the United States dedicated to bringing innovative, highly valued healthcare solutions to patients, payers and healthcare providers;
- partnering with another commercial organization to promote DSUVIA, which will allow us to adjust the number of people in our sales organization and rely on an existing salesforce of a commercial partner;
- potentially expanding the label to include pediatric populations by conducting post-approval clinical trials for DSUVIA; and
- continuing to establish DSUVIA as a suitable choice for moderate-to-severe acute pain in certified medically supervised settings.

If we are unable to establish successful sales and marketing capabilities or enter into agreements with third parties to market and sell our products, we may be unable to generate any product revenue. For a more comprehensive discussion of the risks related to our commercialization, please see "Risk Factors—Risks Related to Commercialization of DSUVIA and Zalviso" appearing elsewhere in this Form 10-K.

Acquisition of Tetraphase Pharmaceuticals

On March 15, 2020, we entered into the Agreement and Plan of Merger, or merger agreement, with Tetraphase Pharmaceuticals, Inc., or Tetraphase, and Consolidation Merger Sub, Inc., a Delaware corporation and indirect wholly owned subsidiary of the Company, or Merger Sub, pursuant to which we will acquire Tetraphase. Pursuant to the merger agreement, each share of Tetraphase common stock issued and outstanding immediately prior to the effective time of the merger will automatically be converted into the right to receive 0.6303 shares of the Company's common stock, subject to certain adjustments pursuant to the terms of the merger agreement, and a contingent value right for additional consideration to be paid to the then former securityholders of Tetraphase upon the achievement of certain sales milestones. The closing of the merger is expected in the second quarter of 2020 subject to customary closing conditions. For additional information regarding the merger, see Note 17 "Subsequent Events" in the accompanying notes to the Consolidated Financial Statements.

Co-Promotion Agreement

On March 15, 2020, we entered into the Co-Promotion Agreement with Tetraphase to co-promote DSUVIA and Tetraphases's XERAVA™ (eravacycline), which is FDA approved for the treatment of complicated intra-abdominal infections. Under the terms of this agreement, each company is responsible for maintaining compliance under the agreed marketing and promotion plan and achieving a minimum number of sales calls for each product. On March 16, 2020, in connection with entering into the Co-Promotion Agreement, we initiated a reduction in headcount, designed to eliminate the overlap with the Tetraphase commercial team to more efficiently commercialize DSUVIA in connection with the Tetraphase commercial team. We have eliminated 30 positions, mainly within the commercial organization. For additional information regarding the Co-Promotion Agreement, see Note 17 "Subsequent Events" in the accompanying notes to the Consolidated Financial Statements.

Collaborative Arrangements

Grünenthal Collaboration

On December 16, 2013, and as amended July 17, 2015 and September 20, 2016, we and Grünenthal entered into the Amended Agreements. Under the terms of the Amended Agreements with Grünenthal, we received an upfront cash payment of $30.0 million in December 2013, a milestone payment of $5.0 million related to the MAA submission, which occurred in July 2014, and a $15.0 million milestone payment due to the EC approval of the MAA for Zalviso in September 2015. Under the Amended Agreements, we are eligible to receive approximately $194.5 million in additional milestone payments, based upon successful regulatory and product development efforts ($28.5 million) and net sales target achievements ($166.0 million). Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, depending on the sales level achieved, on net sales of Zalviso in the Territory. For additional information on the Amended Agreements, see Note 5 "Revenue from Contracts with Customers" in the accompanying notes to the Consolidated Financial Statements.

On September 18, 2015, we sold a majority of the expected royalty stream and commercial milestones from the sales of Zalviso in Europe by Grünenthal to PDL, in a transaction referred to as the Royalty Monetization. We received gross proceeds of $65.0 million in the Royalty Monetization. PDL will receive 75% of the European royalties under the Amended Agreements with Grünenthal, as well as 80% of the first four commercial milestones worth $35.6 million (or 80% of $44.5 million), subject to the capped amount of $195.0 million. For additional information on the Royalty Monetization with PDL, see Note 8 "Liability Related to Sale of Future Royalties" in the accompanying notes to the Consolidated Financial Statements.

Grünenthal is responsible for all commercial activities for Zalviso, including obtaining and maintaining pharmaceutical product regulatory approval in the Territory. We are responsible for obtaining and maintaining device regulatory approval in the Territory and manufacturing and supply of Zalviso to Grünenthal for commercial sales.

Intellectual Property

We seek patent protection in the United States and internationally for DSUVIA, DZUVEO and Zalviso. Our policy is to pursue, maintain and defend patent rights developed internally and to protect the technology, inventions and improvements that are commercially important to the development of our business. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology. We also rely on trade secrets to protect DSUVIA, DZUVEO and Zalviso. Our commercial success also depends in part on our non-infringement of the patents or proprietary rights of third parties. For a more comprehensive discussion of the risks related to our intellectual property, please see "Risk Factors—Risks Related to Our Intellectual Property" appearing elsewhere in this Form 10-K.

Our success will depend significantly on our ability to:

- obtain and maintain patent and other proprietary protection for DSUVIA, DZUVEO and Zalviso;
- defend our patents;
- preserve the confidentiality of our trade secrets; and
- operate our business without infringing the patents and proprietary rights of third parties.

We have established and continue to build proprietary positions for DSUVIA, DZUVEO and Zalviso and related technology in the United States and abroad.

As of December 31, 2019, we are the owner of record of 25 issued U.S. patents, which together provide coverage for sufentanil sublingual tablets, and the device components of Zalviso and DSUVIA. These patents provide coverage to at least 2027. We also hold six issued European patents, each valid in at least eight countries in Europe. In addition, we own seven patents in Japan, seven in China and seven in Korea, and a number of other international patents which provide coverage to at least 2027. We are also pursuing a number of U.S. and foreign patent applications. The patent applications that we have filed and have not yet been granted may fail to result in issued patents in the United States or in foreign countries. Even if the patents do successfully issue, third parties may challenge the patents.

We continue to seek and expand our patent protection for both compositions of matter and delivery devices, as well as methods of treatment related to DSUVIA, DZUVEO and Zalviso. In particular, we are pursuing additional patent protection for our DSUVIA, DZUVEO and Zalviso formulations, our Zalviso device, the combination of drugs and our Zalviso device, our DSUVIA and DZUVEO SDA, as well as to methods of treatment using such drug and device compositions.

We have filed for additional patent coverage in the United States, Europe as well as many other foreign jurisdictions including, Japan, China, India, Canada and Korea. If issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, we expect that these patents will expire between 2027 and 2031, excluding any additional term for patent term adjustments or patent term extensions in the United States. We note that the patent laws of foreign countries differ from those in United States, and the degree of protection afforded by foreign patents may be different from the protection offered by U.S. patents.

Further, we seek trademark protection in the United States and internationally where available and when appropriate. We have registered our ACELRX, DSUVIA and Zalviso marks in Class 5, "Pharmaceutical preparations for treating pain; pharmaceutical preparations for treating anxiety," and Class 10, "Drug delivery systems; medical device, namely, a mechanical and electronic device used to administer medications, perform timed medication delivery, and to provide secure access to and delivery of medications," in the United States.

Our ACELRX, DSUVIA and Zalviso marks are also registered in the European Union, as well as other countries. Our DZUVEO mark is registered in the European Union.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, and medical technology companies. We believe the key competitive factors that will affect the development and commercial success of our products are the safety, efficacy and tolerability profile, the patient and healthcare professional satisfaction with using our products in relation to available alternatives and the reliability, convenience of dosing, price and reimbursement of our products. Over the past year, we have monitored changes in the pharmaceutical industry in response to opioid use in the United States. Pharmaceutical companies engaged in the distribution and sale of opioids, in particular for the treatment of chronic pain, are refocusing their efforts in order to support responsible opioid use. While our products are designed for the treatment of moderate-to-severe acute pain for use in medically supervised settings, rather than for the treatment of chronic pain or for outpatient use, these industry changes could impact the commercial success of DSUVIA, or Zalviso, if approved, in the United States.

DSUVIA competes, and Zalviso, if approved in the U.S., will compete, with a number of existing and future pharmaceuticals and drug delivery devices developed, manufactured and marketed by others. In particular, DSUVIA may compete with a wide variety of products and product candidates including (i) injectable opioid products, such as morphine, fentanyl, hydromorphone and meperidine; (ii) oral opioids such as oxycodone and hydrocodone; (iii) generic injectable local anesthetics, such as bupivacaine or branded formulations thereof; (iv) non-steroidal anti-inflammatory drugs, or NSAIDS, including ketorolac in intranasal or generic IV form, and IV meloxicam; and (v) transmucosal fentanyl products. Zalviso, if approved in the U.S., may compete with a number of opioid-based treatment options, including IV PCA pumps, oral PCA devices, and transdermal opioid PCAs.

Many of our competitors and potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drug candidates, obtaining FDA and other regulatory approval of products, and the commercialization of those products. Accordingly, our competitors may be more successful than we are in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' drugs or drug delivery systems may be more effective, have fewer adverse effects, be less expensive to develop and manufacture, or be more effectively marketed and sold than any product we may seek to commercialize. This may render our products obsolete or non-competitive. We anticipate that we will face intense and increasing competition as new drugs enter the market, additional technologies become available, and competitors establish collaborative or licensing relationships, which may adversely affect our competitive position.

Pharmaceutical Manufacturing and Supply

We currently rely on contract manufacturers to produce sufentanil sublingual tablets for commercial production of DSUVIA and Zalviso under current Good Manufacturing Practices, or cGMP, with oversight by our internal managers. Equipment specific to the pharmaceutical manufacturing process was purchased and customized for us and is currently owned by us. We plan to continue to rely on contract manufacturers and, potentially, collaboration partners to manufacture commercial quantities of our products, if and when approved for marketing by the FDA. We currently rely on a single manufacturer for the commercial supplies of the active pharmaceutical ingredient, or API, for DSUVIA and Zalviso, and are currently working to qualify a second source. We have identified other manufacturers that could satisfy our commercial supply and packaging requirements and we continue to evaluate those manufacturers.

Device Manufacturing and Supply

All contract manufacturers and component suppliers have been selected for their specific competencies in the manufacturing processes and materials that make up DSUVIA and Zalviso. We currently rely on single manufacturers for the commercial supplies of our drug components and packaging for DSUVIA and Zalviso, and do not currently have agreements in place for redundant supply or a second source for either DSUVIA or Zalviso. DSUVIA utilizes an SDA in the delivery of the tablets. FDA regulations require that materials be produced under cGMPs or Quality System Regulation, or QSR, as required for the respective unit operation within the manufacturing process. We outsource injection molding of all the plastic parts for the SDA, and product sub-assemblies; and filling, packaging and labeling of SDAs.

The device components of Zalviso are manufactured by contract manufacturers, component fabricators and secondary service providers. We outsource injection molding of all the plastic parts for the cartridge and device and product sub-assemblies; tablet cartridge filling and packaging; and assembly, packaging and labeling of the dispenser and controller.

Government Regulation

Government authorities in the United States at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, export and import of products such as DSUVIA and Zalviso. Product candidates, such as Zalviso, must be approved by the FDA through the NDA process before they may legally be marketed in the United States.

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and complying with applicable laws and regulations requires the expenditure of substantial time and financial resources. Failure to comply at any time during the product development and approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. The process required by the FDA before a drug product may be marketed in the United States generally involves the following:

- completion of non-clinical laboratory tests, animal trials and formulation studies according to Good Laboratory and Manufacturing Practices regulations;
- submission to the FDA of an investigational new drug, or IND, application which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCP, to establish the clinical safety and efficacy of the proposed drug product for its intended use;
- submission to the FDA of an NDA for a new drug product;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug product and the drug substance(s) are produced to assess compliance with cGMP;
- payment of application, annual program fees; and
- FDA review and approval of the NDA.

The testing and approval process requires substantial time, effort and financial resources and we cannot be certain that approval for our product candidate, Zalviso, will be granted on a timely basis, if at all.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1.* The product is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2.* Involves trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted conditions and to determine dosage tolerance and optimal dosage and schedule.
- *Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical safety and efficacy in an expanded patient population at geographically dispersed clinical trial sites. These trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an Institutional Review Board, or IRB, can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biological product has been associated with unexpected serious harm to patients.

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP and QSR for medical device requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

The results of product development, preclinical trials and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on our drug products, proposed labeling and other relevant information, will be submitted to the FDA as part of an NDA for a new drug product, requesting approval to market the product in the United States. The submission of an NDA is subject to the payment of a substantial user fee; a waiver of such fee may be obtained under certain limited circumstances. During its review of an NDA, the FDA may inspect our manufacturers for GMP and QSR compliance, and our pivotal clinical trial sites for GCP compliance.

In addition, under the Pediatric Research Equity Act, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers.

The approval process is lengthy and difficult, and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA issues a Complete Response Letter at the conclusion of its review if the NDA is not yet deemed ready for approval. A Complete Response Letter generally outlines the deficiencies in the submission and may require substantial additional testing or information for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

If a product candidate does receive regulatory approval, the approval may be limited to specific conditions and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. DSUVIA was approved with a Risk Evaluation and Mitigation Strategy, or REMS, to mitigate the risk of respiratory depression resulting from accidental exposure by ensuring that DSUVIA is dispensed only to patients in certified medically supervised healthcare settings. Zalviso, if approved, will also require a REMS, which can include a medication guide, patient package insert, a communication plan, elements to assure safe use and implementation system, and must include a timetable for assessment of the REMS. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. In addition, the FDA may require post-approval testing which involves clinical trials designed to further assess a drug product's safety and effectiveness after the NDA.

Post-Approval Requirements

Any drug products for which we receive FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated clinical safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. Phase 4 clinical trials are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication or when otherwise requested by the FDA in the form of post marketing requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in withdrawal of NDA approval. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drug products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers of drug products must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Drug product manufacturers and other entities involved in the manufacturing and distribution of approved drug products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, packaging, labeling, storage and shipment of the drug product. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory standards, and test each product batch or lot prior to its release. In the case of Zalviso, the device component must comply with FDA's Quality Systems Regulation.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution or may require substantial resources to correct.

The FDA may withdraw a product approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning letters, holds on clinical trials, product recalls or seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products to the extent we choose to sell any products outside of the United States.

In June 2018, the European Commission, or EC, granted marketing approval of DZUVEO for the treatment of patients with moderate-to-severe acute pain in medically monitored settings. We currently intend to commercialize and promote DZUVEO in Europe with a strategic partner, although we have not yet entered into such an arrangement.

We are responsible for maintaining Zalviso device regulatory approval in the EU in order to support the manufacturing and supply of Zalviso to Grünenthal for commercial sales. We completed the Conformité Européenne approval process for the Zalviso device, more commonly known as a CE Mark approval. We received CE Mark approval in December 2014, which permits the commercial sale of the Zalviso device in the European Union. In connection with the CE Mark approval, we were also granted International Standards Organization, or ISO, 13485:2003 certification of our quality management system. This is an internationally recognized quality standard for medical devices. The CE Mark was originally issued by the British Standards Institution, or BSI, a Notified Body, or NB, located in the United Kingdom, or U.K., or BSI-U.K. We transferred the CE Mark file and certification to the Netherlands NB of BSI, or BSI-NL, to mitigate the uncertainty with regards to Brexit. The ISO certification issued through BSI-U.K. was upgraded in 2019 to the latest version of the standard, ISO 13485:2016 through BSI-U.K. in 2019 and remains in effect, regardless of Brexit. BSI ISO 13485:2016 certification recognizes that consistent quality policies and procedures are in place for the development, design and manufacturing of medical devices. The certification indicates that we have successfully implemented a quality system that conforms to ISO 13485 standards for medical devices. Certification to this standard is one of the key regulatory requirements for a CE Mark in the EU and EEA, as well as to meet equivalent requirements in other international markets.

Controlled Substances Regulations

Sufentanil, a Schedule II controlled substance, is the API in DSUVIA and Zalviso. Controlled substances are governed by the DEA. Similarly, sufentanil is regulated as a controlled substance in Europe and other territories outside of the U.S. The handling of controlled substances and/or drug product by us, our contract manufacturers, analytical laboratories, packagers and distributors, are regulated by the Controlled Substances Act and regulations thereunder.

The Drug Supply Chain Security Act of 2013, or DSCSA, imposes obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements are that manufacturers must provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, manufacturers have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Unforeseen delays to the drug substance and drug product manufacture and supply chain may occur due to delays, errors or other unforeseen problems with the permitting and quota process. Also, any one of our suppliers, contract manufacturers, laboratories, packagers and/or distributors could be the subject of DEA violations and enforcement could lead to delays or even loss of DEA license by the contractors.

Federal and State Fraud and Abuse and Data Privacy and Security and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws restrict certain business practices in the pharmaceutical industry. These laws include, but are not limited to, anti-kickback, false claims, data privacy and security, and transparency statutes and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for, purchasing, leasing, ordering or arranging for the purchasing, leasing or ordering of any item or service reimbursable under Medicare, Medicaid or other federal healthcare program. The term “remuneration” has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and/or formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and practices involving remuneration that may be alleged to be intended to induce purchasing, leasing or ordering may be subject to scrutiny if they do not qualify for an exception or safe harbor. The failure to satisfy all of the requirements of an applicable exception or safe harbor do not make the conduct per se illegal under the 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 of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under an exception or safe harbor.

Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, the Affordable Care Act to a stricter standard such that a person or entity no longer needs to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Rather, if "one purpose" of the remuneration is to induce referrals, the federal Anti-Kickback Statute is violated. In addition, the Affordable Care Act codified case law that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute also constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below).

The federal civil False Claims Act and related laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses. Further, the Civil Monetary Penalties Law imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to, among others, a federal healthcare program that the person knows or should know is for a medical or other item or service that was not provided as claimed or is false or fraudulent.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates that are independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. International laws, such as the European Union General Data Protection Regulation, or GDPR, (EU 2016/679) and Swiss Federal Act on Data Protection, regulate the processing of personal data within the European Union and between countries in the European Union and countries outside of the European Union, including the United States. Failure to provide adequate privacy protections and maintain compliance with safe harbor mechanisms could jeopardize business transactions across borders and result in significant penalties.

Additionally, the federal Physician Payments Sunshine Act within the Affordable Care Act and its implementing regulations, require that certain manufacturers of drugs, devices, biologicals and medical supplies, for which federal healthcare program payment is available, report information related to certain payments or other transfers of value made or distributed to physicians, as defined by law, and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. FDA and some states require the posting of information relating to clinical studies. In addition, certain states such as California require pharmaceutical companies to implement a comprehensive compliance program that includes a limit on expenditures for, or payments to, individual medical or health professionals. Moreover, several states have enacted legislation requiring pharmaceutical manufacturers to, among other things, file periodic reports with the state, make periodic public disclosures on sales and marketing activities, report information related to drug pricing, require the registration of sales representatives, and prohibit certain other sales and marketing practices.

If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Pharmaceutical Coverage, Pricing and Reimbursement

In both domestic and foreign markets, our sales of any approved products will depend in part on the availability of coverage and adequate reimbursement from third-party payers. Third-party payers include government health administrative authorities, managed care providers, private health insurers and other organizations. Sales of our products will depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by third-party payers. These third-party payers are increasingly focused on containing healthcare costs by challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare products. Third-party payers and hospitals may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. Because each third-party payer individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming, costly and sometimes unpredictable process. We may be required to provide scientific and clinical support for the use of any product to each third-party payer and hospital separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. We cannot be certain that DSUVIA and Zalviso, once approved for commercial sale, will be considered cost-effective. Because coverage and reimbursement determinations are made on a payer-by-payer basis, obtaining acceptable coverage and reimbursement from one payer does not guarantee that we will obtain similar acceptable coverage or reimbursement from another payer. If we are unable to obtain coverage of, and adequate reimbursement and payment levels for, our approved products from third-party payers, physicians may limit how much or under what circumstances they will prescribe or administer them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition and future success. Third-party payers, government healthcare programs, wholesalers, group purchasing organizations, and hospitals frequently require that pharmaceutical companies negotiate agreements that provide discounts or rebates from list prices. We expect increasing pressure to offer larger discounts or discounts to a greater number of these organizations to maintain acceptable reimbursement levels for and access to our products. Net prices for drugs may be reduced by these mandatory discounts or rebates required by government healthcare programs, private payers, wholesalers, group purchasing organizations, hospitals, and by any future relaxation of laws that presently restrict imports of drugs from policy and payment limitations in setting their own reimbursement policies. In addition, if our competitors reduce the prices of their products, or otherwise demonstrate that they are better or more cost effective than our products, this may result in a greater level of reimbursement for their products relative to our products, which would reduce sales of our products and harm our results of operations.

There have been, and there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to commercialize our products profitably. We anticipate that the federal and state legislatures and the private sector will continue to consider and may adopt and implement healthcare policies, such as the Affordable Care Act, intended to curb rising healthcare costs. These cost containment measures may include: controls on government-funded reimbursement for drugs; new or increased requirements to pay prescription drug rebates to government health care programs; controls on healthcare providers; challenges to or limits on the pricing of drugs, including pricing controls, or limits or prohibitions on reimbursement for specific products through other means; requirements to try less expensive products or generics before a more expensive branded product; and public funding for cost effectiveness research, which may be used by government and private third-party payers to make coverage and payment decisions.

In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition for our products from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Healthcare Reform

In the United States and foreign 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 affect our future results of operations as we begin to commercialize our products. In particular, there have been and continue to be a number of initiatives at the United States federal and state level that seek to reduce healthcare costs. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our future products will likely be lower than the prices we might otherwise obtain from non-governmental payers. Moreover, private payers often follow federal healthcare coverage policy and payment limitations in setting their own payment rates.

Furthermore, political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental change. Initiatives to reduce the federal deficit and to reform healthcare delivery are increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative benefits, controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability.

In the United States, the Affordable Care Act was enacted in an effort to, among other things, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, impose new taxes and fees on the health industry and impose additional health policy reforms. Aspects of PPACA that may impact our business include:

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- expansion of eligibility criteria for Medicaid programs, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Legislative changes to the Affordable Care Act remain possible and appear likely in the 116th U.S. Congress and under the Trump Administration. There remain judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act. Currently, 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, several 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". Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act's mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. In December 2018, Centers for Medicare & Medicaid Services, or CMS, published a new final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act. We expect that the Affordable Care Act, as currently enacted or as it may be amended or repealed in the future, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to successfully commercialize DSUVIA, and if approved in the United States, Zalviso.

Although the recent U.S. District Court holding that the PPACA is unconstitutional has been appealed, its long-term viability remains unclear. In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. Aggregate reductions of Medicare payments to providers of 2% per fiscal year went into effect on April 1, 2013 and will stay in effect through 2027 unless Congressional action is taken. The American Taxpayer Relief Act further reduced Medicare payments to several providers, including hospitals.

Moreover, the DSCSA imposes additional obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new legislation, manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. AcelRx is engaging Contract Manufacturing Organizations, or CMOs, and solution providers in serialization to implement the requirements of the DSCSA on our products. The acceptability of the approach that AcelRx is implementing will be ultimately subject to review by the FDA.

Legislative and regulatory proposals have been made to expand post-approval requirements and further restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our products, if any, may be.

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 or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our products may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing.

Further, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we are able to charge for our products, or the amounts of reimbursement available for our products. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, price controls or patient access constraints under the Medicaid program, and some states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payer or policy actions, which may include cost containment and other healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidate that receives regulatory approval. In the United States and markets in other countries, sales of DSUVIA, and Zalviso, if approved for commercial sale, will depend, in part, on the extent to which third-party payers provide coverage and establish adequate reimbursement levels for approved products. In the United States, third-party payers include federal and state healthcare programs, government authorities, private managed care providers, private health insurers and other organizations.

Further, third-party payers are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Such payers may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our product candidates, in addition to the costs required to obtain the FDA approvals. Nonetheless, DSUVIA and Zalviso, if approved, may not be considered medically necessary or cost-effective.

Moreover, the process for determining whether a third-party payer will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payer will pay for the drug product. A payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payer's determination to provide coverage for a drug product does not assure that other payers will also provide coverage for the drug product. Adequate third-party reimbursement may not be available to maintain price levels sufficient to realize an appropriate return on our investment.

Employees

As of December 31, 2019, we employed 99 full-time employees. None of our employees are subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate Information

We were originally incorporated as SuRx, Inc. in Delaware on July 13, 2005. We subsequently changed our name to AcelRx Pharmaceuticals, Inc. on August 13, 2006. We file electronically with the U.S. Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make available on our website at www.acelrx.com, free of charge, copies of these reports as soon as reasonably practicable after filing these reports with, or furnishing them to, the SEC.

Item 1A. Risk Factors

Our operations and financial results are subject to various risks and uncertainties. You should carefully consider the risks described below, together with all of the other information in this report, including our financial statements and notes thereto. If any of the following risks actually materialize, our business, financial condition, results of operations, liquidity, and future prospects could be materially harmed, the price of our common stock could decline, and you could lose part or all of your investment.

Risks Related to Our Planned Acquisition of Tetraphase Pharmaceuticals, Inc.

The failure to complete our planned acquisition of Tetraphase Pharmaceuticals, Inc. in a timely manner or at all, may adversely affect our business and our stock price.

Our and Tetraphase Pharmaceuticals, Inc.'s, or Tetraphase's, obligations to consummate our planned acquisition of Tetraphase are subject to the satisfaction or waiver of certain customary conditions, including, among others, (i) the adoption of the Agreement and Plan of Merger by a majority of the stockholders of Tetraphase; (ii) the absence of (A) any temporary restraining order, preliminary or permanent injunction or other order issued by any court of competent jurisdiction enjoining or otherwise preventing the consummation of the merger or (B) any applicable law that makes consummation of the merger illegal; (iii) the absence of certain legal proceedings to which a governmental body is a party relating to the merger; (iv) subject to certain qualifications, the accuracy of the representations and warranties of the parties and compliance by the parties with their respective obligations under the merger agreement; (v) the absence of any material adverse effect on Tetraphase or our company since the date of the merger agreement; (vi) the registration statement on Form S-4 to register our common stock to be issued in the merger being declared effective by the SEC; and (vii) a minimum Tetraphase net cash balance. We cannot provide assurance that these or the other conditions to the completion of the planned acquisition of Tetraphase will be satisfied in a timely manner or at all. In addition, other factors may affect when and whether the acquisition will occur. If our planned acquisition of Tetraphase is not completed, our share price could fall to the extent that our current price reflects an assumption that we will complete the planned acquisition. Furthermore, if the planned acquisition of Tetraphase is not completed and the merger agreement is terminated, we may suffer other consequences that could adversely affect our business, results of operations and share price, including the following:

- we have incurred and will continue to incur costs relating to the planned acquisition (including significant legal and financial advisory fees) and these costs are payable by us whether or not the planned acquisition is completed;
- matters relating to the planned acquisition (including integration planning) may require substantial commitments of time and resources by our management team, which could otherwise have been devoted to other opportunities that may have been beneficial to us;
- we may be subject to legal proceedings related to the acquisition or the failure to complete the acquisition;
- the failure to consummate the acquisition may result in negative publicity and a negative impression of us in the investment community; and
- any disruptions to our business resulting from the announcement and pendency of the acquisition, including any adverse changes in our relationships with our customers, suppliers, collaboration partners and employees, may continue or intensify in the event the merger is not consummated.

Uncertainty about our planned acquisition of Tetraphase may adversely affect our business and stock price, whether or not the planned acquisition is completed.

We are subject to risks in connection with the announcement and pendency of our planned acquisition of Tetraphase, including the pendency and outcome of any legal proceedings against us, our directors and others relating to the planned acquisition and the risks from possibly foregoing opportunities we might otherwise pursue absent the planned acquisition of Tetraphase. Furthermore, uncertainties about the planned acquisition may cause our current and prospective employees to experience uncertainty about their future with us. These uncertainties may impair our ability to retain, recruit or motivate key management and other personnel.

In addition, in response to the announcement of our planned acquisition of Tetraphase, our existing or prospective customers, suppliers or collaboration partners may:

- delay, defer or cease purchasing our products or providing goods or services to us;
- delay or defer other decisions concerning us, or refuse to extend credit terms to us;
- cease further joint development activities; or
- otherwise seek to change the terms on which they do business with us.

While we are attempting to address these potential risks with our existing and prospective customers, suppliers or collaboration partners, they may be reluctant to purchase our products, supply us with goods and service or continue collaborations due to the potential uncertainty about the direction of our product offerings and the support and service of our products after we complete the planned acquisition of Tetraphase.

We may fail to realize the benefits expected from our planned acquisition of Tetraphase, which could adversely affect our stock price.

Our planned acquisition of Tetraphase, if completed, will be our largest acquisition to date. The anticipated benefits we expect from the planned acquisition are, necessarily, based on projections and assumptions about the combined businesses of our company and Tetraphase, which may not materialize as expected or which may prove to be inaccurate. The value of our common stock following the completion of the planned acquisition could be adversely affected if we are unable to realize the anticipated benefits from the acquisition on a timely basis or at all. Achieving the benefits of the planned acquisition of Tetraphase will depend, in part, on our ability to integrate the business, operations and products of Tetraphase successfully and efficiently with our business. The challenges involved in this integration, which will be complex and time-consuming, include the following:

- difficulties entering new markets and integrating new products in which we have no or limited direct prior experience;
- successfully managing relationships with our combined supplier and customer base;
- consolidating and integrating corporate, finance and administrative infrastructures and integrating and harmonizing business systems;
- coordinating sales and marketing efforts to effectively position our capabilities and the direction of product development;
- limitations prior to the completion of the acquisition on the ability of management of our company and of Tetraphase to conduct planning regarding the integration of the two companies;
- the increased scale and complexity of our operations resulting from the acquisition;
- retaining key employees of our company and Tetraphase;
- obligations that we will have to counterparties of Tetraphase that arise as a result of the change in control of Tetraphase; and
- minimizing the diversion of management attention from other important business objectives.

If we do not successfully manage these issues and the other challenges inherent in integrating an acquired business of the size and complexity of Tetraphase, then we may not achieve the anticipated benefits of the acquisition of Tetraphase and our revenue, expenses, operating results and financial condition could be materially adversely affected.

The acquisition of Tetraphase may result in significant charges or other liabilities that could adversely affect the financial results of the combined company.

The financial results of the combined company may be adversely affected by cash expenses and non-cash accounting charges incurred in connection with our integration of the business and operations of Tetraphase. The amount and timing of these possible charges are not yet known. Further, our failure to identify or accurately assess the magnitude of certain liabilities we are assuming in the acquisition could result in unexpected litigation or regulatory exposure, unfavorable accounting charges, unexpected increases in taxes due, a loss of anticipated tax benefits or other adverse effects on our business, operating results or financial condition. The price of our common stock following the acquisition could decline to the extent the combined company's financial results are materially affected by any of these events.

The issuance of shares of our common stock in connection with the planned acquisition of Tetraphase will dilute our shareholders' ownership interest in the company.

If the acquisition of Tetraphase is completed, up to approximately 14 million shares of our common stock will be issued to Tetraphase securityholders, and former Tetraphase securityholders will own, in the aggregate, up to approximately 14.6% of the combined company. This issuance of shares of our common stock will dilute your ownership interest in our company, and you will have a reduced ownership and voting interest in our company following the completion of this transaction. In addition, if we elect to settle any contingent value rights through the issuance of additional shares of common stock, you will experience further dilution.

Risks Related to Commercialization of DSUVIA® and Zalviso®

Our success is highly dependent on our ability to successfully commercialize DSUVIA. To the extent DSUVIA is not commercially successful, our business, financial condition and results of operations will be materially harmed.

We invested a significant portion of our efforts and financial resources to develop and gain regulatory approval for DSUVIA and expect to continue making significant investments to commercialize DSUVIA. We believe our success is highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize DSUVIA in the United States. The commercial success of DSUVIA depends heavily on numerous factors, including:

- our ability to market, sell, and distribute DSUVIA;
- our ability to establish and maintain commercial manufacturing with third parties;
- acceptance of DSUVIA by physicians, patients and the healthcare community;
- acceptance of pricing and placement of DSUVIA on payers' formularies;
- our ability to effectively compete with other medications for the treatment of moderate-to-severe acute pain in medically supervised settings, including IV-opioids and any subsequently approved products;
- effective management of, and compliance with, the DSUVIA Risk Evaluation and Mitigation Strategy, or REMS, program;
- continued demonstration of an acceptable safety profile of DSUVIA; and
- our ability to obtain, maintain, enforce, and defend our intellectual property rights and claims.

If we are unable to successfully commercialize DSUVIA, our business, financial condition, and results of operations will be materially harmed.

The commercial success of DSUVIA and Zalviso, if approved, in the United States, as well as DZUVEO and Zalviso in Europe, will depend upon the acceptance of these products by the medical community, including physicians, nurses, patients, and pharmacy and therapeutics committees.

The degree of market acceptance of DSUVIA and Zalviso, if approved, in the United States, or DZUVEO and Zalviso in Europe, will depend on a number of factors, including:

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and health care payers;
- the use of DSUVIA for the management of moderate-to-severe acute pain by a healthcare professional for patient types that were not specifically studied in our Phase 3 trials;
- the use of Zalviso for the management of moderate-to-severe acute pain in the hospital setting for patient types that were not specifically studied in our Phase 3 trials;
- the prevalence and severity of any adverse events, or AEs, or serious adverse events, or SAEs;
- overcoming any perceptions of sufentanil as a potentially unsafe drug due to its high potency opioid status;
- limitations or warnings contained in the U.S. Food and Drug Administration, or FDA-approved label for DSUVIA, or the European Medicines Agency, or EMA-approved label for DZUVEO, or Zalviso;
- restrictions or limitations placed on DSUVIA due to the REMS program;
- availability of alternative treatments;
- existing capital investment by hospitals in IV PCA technology;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain formulary approval; and,
- our ability to obtain and maintain sufficient third-party coverage and reimbursement.

If our approved products do not achieve an adequate level of acceptance by physicians, nurses, patients and pharmacy and therapeutics committees, we may not generate sufficient revenue and become or remain profitable.

If we are unable to maintain or grow our sales and marketing capabilities or enter into agreements with third parties to market and sell our products outside of the United States, we may be unable to generate sufficient product revenue.

In order to commercialize DSUVIA and Zalviso, if approved, in the United States, we must maintain or grow internal sales, marketing, distribution, managerial and other capabilities or make arrangements with third parties to perform these services. We have entered into agreements with third parties for the distribution of DSUVIA and plan to enter into such agreements for Zalviso, if approved, in the United States; however, if these third parties do not perform as expected or there are delays in establishing such relationships for Zalviso, if approved, our ability to effectively distribute products would suffer.

We have entered into a collaboration with Grünenthal for the commercialization of Zalviso in Europe and Australia and intend to enter into additional strategic partnerships with third parties to commercialize our products outside of the United States. DZUVEO was approved by the EC in June 2018. We have not yet entered into a collaboration agreement with a strategic partner for the commercialization of DZUVEO in Europe, and there can be no assurance that we will successfully enter into such an agreement. We may also consider the option to enter into strategic partnerships for DSUVIA, or Zalviso, if approved, in the United States. We face significant competition in seeking appropriate strategic partners, and these strategic partnerships can be intricate and time consuming to negotiate and document.

We may not be able to negotiate future strategic partnerships on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any strategic partnerships because of the numerous risks and uncertainties associated with establishing strategic partnerships. Our current or future collaboration partners, if any, may not dedicate sufficient resources to the commercialization of Zalviso or DSUVIA/DZUVEO, or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective collaborations to enable the sale of our products to healthcare professionals and in geographical regions that will not be covered by our own marketing and sales force, or if our potential future collaboration partners do not successfully commercialize our products, our ability to generate revenues from product sales will be adversely affected.

If we are unable to maintain or grow adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and become profitable. We compete with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

In March 2020, in connection with the Co-Promotion Agreement with Tetraphase Pharmaceuticals, Inc., we reduced the size of our commercial team to eliminate the overlap with the Tetraphase commercial team and, given our reduced workforce, we may experience difficulties in retaining our existing employees and managing our operations, including our continued commercialization of DSUVIA.

As of December 31, 2019, we had 99 full-time employees. On March 15, 2020, we entered into the Agreement and Plan of Merger and the Co-Promotion Agreement with Tetraphase Pharmaceuticals, Inc., or Tetraphase. In connection with the Co-Promotion Agreement, we reduced the size of our commercial team to eliminate the overlap with the Tetraphase commercial team. The restructuring resulted in the elimination of 30 positions, or approximately 33% of our workforce. We will need to retain and maintain our existing sales, managerial, operational, finance and other personnel and resources in order to continue the commercialization of DSUVIA and manage our operations. Our current infrastructure may be inadequate to support our strategy and our workforce reduction may be disruptive to our operations, may negatively affect our productivity, and constrain our commercialization activities. For example, our workforce reduction could yield unanticipated consequences, such as attrition beyond planned staff reductions, negative impact on employee morale and our corporate culture, or increase difficulties in our day-to-day operations and prevent us from successfully commercializing DSUVIA as rapidly as planned. If we encounter such unanticipated consequences, we may have difficulty retaining and attracting personnel. In addition, the implementation of any additional workforce or expense reduction programs may divert the efforts of our management team and other key employees, which could adversely affect our business. Furthermore, we may not realize, in full or in part, the anticipated benefits, savings and improvements in our cost structure from our cost reduction plan, due to unforeseen difficulties, delays or unexpected costs. If we are unable to realize the expected operational efficiencies and cost savings from the cost reduction plan, our operating results and financial condition would be adversely affected.

Guidelines and recommendations published by government agencies, as well as non-governmental organizations, and existing laws and regulations can reduce the use of DSUVIA, and Zalviso, if approved in the United States.

Government agencies and non-governmental organizations promulgate regulations and guidelines applicable to certain drug classes that may include DSUVIA and Zalviso, if approved in the United States. Recommendations of government agencies or non-governmental organizations may relate to such matters as maximum quantities dispensed to patients, dosage, route of administration, and use of concomitant therapies. Government agencies and non-governmental organizations have offered commentary and guidelines on the use of opioid-containing products. We are uncertain how these activities and guidelines may impact DSUVIA and our ability to gain marketing approval of Zalviso in the United States. Regulations or guidelines suggesting the reduced use of certain drug classes that may include DSUVIA or Zalviso, or the use of competitive or alternative products as the standard-of-care to be followed by patients and healthcare providers, could result in decreased use of DSUVIA or Zalviso, if approved, or negatively impact our ability to gain market acceptance and market share. The U.S. government and state legislatures have prioritized combatting the growing misuse and addiction to opioids and opioid overdose deaths and have enacted legislation and regulations as well as other measures intended to fight the opioid epidemic. Addressing opioid drug abuse is a priority for the current U.S. administration and the FDA and is part of a broader initiative led by the HHS. Overall, there is greater scrutiny of entities involved in the manufacture, sale and distribution of opioids. These initiatives, existing laws and regulations, and any negative publicity related to opioids may have a material impact on our business and our ability to manufacture opioid products.

Governmental investigations, inquiries, and regulatory actions and lawsuits brought against us by government agencies and private parties with respect to our commercialization of opioids could adversely affect our business, financial condition, results of operations and cash flows.

As a result of greater public awareness of the public health issue of opioid abuse, there has been increased scrutiny of, and investigation into, the commercial practices of opioid manufacturers by state and federal agencies. As a result of our manufacturing and commercial sale of DSUVIA in the United States and Zalviso in Europe, we could become the subject of federal, state and foreign government investigations and enforcement actions, focused on the misuse and abuse of opioid medications.

In addition, a significant number of lawsuits have been filed against opioid manufacturers, distributors, and others in the supply chain by cities, counties, state Attorney's General and private persons seeking to hold them accountable for opioid misuse and abuse. The lawsuits assert a variety of claims, including, but not limited to, public nuisance, negligence, civil conspiracy, fraud, violations of the Racketeer Influenced and Corrupt Organizations Act, or RICO, or similar state laws, violations of state Controlled Substance Act or state False Claims Act, product liability, consumer fraud, unfair or deceptive trade practices, false advertising, insurance fraud, unjust enrichment and other common law and statutory claims arising from defendants' manufacturing, distribution, marketing and promotion of opioids and seek restitution, damages, injunctive and other relief and attorneys' fees and costs. The claims generally are based on alleged misrepresentations and/or omissions in connection with the sale and marketing of prescription opioid medications and/or an alleged failure to take adequate steps to prevent abuse and diversion. While DSUVIA is designed for use solely in certified medically supervised healthcare settings and administered only by a healthcare professional in these settings, and is not distributed or available at retail pharmacies to patients by prescription, we can provide no assurance that parties will not file lawsuits of this type against us in the future. In addition, current public perceptions of the public health issue of opioid abuse may present challenges to favorable resolution of any potential claims. Accordingly, we cannot predict whether we may become subject to these kinds of investigations and lawsuits in the future, and if we were to be named as a defendant in such actions, we cannot predict the ultimate outcome. Any allegations against us may negatively affect our business in various ways, including through harm to our reputation.

If we were required to defend ourselves in these matters, we would likely incur significant legal costs and could in the future be required to pay significant amounts as a result of fines, penalties, settlements or judgments. It is unlikely that our current product liability insurance would fully cover these potential liabilities, if at all. Moreover, we may be unable to maintain insurance in the future on acceptable terms or with adequate coverage against potential liabilities or other losses. For more information about our product liability insurance and exclusions therefrom, please see the risk factor entitled "We face potential product liability claims, and, if such claims are successful, we may incur substantial liability" elsewhere in this section. The resolution of one or more of these matters could have a material adverse effect on our business, financial condition, results of operations and cash flows.

Furthermore, in the current climate, stories regarding prescription drug abuse and the diversion of opioids and other controlled substances are frequently in the media or advocated by public interest groups. Unfavorable publicity regarding the use or misuse of opioid drugs, the limitations of abuse-deterrent formulations, the ability of drug abusers to discover previously unknown ways to abuse opioid products, public inquiries and investigations into prescription drug abuse, litigation, or regulatory activity regarding sales, marketing, distribution or storage of opioids could have a material adverse effect on our reputation and impact on the results of litigation.

Finally, various government entities, including Congress, state legislatures or other policy-making bodies, or public interest groups have in the past and may in the future hold hearings, conduct investigations and/or issue reports calling attention to the opioid crisis, and may mention or criticize the perceived role of manufacturers, including us, in the opioid crisis. Similarly, press organizations have and likely will continue to report on these issues, and such reporting may result in adverse publicity for us, resulting in reputational harm.

A key part of our business strategy is to establish collaborative relationships to commercialize and fund development and approval of our products, particularly outside of the United States. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our products successfully, if at all.

We will need to establish and maintain successful collaborative relationships to obtain international sales, marketing and distribution capabilities for our products. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty. For example:

- our partners may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical or regulatory results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- our contracts for collaborative arrangements are or may be terminable at will on written notice and may otherwise expire or terminate, and we may not have alternatives available to achieve the potential for our products in those territories or markets;
- our partners may choose to pursue alternative technologies, including those of our competitors;
- we may have disputes with a partner that could lead to litigation or arbitration;
- we have limited control over the decisions of our partners, and they may change the priority of our programs in a manner that would result in termination of the agreement or add significant delays to the partnered program;
- our ability to generate future payments and royalties from our partners depends upon the abilities of our partners to establish the safety and efficacy of our drugs, maintain regulatory approvals and our ability to successfully manufacture and achieve market acceptance of our products;
- we or our partners may fail to properly initiate, maintain or defend our intellectual property rights, where applicable, or a party may use our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability;
- our partners may not devote sufficient capital or resources towards our products; and
- our partners may not comply with applicable government regulatory requirements necessary to successfully market and sell our products.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, any research, clinical development, manufacturing or commercialization efforts pursuant to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully and timely transition terminated collaborative agreements, we may have to undertake development and commercialization activities at our own expense or find alternative sources of capital.

Approval of Zalviso and DZUVEO in Europe has resulted in a variety of risks associated with international operations that could materially adversely affect our business.

Our existing collaboration with Grünenthal for Zalviso requires us to supply product to support the European commercialization of Zalviso. In addition, with the June 2018 approval of DZUVEO in Europe, we intend to enter into agreements with third parties to market DZUVEO in Europe, which may also require us to supply product to those third parties. We may be subject to additional risks related to entering into international business relationships, including:

- multiple, conflicting, and changing laws and regulations such as privacy and data regulations, transparency regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, including for drug approvals, and other governmental approvals, permits, and licenses;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different payer reimbursement regimes, governmental payers, patient self-pay systems and price controls;

- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

Any of these factors could have a material adverse effect on our business.

If we, or current and potential partners, are unable to compete effectively, our products may not reach their commercial potential.

The U.S. biotechnology and pharmaceutical industries are characterized by intense competition and cost pressure. DSUVIA competes, and Zalviso, if approved in the U.S., will compete, with a number of existing and future pharmaceuticals and drug delivery devices developed, manufactured and marketed by others. In particular, DSUVIA may compete with a wide variety of products and product candidates including (i) injectable opioid products, such as morphine, fentanyl, hydromorphone and meperidine; (ii) oral opioids such as oxycodone and hydrocodone; (iii) generic injectable local anesthetics, such as bupivacaine or branded formulations thereof; (iv) non-steroidal anti-inflammatory drugs, or NSAIDS, including ketorolac in intranasal or generic IV form, and IV meloxicam; and (v) transmucosal fentanyl products. Zalviso, if approved in the U.S., may compete with a number of opioid-based treatment options, including IV PCA pumps, oral PCA devices, and transdermal opioid PCAs.

Key competitive factors affecting the commercial success of our approved products are likely to be efficacy, safety profile, reliability, convenience of dosing, price and reimbursement. Many of our competitors and potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drug candidates, obtaining FDA and other regulatory approval of products, and the commercialization of those products. Accordingly, our competitors may be more successful than we are in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' drugs or drug delivery systems may be more effective, have fewer adverse effects, be less expensive to develop and manufacture, or be more effectively marketed and sold than any product we may seek to commercialize. This may render our products obsolete or non-competitive. We anticipate that we will face intense and increasing competition as new drugs enter the market, additional technologies become available, and competitors establish collaborative or licensing relationships, which may adversely affect our competitive position. These and other competitive risks may materially adversely affect our ability to attain or sustain profitable operations.

Hospital or other health care facility formulary approvals for DSUVIA or Zalviso, if approved, in the United States may not be achieved, or could be subject to certain restrictions, which could make it difficult for us to sell our products.

Obtaining hospital or other health care facility formulary approvals can be an expensive and time-consuming process. We cannot be certain if and when we will obtain formulary approvals to allow us to sell our products into our target markets. Failure to obtain timely formulary approval will limit our commercial success. If we are successful in obtaining formulary approvals, we may need to complete evaluation programs whereby DSUVIA, or Zalviso, if approved, is used on a limited basis for certain patient types. The evaluation period may last several months and there can be no assurance that use during the evaluation period will lead to formulary approvals of DSUVIA, or Zalviso, if approved. Further, even successful formulary approvals may be subject to certain restrictions based on patient type or hospital protocol. Failure to obtain timely formulary approvals for DSUVIA, or Zalviso, if approved, would materially adversely affect our ability to attain or sustain profitable operations.

Coverage and adequate reimbursement may not be available for DSUVIA or Zalviso, if approved, in the United States, or DZUVEO or Zalviso in Europe, which could make it difficult for us, or our partners, to sell our products profitably.

Our ability to commercialize DSUVIA or Zalviso, if approved, in the United States, any future collaboration partner's ability to commercialize DZUVEO in Europe, or Grünenthal's ability to expand sales of Zalviso in Europe successfully will depend, in part, on the extent to which coverage and adequate reimbursement will be available from government payer programs at the federal and state levels, authorities, including Medicare and Medicaid, private health insurers, managed care plans and other third-party payers.

No uniform policy requirement for coverage and reimbursement for drug products exists among third-party payers in the United States or Europe. Therefore, coverage and reimbursement can differ significantly from payer to payer. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payer separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Our inability to promptly obtain coverage and adequate reimbursement rates from third party payers could significantly harm our operating results, our ability to raise capital needed to commercialize our approved drugs and our overall financial condition.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell our products profitably. These legislative and/or regulatory changes may negatively impact the reimbursement for our products, following approval. The availability of numerous generic pain medications may also substantially reduce the likelihood of reimbursement for DSUVIA or Zalviso, if approved, in the United States, and DSUVIA/DZUVEO and Zalviso in Europe and elsewhere. The application of user fees to generic drug products may expedite the approval of additional pain medication generic drugs. We expect to experience pricing pressures in connection with our sales of DSUVIA and Zalviso, if approved, in the United States, Grünenthal's European sales of Zalviso, and future product sales of DZUVEO, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. If we fail to successfully secure and maintain reimbursement coverage for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and our business will be harmed.

Furthermore, market acceptance and sales of our products will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third-party payers, such as private health insurers, hospitals and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that reimbursement will be available for DSUVIA or Zalviso, if approved, in the United States, or DZUVEO or Zalviso in Europe. Also, reimbursement amounts may reduce the demand for, or the price of, our products. For example, we anticipate we may need comparator studies of DZUVEO in Europe to ensure premium reimbursement in certain countries. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize DSUVIA or Zalviso, if approved, in the United States, or DZUVEO or Zalviso in Europe.

Additionally, the regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues able to be generated from the sale of the product in that country. For example, separate pricing and reimbursement approvals may impact Grünenthal's ability to market and successfully commercialize Zalviso in the 28 EU member states, at the time of the agreement, plus Switzerland, Liechtenstein, Iceland, Norway and Australia, or the Territory. Adverse pricing limitations may hinder our ability to recoup our investment in DSUVIA in the United States, or Zalviso, even after obtaining FDA marketing approval.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If we are found to have improperly promoted off-label uses of our products, including DSUVIA or Zalviso, if approved, in the United States, we may become subject to significant liability. Such enforcement has become more common in the industry. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription drug products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. While we have received marketing approval for DSUVIA for our proposed indication, physicians may nevertheless use our products for their patients in a manner that is inconsistent with the approved label, if the physicians personally believe in their professional medical judgment it could be used in such manner. However, if the FDA determines that our promotional materials or training constitutes promotion of an off-label use, it could request that we modify our training or promotional materials or subject us to regulatory or enforcement actions, including the issuance of an untitled letter, a warning letter, injunction, seizure, civil fine or criminal penalties and a requirement for corrective advertising, including Dear Doctor letters. It is also possible that other federal, state or foreign enforcement authorities might take action if they consider our promotional or training materials to constitute promotion of an off-label use, which could result in significant civil, criminal and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government-funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, increased losses and diminished profits and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. The FDA or other enforcement authorities could also request that we enter into a consent decree or a corporate integrity agreement or seek a permanent injunction against us under which specified promotional conduct is monitored, changed or curtailed. If we cannot successfully manage the promotion of DSUVIA or Zalviso, if approved, in the United States, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

If we are unable to establish and maintain relationships with group purchasing organizations any future revenues or future profitability could be jeopardized.

Many end-users of pharmaceutical products have relationships with group purchasing organizations, or GPOs, whereby such GPOs provide such end-users access to a broad range of pharmaceutical products from multiple suppliers at competitive prices and, in certain cases, exercise considerable influence over the drug purchasing decisions of such end-users. Hospitals and other end-users contract with the GPO of their choice for their purchasing needs. We expect to derive revenue from end-user customers that are members of GPOs for DSUVIA and Zalviso, if approved. Establishing and maintaining strong relationships with these GPOs will require us to be a reliable supplier, remain price competitive and comply with FDA regulations. The GPOs with whom we have relationships may have relationships with manufacturers that sell competing products, and such GPOs may earn higher margins from these products or combinations of competing products or may prefer products other than ours for other reasons. If we are unable to establish or maintain our GPO relationships, sales of DSUVIA and Zalviso, if approved, and related revenues could be negatively impacted.

We intend to rely on a limited number of pharmaceutical wholesalers to distribute DSUVIA and Zalviso, if approved, in the United States.

We intend to rely primarily upon pharmaceutical wholesalers in connection with the distribution of DSUVIA and Zalviso, if approved, in the United States. As part of the DSUVIA REMS program, we monitor distribution and audit wholesalers' data. If our wholesalers do not comply with the DSUVIA REMS requirements, or if we are unable to establish or maintain our business relationships with these pharmaceutical wholesalers on commercially acceptable terms, or if our wholesalers are unable to distribute our drugs for regulatory, compliance or any other reason, it could have a material adverse effect on our sales and may prevent us from achieving profitability.

Risks Related to Clinical Development and Regulatory Approval

Existing and future legislation may increase the difficulty and cost for us to commercialize our products and affect the prices we may obtain.

In the United States and some foreign jurisdictions, the legislative landscape continues to evolve, including changes to the regulation of opioid-containing products. There have been a number of legislative and regulatory changes and proposed changes regarding healthcare systems that could prevent or delay marketing approval of Zalviso outside of Europe. These changes will restrict or regulate post-approval activities for DSUVIA, DZUVEO and Zalviso, and affect our ability to profitably sell any products for which we obtain marketing approval. For example, 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 FDA announced that it intended to review product and labeling decisions and re-examine the risk-benefit paradigm for opioids. In June 2019, the FDA issued draft guidance related to a new benefit/risk framework for new opioid analgesic products, which proposes that the new product candidate show some benefit over an existing product. In July 2019, the FDA informed two New Drug Application, or NDA, applicants with August 2019 Prescription Drug User Fee Act, or PDUFA, dates for their opioid candidate products that the FDA was postponing product-specific advisory committee meetings for opioid analgesics while it continues to consider a number of scientific and policy issues relating to this class of drug. In September 2019, the FDA held a public hearing to receive stakeholder input on the approval process for new opioids. The timing of the resubmission of the Zalviso NDA is dependent upon the finalization of the FDA's new opioid approval guidelines and process.

In the European Union, or EU, the pricing of prescription drugs is subject to government control. In addition, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use.

In the United States, the Affordable Care Act (as defined below) was enacted in an effort to, among other things, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, impose new taxes and fees on the health industry and impose additional health policy reforms. Aspects of the Affordable Care Act that may impact our business include:

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- expansion of eligibility criteria for Medicaid programs, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

The Affordable Care Act has the potential to substantially change health care financing and delivery by both governmental and private insurers and may also increase our regulatory burdens and operating costs.

There remain judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed two Executive Orders and other directives 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, several 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 that repealed, 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". Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act's mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax, and effective January 1, 2021, also eliminates the health insurer tax. In December 2018, the Centers for Medicare & Medicaid Services, or CMS, published a new final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amended the Affordable Care Act, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. While this ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act. We expect that the Affordable Care Act, as currently enacted or as it may be amended or repealed in the future, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to successfully commercialize our products. 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 or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our products may lose regulatory approval and we may not achieve or sustain profitability, which would adversely affect our business.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. Aggregate reductions of Medicare payments to providers of 2% per fiscal year went into effect on April 1, 2013 and will stay in effect through 2027 unless Congressional action is taken. The American Taxpayer Relief Act further reduced Medicare payments to several providers, including hospitals.

Moreover, the Drug Supply Chain Security Act of 2013 imposes additional obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this legislation, manufacturers are required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product.

In the United States, there has been increasing legislative and enforcement interest with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Additionally, the Trump Administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. HHS has begun soliciting feedback on some of these measures and, at the same time, has implemented others under its existing authority. For example, in September 2018, Centers for Medicare & Medicaid Services, or CMS, announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019. Although these, and other measures will require additional authorization to become effective, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. Furthermore, even after initial price and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple factors, including reference pricing systems and publication of discounts by third party payers or authorities in other countries. In Europe, prices can be reduced further by parallel distribution and parallel trade, i.e. arbitrage between low-priced and high-priced countries. If any of these events occur, revenue from sales of Zalviso and DZUVEO in Europe would be negatively affected.

Legislative and regulatory proposals have been made to expand post-approval requirements and further restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our products, if any, may be.

We expect that additional healthcare reform measures will be adopted within and outside the United States in the future, any of which could negatively impact our business. The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect the demand for any drug products for which we have obtained or may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

We may experience market resistance, delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy regarding opioids generally, and sufentanil specifically.

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 FDA announced that it intended to review product and labeling decisions and re-examine the risk-benefit paradigm for opioids. In June 2019, the FDA issued draft guidance related to a new benefit/risk framework for new opioid analgesic products, which proposes that the new product candidate show some benefit over an existing product. In September 2019, the FDA held a public hearing to receive stakeholder input on the approval process for new opioids. The timing of the resubmission of the Zalviso NDA is dependent upon the finalization of the FDA's new opioid approval guidelines and process.

In May 2017, an Opioid Policy Steering Committee was established to address and advise regulators on opioid use. The Committee was charged with three initial questions: (i) should the FDA require mandatory education for healthcare professionals, or HCPs, who prescribe opioids; (ii) should the FDA take steps to ensure the number of prescribed opioid doses is more closely tailored to the medical indication; and (iii) is the FDA properly considering the risk of abuse and misuse of opioids during its drug review process. Zalviso has not been designed with an abuse-deterrent formulation and is not tamper-resistant. As a result, Zalviso has not undergone testing for tamper-resistance or abuse deterrence.

The FDA can delay, limit or deny marketing approval for many reasons, including:

- a product candidate may not be considered safe or effective;
- the manufacturing processes or facilities we have selected may not meet the applicable requirements; and,
- changes in their approval policies or adoption of new regulations may require additional work on our part.

Part of the regulatory approval process includes compliance inspections of manufacturing facilities to ensure adherence to applicable regulations and guidelines. The regulatory agency may delay, limit or deny marketing approval of our product candidate, Zalviso, as a result of such inspections. In June 2014, the FDA completed an inspection at our corporate offices. We received a single observation on a Form 483 as a result of the inspection. Although we believe we have adequately addressed this observation in revised standard operating procedures, we, our contract manufacturers, and their vendors, are all subject to preapproval and post-approval inspections at any time. The results of these inspections could impact our ability to obtain FDA approval for Zalviso and, if approved, our ability to launch and successfully commercialize Zalviso in the United States. In addition, results of FDA inspections could impact our ability to maintain FDA approval of DSUVIA, and our ability to expand and sustain commercial sales of DSUVIA in the United States.

Any delay in, or failure to receive or maintain, approval for Zalviso in the United States could prevent us from generating meaningful revenues or achieving profitability. Zalviso may not be approved even if we believe it has achieved its endpoints in clinical trials. Regulatory agencies, including the FDA, or their advisors, may disagree with our trial design and our interpretations of data from preclinical studies and clinical trials. Regulatory agencies may change requirements for approval even after a clinical trial design has been approved. The FDA exercises significant discretion over the regulation of combination products, including the discretion to require separate marketing applications for the drug and device components in a combination product. Zalviso is being regulated as a drug product under the NDA process administered by the FDA. The FDA could in the future require additional regulation of Zalviso, or DSUVIA, under the medical device provisions of the Federal Food, Drug and Cosmetic Act, or FDCA. We must comply with the Quality Systems Regulation, or QSR, which sets forth the FDA's current good manufacturing practice, or cGMP, requirements for medical devices, and other applicable government regulations and corresponding foreign standards for drug cGMPs. If we fail to comply with these regulations, it could have a material adverse effect on our business and financial condition.

Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing trials. For example, DSUVIA is subject to a deferred post-marketing requirement for study in the pediatric population ages 6-17 years. Our protocol for this trial is not due until August 2020. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. For example, we intend to seek approval of Zalviso for the management of moderate-to-severe acute pain in adult patients in the hospital setting; however, our clinical trial data was generated exclusively from the post-operative segment of this population, and the FDA may restrict any approval to post-operative patients only, which would reduce our commercial opportunity.

The success of Zalviso relies, in part, on obtaining regulatory approval in the United States.

The success of Zalviso relies, in part, upon our ability to develop and receive regulatory approval of this product candidate in the United States for the management of moderate-to-severe acute pain in adult patients in the hospital setting. Our Phase 3 program for Zalviso initially consisted of three Phase 3 clinical trials. We reported positive top-line data from each of these trials and submitted an NDA for Zalviso to the FDA in September 2013, which the FDA then accepted for filing in December 2013. In July 2014, the FDA issued a Complete Response Letter, or CRL, for our NDA for Zalviso, or the Zalviso CRL. The Zalviso CRL contained requests for additional information on the Zalviso System to ensure proper use of the device. The requests include submission of data demonstrating a reduction in the incidence of device errors, changes to address inadvertent dosing, among other items, and submission of additional data to support the shelf life of the product. Furthermore, in March 2015, we received correspondence from the FDA stating that in addition to the bench testing and two Human Factors studies we had performed in response to the issues identified in the Zalviso CRL, a clinical trial was needed to assess the risk of inadvertent dispensing and overall risk of dispensing failures. Based on the results of our Type C meeting with the FDA in September 2015, we completed the protocol review with the FDA and initiated this study, IAP312, in September 2016.

IAP312 was a Phase 3 study in post-operative patients designed to evaluate the effectiveness of changes made to the functionality and usability of the Zalviso device and to take into account comments from the FDA on the study protocol. The IAP312 study was designed to rule out a 5% device failure rate. The study design required a minimum of 315 patients. In the IAP312 study, sites proactively looked for tablets that were dispensed by the patient but failed to be placed under the tongue, known as dropped tablets. The FDA refers to dropped tablets as inadvertent dispensing. Correspondence from the FDA suggests that they may include the rate of inadvertent dispensing along with the device failures to calculate a total error rate. The IAP312 study evaluated all incidents of misplaced tablets; however, per the protocol, the error rate calculation does not include the rate of inadvertent dispensing. If the FDA includes the rate of inadvertent dispensing along with the device failures to calculate a total error rate, the resulting error rate may be unacceptable to the FDA. Further, the correspondence from the FDA suggests that we may need to modify the REMS program for Zalviso to address dropped tablets. The IAP312 results will supplement the three Phase 3 trials already completed in the Zalviso NDA resubmission. The timing of the resubmission of the Zalviso NDA is dependent upon the finalization of the FDA's new opioid approval guidelines and process.

There is no guarantee that the additional work we performed related to Zalviso, including the IAP312 trial, will result in our successfully obtaining FDA approval of Zalviso in a timely fashion, if at all. Although we believe the IAP312 study met safety, satisfaction and device usability expectations, there is no guarantee the IAP312 trial results will address the issues raised by the FDA. For example, the FDA may include the rate of inadvertent dispensing along with the device failures to calculate a total error rate and the resulting error rate may be unacceptable to the FDA, or the FDA may still have concerns regarding the performance of the device, inadvertent dosing (dropped tablets), or other issues. At any future point in time, the FDA could require us to complete further clinical, Human Factors, pharmaceutical, reprocessing or other studies, which could delay or preclude any NDA resubmission or approval of the NDA and could require us to obtain significant additional funding. We may not be able to identify appropriate remediations to issues that the FDA may raise, and we may not have sufficient time or financial resources to conduct future activities to remediate issues raised by the FDA. We intend to seek a label indication for Zalviso for the management of moderate-to-severe acute pain in adult patients in the hospital setting. However, our clinical trial data was generated exclusively from the post-operative segment of this population, and the FDA may restrict any approval to post-operative patients only, which would reduce our commercial opportunity.

Upon resubmission of the Zalviso NDA, the FDA may hold an advisory committee meeting to obtain committee input on the safety and efficacy of Zalviso. Typically, advisory committees will provide responses to specific questions asked by the FDA, including the committee's view on the approvability of the drug under review. Advisory committee decisions are not binding, but an adverse decision at the advisory committee may have a negative impact on the regulatory review of Zalviso. Additionally, we may choose to engage in the dispute resolution process with the FDA.

Our proposed trade name of Zalviso has been approved by the EMA and is currently being used in Europe. It has also been conditionally approved by the FDA, which must approve all drug trade names to avoid medication errors and misbranding. However, the FDA may withdraw this approval in which case any brand recognition or goodwill that we establish with the name Zalviso prior to commercialization may be worthless.

Any delay in approval by the FDA of the Zalviso NDA, once it is resubmitted, may negatively impact our stock price and harm our business operations. Any delay in obtaining, or inability to obtain, regulatory approval would prevent us from commercializing Zalviso in the United States, generating revenues and potentially achieving profitability. If any of these events occur, we may be forced to delay or abandon our development efforts for Zalviso, which would have a material adverse effect on our business.

Positive clinical results obtained to date for Zalviso may be disputed in FDA review, do not guarantee regulatory approval and may not be obtained from future clinical trials.

We have reported positive top-line data from each of our four Zalviso Phase 3 clinical trials completed to date, as well as our Phase 2 clinical trials for Zalviso. However, even if we believe that the data obtained from clinical trials is positive, the FDA has, and in the future could, determine that the data from our trials was negative or inconclusive or could reach a different conclusion than we did on that same data. Negative or inconclusive results of a clinical trial or difference of opinion could cause the FDA to require us to repeat the trial or conduct additional clinical trials prior to obtaining approval for commercialization, and there is no guarantee that additional trials would achieve positive results or that the FDA will agree with our interpretation of the results. If the FDA were to require any additional clinical trials for Zalviso, our development efforts would be further delayed, which would have a material adverse effect on our business. Any such determination by the FDA would delay the timing of our commercialization plan for Zalviso and adversely affect our business operations.

Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales.

We have experienced and may in the future experience delays in clinical trials of our product candidates. While we have completed four Phase 3 clinical trials and several Phase 2 clinical trials for Zalviso, future clinical trials may not begin on time, have an effective design, enroll a sufficient number of patients or be completed on schedule, if at all. For example, we postponed the start of IAP312, originally planned for the first quarter of 2016, to September 2016. The postponement was due to a delay in the receipt and testing of final clinical supplies for this trial. As a result, the development timeline for Zalviso was further extended.

Our post-approval clinical trials for DSUVIA, or any future FDA-required clinical trials for Zalviso, could be delayed for a variety of reasons, including:

- inability to raise funding necessary to initiate or continue a trial;
- delays in obtaining regulatory approval to commence a trial;
- delays in reaching agreement with the FDA on final trial design;
- imposition of a clinical hold by the FDA, Institutional Review Board, or IRB, or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- delays in obtaining required IRB approval at each site;
- delays in recruiting suitable patients to participate in a trial;
- delays in the testing, validation, manufacture and delivery of the tablets and device components of DSUVIA or Zalviso;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical sites dropping out of a trial to the detriment of enrollment or being delayed in entering data to allow for clinical trial database closure;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

If any future FDA-required clinical trials are delayed for any reason, our development costs may increase, our approval process for Zalviso could be delayed, our ability to commercialize and commence sales of Zalviso could be materially harmed, and our ability to maintain FDA approval of DSUVIA could be jeopardized, which could have a material adverse effect on our business.

Zalviso may cause adverse effects or have other properties that could delay or prevent regulatory approval or limit the scope of any approved label or market acceptance. DSUVIA may cause adverse effects or have other properties that could limit market acceptance.

Adverse events, or AEs, caused by Zalviso could cause us, other reviewing entities, clinical trial sites or regulatory authorities to interrupt, delay or halt any future FDA-required clinical trials and could result in the denial of regulatory approval. Phase 2 clinical trials we conducted with Zalviso did generate some AEs, but no significant adverse events, or SAEs, related to the trial drug. In our Phase 3 active-comparator clinical trial (IAP309), 8% of Zalviso-treated patients dropped out of the trial prematurely due to an AE (11% in the IV patient-controlled morphine group), and we observed three serious adverse events, or SAEs, that were assessed as possibly or probably related to study drug (one- respiratory depression in the Zalviso group and two- abdominal distension and ileus in the IV patient-controlled morphine group). In our Phase 3, double-blind, placebo-controlled, abdominal surgery trial (IAP310), 6% of Zalviso-treated patients dropped out of the trial prematurely due to an AE (9% in placebo group). There were no SAEs determined to be related to study drug. In our Phase 3, double-blind, placebo-controlled, orthopedic surgery trial (IAP311), 7% of Zalviso-treated patients dropped out of the trial prematurely due to an AE (7% in placebo group). Four patients (three in the Zalviso group and one in the placebo group) experienced an SAE considered possibly or probably related to the trial drug by the investigator. The SAEs possibly or probably attributed to Zalviso were severe oxygen saturation decrease, sinus tachycardia and confusional state. In our Phase 3 multicenter, open-label study of Zalviso (IAP312), 3% of patients dropped out prematurely due to an AE. Five patients experienced SAEs in the IAP312 study and none of these were considered possibly or probably related to the study drug by the investigator.

In our Phase 2 DSUVIA placebo-controlled bunionectomy study (SAP202), two patients in the DSUVIA 30 mcg group (5%) discontinued treatment due to an AE, one unrelated to study drug and the other probably related to study drug. There were no SAEs deemed related to study drug. In our Phase 3 placebo-controlled abdominal surgery study (SAP301), one DSUVIA-treated patient (1%) dropped out of the trial prematurely due to an AE (4% in placebo group). There were two SAEs determined to be related to study drug in the placebo-treated group and no related SAEs in the DSUVIA group. In our Phase 3 open-label, single-arm emergency room study (SAP302), no DSUVIA-treated patients dropped out of the trial prematurely due to an AE. One patient had an SAE - angina pectoris - possibly related to study drug. In our post-operative study in patients aged 40 years or older (SAP303), 3% of DSUVIA-treated patients dropped out of the trial prematurely due to an AE. There were no SAEs deemed related to study drug.

If DSUVIA or, if approved, Zalviso cause serious or unexpected side effects after receiving marketing approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified REMS program;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; or,
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of DSUVIA or, if approved, Zalviso, and could substantially increase the costs of commercializing our products.

Additional time may be required to obtain U.S. regulatory approval for Zalviso because it is a drug/device combination product candidate.

DSUVIA and Zalviso are combination products with both drug and device components. The FDA requires both the drug and device components of combination product candidates to be reviewed as part of an NDA submission. There are very few examples of the FDA approval process for drug/device combination products such as DSUVIA and Zalviso. As a result, we experienced delays in the development and commercialization of DSUVIA, and may experience future delays in the development and commercialization of Zalviso, due to regulatory uncertainties in the product development and approval process, in particular as it relates to a drug/device combination product approval under an NDA.

The process for obtaining approval of an NDA is time consuming, subject to unanticipated delays and costs, and requires the commitment of substantial resources.

If the FDA determines that any of the clinical work submitted, including the clinical trials, Human Factors studies and bench testing submitted for a product candidate in support of an NDA were not conducted in full compliance with the applicable protocols for these trials, studies and testing as well as with applicable regulations and standards, or if the FDA does not agree with our interpretation of the results of such trials, studies and testing, the FDA may reject the data and results. The FDA may audit some or all of our clinical trial sites to determine the integrity of our clinical data. The FDA may audit some or all of our Human Factors study sites to determine the integrity of our data and may audit the data and results of bench testing. Any rejection of any of our data would negatively impact our ability to obtain marketing authorization for our product candidate, Zalviso, and would have a material adverse effect on our business and financial condition. In addition, an NDA may not be approved, or approval may be delayed, as a result of changes in FDA policies for drug approval during the review period. For example, although many products have been approved by the FDA in recent years under Section 505(b)(2) of the FDCA, objections have been raised to the FDA's interpretation of Section 505(b)(2). If challenges to the FDA's interpretation of Section 505(b) (2) are successful, the FDA may be required to change its interpretation, which could delay or prevent the approval of such an NDA. More generally, the FDA's comprehensive action plan to take concrete steps towards reducing the impact of opioid abuse on American families and communities may result in delays and challenges in obtaining NDA approval. Any significant delay in the acceptance, review or approval of an NDA that we have submitted would have a material adverse effect on our business and financial condition and would require us to obtain significant additional funding.

Although we have obtained regulatory approval for DSUVIA, and even if we obtain regulatory approval for Zalviso in the United States, we and our collaborators face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Although we have obtained regulatory approval for DSUVIA, and even if we obtain regulatory approval for Zalviso in the United States, the FDA may impose significant restrictions on the indicated uses or marketing of our products or impose ongoing requirements for potentially costly post-approval trials or post-market surveillance. For example, DSUVIA is subject to a deferred post-marketing requirement for study in the pediatric population ages 6-17 years. Our protocol for this trial is not due until August 2020. Additionally, the labeling approved for DSUVIA includes restrictions on use due to the opioid nature of sufentanil. If approved, the labeling for Zalviso will likely include similar restrictions on use.

DSUVIA in the United States is also subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping and reporting of safety and other post-market information. The holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. If approved, Zalviso will be subject to these same requirements.

We must also register and obtain various state prescription drug distribution licenses and controlled substance permits, and any delay or failure to obtain or maintain these licenses or permits may limit our market and materially impact our business. In certain states we cannot apply for a license until a drug is approved by the FDA. The state licensing process may take several months which would delay commercialization in those states. In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMPs and adherence to commitments made in the NDA. If we, or a regulatory agency, discover previously unknown problems with a product, such as AEs of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facilities, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of our products, a regulatory agency may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize DSUVIA, or, if approved, Zalviso, and generate revenues.

Except for Zalviso and DZUVEO, which are both approved in Europe, we may never obtain additional regulatory approvals for our products and product candidates outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we or our commercial partners, including Grünenthal in Europe, must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. On September 22, 2015, we announced that the EC had approved Grünenthal's MAA for Zalviso for the management of acute moderate-to-severe post-operative pain in adult patients. In April 2016, Grünenthal completed the first commercial sale of Zalviso. In June 2018, we announced that the EC had granted marketing approval of DZUVEO for the treatment of patients with moderate-to-severe acute pain in medically monitored settings. We have not yet entered into a collaboration agreement with a strategic partner for the commercialization of DZUVEO in Europe and there can be no assurance that we will successfully enter into such an agreement.

Part of the foreign regulatory approval process includes compliance inspections of manufacturing facilities to ensure adherence to applicable regulations and guidelines. The foreign regulatory agency may delay, limit or deny marketing approval as a result of such inspections. We, our contract manufacturers, and their vendors, are all subject to preapproval and post-approval inspections at any time. The results of these inspections could impact our ability to obtain regulatory approval of DSUVIA and Zalviso in countries outside of the United States and Europe, or our ability to launch and successfully commercialize these products, once approved. In addition, results of EMA inspections could impact our ability to maintain EC approval of Zalviso and DZUVEO, and Grünenthal's ability to expand and sustain commercial sales of Zalviso in Europe.

Outside of Europe, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional non-clinical trials or clinical trials, which could be costly and time consuming. Regulatory requirements can vary widely from country-to-country and could delay or prevent the introduction of our products in those countries. Our current clinical trial data may not be sufficient to support marketing approval or premium reimbursement in all territories. For example, we anticipate we may need comparator studies for DZUVEO in Europe to ensure premium reimbursement in certain countries. Grünenthal does have products approved in international markets; however, Grünenthal's experience in international markets does not guarantee compliance with regulatory requirements in those markets. Similarly, while we have obtained approval of DZUVEO in Europe, even if we are successful in entering into a collaboration agreement with a commercial partner, we will be substantially dependent on that commercial partner to comply with regulatory requirements. If we, or our commercial partners, fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

DSUVIA requires, and, if approved, Zalviso will require, a REMS program.

DSUVIA was approved in the United States with a REMS program. If Zalviso is approved in the United States, it will also require a REMS program. The DSUVIA REMS program includes restrictions on product distribution and use only in certified medically supervised settings. Before DSUVIA is distributed, an authorized representative from each medically supervised setting must sign an attestation that they have the ability to manage acute opioid overdose and will train all relevant staff on administration of DSUVIA, including the importance of only dispensing the product in a medically supervised setting. Therefore, REMS-certification is a key gating item to generating product revenues for DSUVIA. In addition, the REMS program for DSUVIA may significantly increase our costs to commercialize this product. While we have received pre-clearance from the FDA regarding certain aspects of the proposed required REMS program for Zalviso, we cannot predict the final REMS program to be required as part of any FDA approval of Zalviso. Depending on the extent of the REMS requirements, any U.S. launch may be delayed, the costs to commercialize Zalviso may increase substantially and the potential commercial market could be restricted. Furthermore, risks of sufentanil that are not adequately addressed through the proposed REMS program for Zalviso may also prevent or delay its approval for commercialization.

Risks Related to Our Financial Condition and Need for Additional Capital

We have incurred significant losses since our inception, anticipate that we will continue to incur significant losses in 2020 and may continue to incur losses in the future.

We have incurred significant net losses in each year since our inception in July 2005, and as of December 31, 2019, we had an accumulated deficit of $398.1 million.

We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. To date, we have financed our operations primarily through the sale of equity securities, debt, government contract funding, the sale of royalties and milestones, and proceeds from our commercial partner, Grünenthal. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to generate revenues. We expect to continue to incur substantial expenses as we support commercialization activities for DSUVIA, conduct research and development activities, including the FDA regulatory review of the Zalviso NDA, once resubmitted, and support the manufacturing and supply of Zalviso in Europe for Grünenthal. While Grünenthal has begun European commercial sales of Zalviso, if DSUVIA is not successfully commercialized, or if Zalviso is not successfully developed or commercialized, or if revenues are insufficient following marketing approval, we will not achieve profitability and our business may fail. Our success is also dependent on current and future collaborations to market our products outside of the United States, which may not materialize or prove to be successful.

We have not yet generated significant product revenue and may never be profitable.

Our ability to generate revenue from commercial sales and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize our products. Although we received FDA approval of DSUVIA, and recently began the commercial launch of DSUVIA in the United States, we may never generate enough revenues from sales of DSUVIA, or Zalviso, if approved, in the United States to become profitable. Although DZUVEO was approved by the EC in June 2018, we have not yet entered into a collaboration agreement with a strategic partner to commercialize DZUVEO in Europe and there can be no assurance that we will successfully enter into such an agreement. While we have a collaboration agreement with Grünenthal for commercialization of Zalviso in Europe and Australia, Grünenthal may not achieve a level of commercial sales of Zalviso for which we would receive sales milestone payments.

In September 2015, we consummated a monetization transaction with PDL BioPharma, Inc., or PDL, pursuant to which we sold to PDL for $65.0 million 75% of the European royalties from sales of Zalviso and 80% of the first four commercial milestones under the License Agreement, subject to a capped amount, referred to as the Royalty Monetization. Accordingly, even if Grünenthal is successful in commercializing Zalviso in the Territory, we will receive only 25% of the royalties and 20% of the first four commercial milestones under the License Agreement, and 100% of the royalties after the capped amount is reached. We do not anticipate generating significant near-term revenues from DSUVIA or Zalviso, if approved, in the United States. Our ability to generate future revenues from product sales depends heavily on our success in:

- maintaining regulatory approval for DSUVIA and obtaining and maintaining regulatory approval for Zalviso in the United States; and
- launching and commercializing DSUVIA and Zalviso, if approved, in the United States by building, internally or through collaborations, an institutionally focused sales force, and launching and commercializing DZUVEO and Zalviso internationally by entering into collaborations, including with Grünenthal, which may require additional funding.

Because of the numerous risks and uncertainties associated with launching a commercial pharmaceutical product, pharmaceutical product development and the regulatory environment, we are unable to predict the timing or amount of increased expenses, or when, or if, we will be able to achieve or maintain profitability. Our expenses could increase beyond expectations if we are delayed in receiving regulatory approval for Zalviso in the United States, or if we are required by the FDA to complete activities in addition to those we currently anticipate or have already completed.

We anticipate continuing to incur significant costs associated with commercializing DSUVIA in the United States. Even if we are able to generate revenues from the sale of DSUVIA or Zalviso, if approved, in the United States, we may not become profitable and may need to obtain additional funding to continue operations.

We are substantially dependent on our commercial partner, Grünenthal, to successfully commercialize Zalviso in Europe.

Under our agreements with Grünenthal, we granted Grünenthal rights to commercialize Zalviso in the Territory for human use in pain treatment within, or dispensed by, hospitals, hospices, nursing homes and other medically supervised settings. In September 2015, the EC approved Grünenthal's MAA for Zalviso for the management of acute moderate-to-severe post-operative pain in adult patients, and Grünenthal began its European launch of Zalviso with the first commercial sale occurring in April 2016. There is no guarantee that Grünenthal will achieve commercial success in its Zalviso launch in the European Union or anywhere in the Territory.

During the pilot and launch phases in the various European countries, Grünenthal reported certain issues from HCPs with the initial set up of the Zalviso controllers before being given to patients for use. To address the issues, we have assisted Grünenthal with implementing additional training for HCPs and we have revised the controller software. Controllers with the revised software, which were delivered in December 2016, have undergone extensive bench testing and we believe we have successfully addressed the issues as presented. Additional devices were delivered beginning in early 2017. Controllers with the U.S. version of the revised software were also used in the IAP312 clinical study that was initiated in September 2016. There can be no assurance that the issues identified in the initial pilot and launch phases by Grünenthal will not have a material adverse impact on the current and future sales of Zalviso in Europe. Further, if new issues occur, there may be a material adverse impact on the future sales of Zalviso in Europe which may have a negative impact on future revenues received and recognized by us.

We may not realize the expected benefits from our collaboration with Grünenthal due to a number of important factors, including:

- The timing and amount of any payments we may receive under our agreements will depend on, among other things, the efforts, allocation of resources, and successful commercialization of Zalviso by Grünenthal in Europe;
- Grünenthal may change the focus of its commercialization efforts or pursue higher-priority programs;
- Grünenthal may reduce or stop its commercialization efforts in countries where it has the sole right to commercialize Zalviso; and
- Grünenthal may terminate its agreements with us, adversely affecting our potential revenue from Zalviso;

Any failures in commercialization of Zalviso outside the United States could have a material adverse impact on our business, including an adverse impact on the commercialization of DSUVIA or the development of Zalviso in the United States, if related to issues underlying the sufentanil sublingual tablet technology, safety or efficacy. Additionally, we agreed to certain representations and covenants relating to the Amended Agreements under our agreements with PDL, and, if we breach those representations or covenants, we may become subject to indemnification claims by PDL and liable to PDL for its indemnifiable losses relating to such breaches. The amount of such losses could be material and could have a material adverse impact on our business.

We have not yet entered into a collaboration agreement with a strategic partner for the commercialization of DZUVEO in Europe.

DZUVEO was approved by the EC in June 2018, but we have not yet entered into a collaboration agreement with a strategic partner to commercialize DZUVEO in Europe. If we are unable to enter into such an agreement, we may never generate revenues from sales of DZUVEO. If we are successful in identifying a commercial partner and entering into a collaboration agreement, we will be substantially dependent on this partner to successfully commercialize DZUVEO in Europe. Any failures in the commercialization of DZUVEO in Europe could have a significant adverse impact on our revenues and operating results.

Any future collaboration agreement for DZUVEO will likely require us to support the manufacturing and supply of the product in Europe for our commercial partner. In addition, we anticipate we may need comparator studies in Europe to ensure premium reimbursement in certain countries. Our inability to profitably manufacture and supply DZUVEO to any future commercial partner, or to successfully complete these additional comparator studies and obtain premium reimbursement in certain countries, may prevent, limit or delay commercialization and any associated future revenues from DZUVEO in Europe.

We may be unable to achieve the manufacturing cost reductions required in order to accommodate the declining transfer prices under the Amended Agreements without a corresponding decrease in our gross margin.

Under the Amended Agreements with Grünenthal, we sell Zalviso at a predetermined transfer price that is currently less than the direct cost of manufacture at our contract manufacturers. In addition, we do not recover internal indirect costs as part of the transfer price. Furthermore, the Amended Agreements include declining maximum transfer prices over the term of the contract with Grünenthal. These transfer prices were agreed to assuming economies of scale that would occur with increasing production volumes (from the potential approval of Zalviso in the U.S. and an increase in demand in Europe) and corresponding decreases in manufacturing costs. We do not have long-term supply agreements with our contract manufacturers and prices are subject to periodic changes. To date, we have not received U.S. approval of Zalviso and sales by Grünenthal in Europe have not been substantial. We do not expect sales by Grünenthal in Europe to be substantial in the foreseeable future. If we do not receive timely approval of Zalviso in the U.S., are unable to successfully launch Zalviso in the U.S., or the volume of Grünenthal sales does not increase significantly, we are unlikely to achieve the manufacturing cost reductions required in order to accommodate these declining transfer prices without a corresponding decrease in our gross margin on Zalviso product sales.

We have limited experience commercializing DSUVIA, which may make it difficult to predict our future performance or evaluate our business and prospects.

Since inception, our operations have been primarily focused on developing our technology and undertaking pharmaceutical development and clinical trials for DSUVIA and Zalviso, understanding the market potential for DSUVIA and Zalviso, and preparing for the commercialization of DSUVIA and the potential commercialization of Zalviso in the United States. We launched commercialization efforts for DSUVIA in February 2019. As a result of our limited commercialization experience, any predictions that are made about our future performance, or viability, or evaluation of our business and prospects, may not be accurate.

We will require additional capital and may be unable to raise capital, which would force us to delay, reduce or eliminate our commercialization efforts and product development programs and could cause us to cease operations.

Launch of a commercial pharmaceutical product and pharmaceutical development activities can be time consuming and costly. We expect to incur significant expenditures in connection with our ongoing activities including the commercial launch of DSUVIA in the United States and support for FDA regulatory review of the Zalviso NDA, once resubmitted. While we believe we have sufficient capital resources to continue planned operations through the end of the first quarter of 2021, we will need additional capital to pursue full commercialization of DSUVIA and Zalviso, if approved.

Clinical trials, regulatory reviews, and the launch of commercial product are expensive activities. In addition, commercialization costs for DSUVIA and Zalviso, if approved, in the United States may be significantly higher than estimated as a result of technical difficulties or otherwise. Revenues may be lower than expected and costs to produce such revenues may exceed those revenues. We will need to seek additional capital to continue operations. Such capital demands could be substantial. In the future, we may seek to sell additional equity securities, including under the Sales Agreement with Cantor, and debt securities, monetize or securitize certain assets including future royalty streams and milestones, refinance our loan agreement, obtain a revolving credit facility, enter into product development, license or distribution agreements with third parties, or divest DSUVIA or Zalviso. Such arrangements may not be available on favorable terms, if at all.

Future events and circumstances, including those beyond our control, may cause us to consume capital more rapidly than we currently anticipate. Furthermore, any product development, licensing, distribution or sale agreements that we enter into may require us to relinquish valuable rights. We may not be able to obtain sufficient additional funding or enter into a strategic transaction in a timely manner. If adequate funds are not available, we would be required to reduce our workforce, reduce the scope of, or cease, the commercial launch of DSUVIA, or the development of Zalviso in advance of the date on which we exhaust our cash resources to ensure that we have sufficient capital to meet our obligations and continue on a path designed to preserve stockholder value.

Securing additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to commercialize DSUVIA or develop Zalviso. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly scale back or discontinue the commercialization of DSUVIA, or the development of Zalviso;
- seek additional corporate partners for Zalviso on terms that might be less favorable than might otherwise be available;
- seek corporate partners for DSUVIA/DZUVEO on terms that might be less favorable than might otherwise be available; or
- relinquish, or license on unfavorable terms, our rights to technologies or products that we otherwise would seek to develop or commercialize ourselves.

To fund our operations, we may sell additional equity securities, which may result in dilution to our stockholders, or debt securities, which may impose restrictions on our business.

We expect that significant additional capital will be needed in the future to continue our planned operations. In order to raise additional funds to support our operations, we may sell additional equity securities, including under the Controlled Equity Offering℠ Sales Agreement, or the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent. We may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. Selling additional equity securities may result in dilution to our existing stockholders and new investors may be materially diluted by subsequent sales. Incurring additional indebtedness, including through the sale of debt securities, would result in increased fixed payment obligations and could also result in additional restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions, such as minimum cash balances, that could adversely impact our ability to conduct our business. Sales of equity or debt securities may also provide new investors with rights superior to our existing stockholders. If we are unable to expand our operations or otherwise capitalize on our business opportunities, our business, financial condition and results of operations could be materially adversely affected, and we may not be able to meet our debt service obligations.

The terms of our loan agreement with Oxford may restrict our current and future operations, particularly our ability to respond to changes in business or to take certain actions, including to pay dividends to our stockholders.

On May 30, 2019, the Company entered into the Loan Agreement with Oxford Finance LLC, or Oxford, a Delaware limited liability company, as the Lender. The Loan Agreement contains, and any future indebtedness we incur will likely contain, a number of restrictive covenants that impose operating restrictions, including restrictions on our ability to engage in acts that may be in our best long-term interests. The Loan Agreement includes covenants that, among other things, restrict our ability to (i) declare dividends or redeem or repurchase equity interests; (ii) incur additional liens; (iii) make loans and investments; (iv) incur additional indebtedness; (v) engage in mergers, acquisitions, and asset sales; (vi) transact with affiliates; (vii) undergo a change in control; (viii) add or change business locations; and (ix) engage in businesses that are not related to our existing business. The Loan Agreement also requires that we at all times maintain unrestricted cash of not less than $5.0 million.

A breach of any of these covenants could result in an event of default under the Loan Agreement. Upon the occurrence of such an event of default, a default interest rate of an additional 5% may be applied to the outstanding loan balances and all outstanding obligations under the Loan Agreement can be declared to be immediately due and payable If our indebtedness is accelerated, we cannot assure you that we will have sufficient assets to repay the indebtedness. The restrictions and covenants in the Loan Agreement and any future financing agreements may adversely affect our ability to finance future operations or capital needs or to engage in other business activities.

We might be unable to service our existing debt due to a lack of cash flow and might be subject to default.

As of December 31, 2019, we have approximately $24.2 million of accrued debt under the Loan Agreement. The Loan Agreement has a scheduled maturity date of June 1, 2023 and is secured by a first priority security interest in substantially all of our assets, with the exception of our intellectual property and those assets sold under the Royalty Monetization, where the security interest is limited to proceeds of intellectual property if it is licensed or sold.

If we do not make the required payments when due, either at maturity, or at applicable installment payment dates, or if we breach the agreement or become insolvent, the Lender could elect to declare all amounts outstanding, together with accrued and unpaid interest, and other payments, to be immediately due and payable. Additional capital may not be available on terms acceptable to us, or at all. Even if we were able to repay the full amount in cash, any such repayment could leave us with little or no working capital for our business. If we are unable to repay those amounts, the Lender will have a first claim on our assets pledged under the Loan Agreement. If the Lender should attempt to foreclose on the collateral, it is unlikely that there would be any assets remaining after repayment in full of such secured indebtedness. Any default under the Loan Agreement and resulting foreclosure would have a material adverse effect on our financial condition and our ability to continue our operations.

Risks Related to Our Reliance on Third Parties

We rely on third party manufacturers to produce commercial supplies of DSUVIA in the United States, commercial supplies of Zalviso in Europe, and clinical supplies of Zalviso in the United States. The failure of third party manufacturers to provide us with adequate commercial and clinical supplies could result in a material adverse effect on our business.

Third party manufacturers produce commercial and clinical supplies of our products and product candidates. Reliance on third party manufacturers entails many risks including:

- the inability to meet our product specifications and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to maintain in good order our production and manufacturing equipment for our products;
- a failure to comply with cGMP and similar foreign standards;
- the inability to negotiate manufacturing or supply agreements with third parties under commercially reasonable terms;

- termination or nonrenewal of manufacturing or supply agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our products in a timely fashion, in sufficient quantities or under acceptable terms;
- the lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control; and
- the failure to deliver our products under specified storage conditions and in a timely manner.

Any of these events could lead to stock outs, inability to successfully commercialize our products, clinical trial delays, or failure to obtain regulatory approval. Some of these events could be the basis for FDA action, including injunction, recall, seizure, or total or partial suspension of production.

In addition, we have not yet entered into a collaboration agreement for the sale of DZUVEO in Europe, but we anticipate that any future collaboration agreement will likely require us to manufacture and supply DZUVEO to our commercial partner. As mentioned above, we are obligated to manufacture and supply Zalviso under the Amended Agreements with Grünenthal for use in Europe and their other licensed territories. If we are unable to establish a reliable commercial supply of Zalviso for Grünenthal's Territory, we may be unable to satisfy our obligations under the Amended Agreements in a timely manner or at all, and we may, as a result, be in breach of the Amended Agreements. If any such breach, or other breach, were to be material and remain uncured, it could result in Grünenthal terminating the Amended Agreements, which in turn could result in us being responsible for indemnification of losses suffered by PDL under the Royalty Monetization. If any of these events were to occur, our business would be materially adversely affected.

We rely on limited sources of supply for the active pharmaceutical ingredient, or API, of DSUVIA and Zalviso and any disruption in the chain of supply may cause a delay in commercializing DSUVIA and developing Zalviso.

Currently we only have one supplier qualified as a vendor for the manufacture of DSUVIA, known as DZUVEO in Europe, and Zalviso with the FDA and EMA, respectively. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. For example, our API provider for DSUVIA is changing its process for manufacturing our drug, which could impact our commercial supply of API for DSUVIA. This change in process requires a regulatory submission to the FDA. The European Health Authority has approved the change in process for both DZUVEO and Zalviso in the EU. In the U.S. a regulatory submission has been submitted to support the use of the API made with the new manufacturing process, but there is no guarantee that the FDA will approve the submission. For example, in July 2019, we received notice from the FDA that a deficiency in the API manufacturer's drug master file will need to be addressed before the submission can be approved. Any alternate vendor would need to be qualified through an NDA supplement and/or an MAA variation which could result in delays. The FDA or other regulatory agencies outside of the United States may also require additional trials if a new sufentanil supplier is relied upon for commercial production.

Manufacture of sufentanil sublingual tablets requires specialized equipment and expertise.

Ethanol, which is used in the manufacturing process for our sufentanil sublingual tablets, is flammable, and sufentanil is a highly potent, Schedule II controlled substance. These factors necessitate the use of specialized equipment and facilities for manufacture of sufentanil sublingual tablets. There are a limited number of facilities that can accommodate our manufacturing process and we need to use dedicated equipment throughout development and commercial manufacturing to avoid the possibility of cross-contamination. If our equipment breaks down or needs to be repaired or replaced, it may cause significant disruption in clinical or commercial supply, which could result in delay in the process of obtaining approval for or sale of our products. Furthermore, we are using one manufacturer to produce our sufentanil sublingual tablets. Any problems with our existing facility or equipment, including ongoing expansion, may impair our ability to successfully commercialize DSUVIA or Zalviso, if approved, complete our clinical trials and increase our cost.

Manufacturing issues may arise that could delay or increase costs related to commercialization, product development and regulatory approval.

Our experience with manufacturing and shipping both DSUVIA and Zalviso is limited. We have relied, and will continue to rely, on contract manufacturers, component fabricators and third-party service providers to produce the necessary DSUVIA single-dose applicator, or SDA, and Zalviso devices for the commercial marketplace. We currently outsource manufacturing and packaging of the DSUVIA SDA and the controller, dispenser and cartridge components of the Zalviso device to third parties and intend to continue to do so. Some of these component purchases were made and will continue to be made utilizing short-term purchase agreements and we may not be able to enter into long-term agreements for commercial supply of DSUVIA, DZUVEO or Zalviso devices with each of the third-party manufacturers or may be unable to do so on acceptable terms. In addition, we have encountered and may continue to encounter production issues with our current or future contract manufacturers and other third party service providers, including the reliability of the production equipment, quality of the components produced, their inability to meet demand or other unanticipated delays including scale-up and automating processes, which could adversely impact our ability to supply our customers with DSUVIA, Zalviso and DZUVEO in Europe, and, if approved, Zalviso in the U.S. and any other foreign territories.

As we scale up manufacturing of DSUVIA and Zalviso, if approved, and conduct required stability testing, product, packaging, equipment and process-related issues may require refinement or resolution. For example, as we scale up, we may identify significant issues which could result in failure to maintain regulatory approval of DSUVIA, increased scrutiny by regulatory agencies, delays in clinical program and regulatory approval, increases in our operating expenses, or failure to obtain approval for Zalviso in the United States.

We have built out a suite within Patheon's production facility in Cincinnati, Ohio that serves as a manufacturing facility for clinical and commercial supplies of sufentanil sublingual tablets. Late stage development and manufacture of registration stability lots, which were utilized in clinical trials, were manufactured at this location. While we have produced a number of commercial lots at Patheon to support Grünenthal's launch in Europe, our experience is limited, which has impacted, and may in the future impact, our ability to deliver commercial supplies to Grünenthal on a timely basis.

In January 2013, we entered into a Manufacturing Services Agreement, or the Services Agreement, with Patheon under which Patheon has agreed to manufacture, supply, and provide certain validation and stability services with respect to Zalviso for potential sales in the United States, Canada, Mexico and other countries, subject to agreement by the parties to any additional fees for such other countries. On August 22, 2017, we entered into an amendment to the Services Agreement with Patheon under which Patheon has agreed to manufacture, supply, and provide certain validation and stability services with respect to DSUVIA for sales in the United States, and potential sales in Canada and Mexico, and other countries. There is no guarantee that Patheon's services will be satisfactory or that they will continue to meet the strict regulatory guidelines of the FDA or other foreign regulatory agencies. If Patheon cannot provide us with an adequate supply of sufentanil sublingual tablets, we may be required to pursue alternative sources of manufacturing capacity. Switching or adding commercial manufacturing capability can involve substantial cost and require extensive management time and focus, as well as additional regulatory filings which may result in significant delays. In addition, there is a natural transition period when a new manufacturing facility commences work. As a result, delays may occur, which can materially impact our ability to meet our desired commercial timelines, thereby increasing our costs and reducing our ability to generate revenue.

The facilities of any of our future manufacturers of sufentanil-containing sublingual tablets must be approved by the FDA or the relevant foreign regulatory agency, such as the EMA, before commercial distribution from such manufacturers occurs. We do not fully control the manufacturing process of sufentanil sublingual tablets and are completely dependent on these third-party manufacturing partners for compliance with the FDA or other foreign regulatory agency's requirements for manufacture. In addition, although our third-party manufacturers are well-established commercial manufacturers, we are dependent on their continued adherence to cGMP manufacturing and acceptable changes to their process. If our manufacturers do not meet the FDA or other foreign regulatory agency's strict regulatory requirements, they will not be able to secure FDA or other foreign regulatory agency approval for their manufacturing facilities. Although European inspectors have approved our tablet manufacturing site, our third-party manufacturing partner is responsible for maintaining compliance with the relevant foreign regulatory agency's requirements. If the FDA or the relevant foreign regulatory agency does not approve these facilities for the commercial manufacture of sufentanil sublingual tablets, we will need to find alternative suppliers, which would result in significant delays in obtaining FDA approval for Zalviso, and other foreign regulatory agency approval of DSUVIA/DZUVEO and Zalviso outside Europe. These challenges may have a material adverse impact on our business, results of operations, financial condition and prospects.

We may not be able to establish additional sources of supply for sufentanil-containing sublingual tablets or device manufacture. Such suppliers are subject to FDA and other foreign regulatory agency's regulations requiring that materials be produced under cGMPs or Quality System Regulations, or QSR, or in ISO 13485 accredited manufacturers, and subject to ongoing inspections by regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in delays and interruptions to our product supply while we seek to secure another supplier that meets all regulatory requirements. In addition, if we are unable to establish a reliable commercial supply of Zalviso for Grünenthal's Territory, we may be unable to satisfy our obligations under the Amended Agreements in a timely manner or at all, and we may, as a result, be in breach of the Amended Agreements.

For DSUVIA, we currently package the finished goods under a manual process at the Sharp facility and would package finished goods of DZUVEO at the Sharp facility in the same manner. The capacity and cost to package the finished goods under this manual process is not optimal to support successful future sales of DSUVIA and DZUVEO. We have initiated the process to purchase an automated filling and packaging line to support increased capacity packaging for DSUVIA and DZUVEO. We expect to complete the acquisition and installation of this line in 2020. There is no assurance that we will be able to successfully purchase, install or validate the automated filling and packaging line for DSUVIA and DZUVEO. If we are successful in the purchase, installation and validation of this equipment and process, there can be no assurance that we will be able to obtain the necessary regulatory approvals to manufacture product on this line.

We rely on third parties to conduct, supervise and monitor our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We utilized contract research organizations, or CROs, for the conduct of the Phase 2 and 3 clinical trials of DSUVIA, as well as our Phase 3 clinical program for Zalviso. We rely on CROs, as well as clinical trial sites, to ensure the proper and timely conduct of our clinical trials and document preparation. While we have agreements governing their activities, we have limited influence over their actual performance. We have relied and plan to continue to rely upon CROs to monitor and manage data for our post-approval clinical programs for DSUVIA and any FDA-required clinical programs for Zalviso, as well as the execution of nonclinical and clinical trials. We control only certain aspects of our CROs' activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We, and our CROs, are required to comply with the FDA's current good clinical practices, or cGCPs, which are regulations and guidelines enforced by the FDA for all product candidates in clinical development. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA may determine that our clinical trials do not comply with cGCPs. Accordingly, if our CROs or clinical trial sites fail to comply with these regulations, we may be required to repeat clinical trials, which would delay the regulatory process.

Our CROs are not our employees, and we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may allow our potential competitors to access our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize Zalviso. As a result, our financial results and the commercial prospects for Zalviso, if approved, would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

Risks Related to Our Business Operations and Industry

Failure to receive required quotas of controlled substances or comply with the Drug Enforcement Agency regulations, or the cost of compliance with these regulations, may adversely affect our business.

Our sufentanil-based products are subject to extensive regulation by the DEA, due to their status as scheduled drugs. Sufentanil is classified as a Schedule II controlled substance, considered to present a high risk of abuse. The manufacture, shipment, storage, sale and use of controlled substances are subject to a high degree of regulation, including security, record-keeping and reporting obligations enforced by the DEA and also by comparable state agencies. In addition, our contract manufacturers are required to maintain relevant licenses and registrations. This high degree of regulation can result in significant compliance costs, which may have an adverse effect on the commercialization of DSUVIA and the development and commercialization of Zalviso, if approved.

The DEA limits the availability and production of all Schedule II controlled substances, including sufentanil, through a quota system. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. Our contract manufacturers apply for quotas on our behalf. We will need significantly greater amounts of sufentanil to successfully commercialize DSUVIA, implement Grünenthal's European commercialization plans for Zalviso, to support European commercialization of DZUVEO and to commercialize Zalviso, if approved in the United States. Any delay by the DEA in establishing the procurement quota, reduction in our quota for sufentanil, failure to increase our quota over time to meet anticipated increases in demand, or refusal by the DEA to establish the procurement quota could delay or stop the commercial sale of our approved products or the clinical development of Zalviso in the United States. This, in turn, could have a material adverse effect on our business, results of operations, financial condition and prospects.

Our relationships with clinical investigators, health care professionals, consultants, commercial partners, third-party payers, hospitals, and other customers are subject to applicable anti-kickback, fraud and abuse and other healthcare laws, which could expose us to penalties.

Healthcare providers, physicians and others play a primary role in the recommendation and prescribing of any products for which we may obtain marketing approval. Our business operations and arrangements with investigators, healthcare professionals, consultants, commercial partners, hospitals, third-party payers and customers may expose us to broadly applicable fraud and abuse and other healthcare laws. These laws may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute the products for which we obtain marketing approval. Applicable federal and state healthcare laws include, but are not limited to, the following:

- the federal healthcare Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which, among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payer (e.g., public or private) and knowingly or willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which impose certain obligations, including mandatory contractual terms, on covered healthcare providers, health plans and clearinghouses, as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- foreign laws, regulations, standards and regulatory guidance which govern the collection, use, disclosure, retention, security and transfer of personal data, including the European Union General Data Privacy Regulation, or GDPR, which introduces strict requirements for processing personal data of individuals within the European Union;

- the federal transparency law, enacted as part of the Affordable Care Act, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologicals and medical supplies to report annually to the CMS information related to payments and other transfers of value provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- analogous state laws that may apply to our business practices, including but not limited to, state laws that require pharmaceutical companies to implement compliance programs and/or comply with the pharmaceutical industry's voluntary compliance guidelines; state laws that impose restrictions on pharmaceutical companies' marketing practices and require manufacturers to track and file reports relating to pricing and marketing information, which requires tracking and reporting gifts, compensation and other remuneration and items of value provided to healthcare professionals and entities, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, with differing effects; and,

- the federal Foreign Corrupt Practices Act of 1977, United Kingdom Bribery Act 2010 and other similar anti-bribery laws in other jurisdictions which generally prohibit companies and their intermediaries from providing money or anything of value to officials of foreign governments, foreign political parties, or international organizations with the intent to obtain or retain business or seek a business advantage.

Recently, there has been a substantial increase in anti-bribery law enforcement activity by U.S. regulators, with more frequent and aggressive investigations and enforcement proceedings by both the Department of Justice and the SEC. A determination that our operations or activities are not, or were not, in compliance with United States or foreign laws or regulations could result in the imposition of substantial fines, interruptions of business, loss of supplier, vendor or other third-party relationships, termination of necessary licenses and permits, and other legal or equitable sanctions. Other internal or government investigations or legal or regulatory proceedings, including lawsuits brought by private litigants, may also follow as a consequence.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of these or any other healthcare regulatory laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, increased losses and diminished profits, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations any of which could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses or divert our management's attention from the operation of our business.

In order to supply the Zalviso device to Grünenthal for commercial sales, we must maintain conformity of our quality system to applicable ISO standards and must comply with applicable European laws and directives.

We underwent a Conformité Européenne approval process for the Zalviso device, more commonly known as a CE Mark approval process. We received CE Mark approval in December 2014, which permits the commercial sale of the Zalviso device in Europe. In connection with the CE Mark approval, we were also granted International Standards Organization, or ISO, 13485:2003 certification of our quality management system in November 2014. This is an internationally recognized quality standard for medical devices. The CE Mark was originally issued by the British Standards Institution, or BSI, a Notified Body, or NB, located in the United Kingdom, or U.K., or BSI-U.K. The CE Mark file and certification has been transferred to the Netherlands NB of BSI, or BSI-NL, to mitigate the uncertainty with regards to Brexit. The ISO certification issued through BSI-U.K. was recently upgraded to the latest version of the standard, ISO 13485:2016 through BSI-U.K. and remains in effect. BSI ISO 13485:2016 certification recognizes that consistent quality policies and procedures are in place for the development, design and manufacturing of medical devices. The certification indicates that we have successfully implemented a quality system that conforms to ISO 13485 standards for medical devices. Certification to this standard is one of the key regulatory requirements for a CE Mark in the EU and European Economic Area (which includes the 27 EU member states as well as Norway, Iceland and Liechtenstein), or EEA, as well as to meet equivalent requirements in other international markets. The certification applies to the Redwood City, California location which designs, manufactures and distributes finished medical devices, and includes critical suppliers. If we fail to remain in compliance with applicable European laws and directives, we would be unable to continue to affix the CE Mark to our Zalviso device, which would prevent Grünenthal from selling these devices within the EU and EEA.

Significant disruptions of our information technology systems or data security incidents could result in significant financial, legal, regulatory, business and reputational harm to us.

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, store, process and transmit large amounts of sensitive information, including intellectual property, proprietary business information, personal information and other confidential information. It is critical that we do so in a secure manner to maintain the confidentiality, integrity and availability of such sensitive information. We have also outsourced elements of our operations (including elements of our information technology infrastructure) to third parties, and as a result, we manage a number of third-party vendors who may or could have access to our computer networks or our confidential information. In addition, many of those third parties in turn subcontract or outsource some of their responsibilities to third parties. While all information technology operations are inherently vulnerable to inadvertent or intentional security breaches, incidents, attacks and exposures, the accessibility and distributed nature of our information technology systems, and the sensitive information stored on those systems, make such systems potentially vulnerable to unintentional or malicious internal and external attacks on our technology environment. Potential vulnerabilities can be exploited from inadvertent or intentional actions of our employees, third-party vendors, business partners, or by malicious third parties. Attacks of this nature are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives (including, but not limited to, industrial espionage) and expertise, including organized criminal groups, "hacktivists," nation states and others. In addition to the extraction of sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. In addition, the prevalent use of mobile devices increases the risk of data security incidents.

Significant disruptions of our third-party vendors' and/or business partners' information technology systems or other similar data security incidents could adversely affect our business operations and result in the loss, misappropriation, and/or unauthorized access, use or disclosure of, or the prevention of access to, sensitive information, which could result in financial, legal, regulatory, business and reputational harm to us. In addition, information technology system disruptions, whether from attacks on our technology environment or from computer viruses, natural disasters, terrorism, war and telecommunication and electrical failures, could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

There is no way of knowing with certainty whether we have experienced any data security incidents that have not been discovered. While we have no reason to believe this to be the case, attackers have become very sophisticated in the way they conceal access to systems, and many companies that have been attacked are not aware that they have been attacked. Any event that leads to unauthorized access, use or disclosure of personal information, including but not limited to personal information regarding our patients or employees, could disrupt our business, harm our reputation, compel us to comply with applicable federal and state breach notification laws and foreign law equivalents, subject us to time consuming, distracting and expensive litigation, regulatory investigation and oversight, mandatory corrective action, require us to verify the correctness of database contents, or otherwise subject us to liability under laws, regulations and contractual obligations, including those that protect the privacy and security of personal information. This could result in increased costs to us, and result in significant legal and financial exposure and/or reputational harm. In addition, any failure or perceived failure by us or our vendors or business partners to comply with our privacy, confidentiality or data security-related legal or other obligations to third parties, or any further security incidents or other inappropriate access events that result in the unauthorized access, release or transfer of sensitive information, which could include personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation, or public statements against us by advocacy groups or others, and could cause third parties, including clinical sites, regulators or current and potential partners, to lose trust in us or we could be subject to claims by third parties that we have breached our privacy- or confidentiality-related obligations, which could materially and adversely affect our business and prospects. Moreover, data security incidents and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or security incidents.

Business interruptions could delay us in the process of developing our products and could disrupt our sales.

Our headquarters is located in the San Francisco Bay Area, near known earthquake fault zones and is vulnerable to significant damage from earthquakes. Our contract manufacturers, suppliers, clinical trial sites and local and national transportation vendors are all subject to business interruptions due to weather, outbreaks of pandemic diseases, natural disasters, or man-made incidents.

In addition, our business could be adversely affected by the effects of health epidemics, including the recent COVID-19 outbreak. If the COVID-19 outbreak continues to spread, we may need to limit operations or implement limitations, including work from home policies. Moreover, if hospitals or other healthcare facilities begin implementing policies that limit access of our sales representatives to such facilities, we may be delayed or thwarted in selling our product. In addition, if hospitals and doctors, as a measure to combat the further spread of COVID-19, reduce the number of procedures in which DSUVIA is administered as part of the pain treatment program, or if surgeons temporarily halt performing elective surgeries, the levels of our sales could be adversely effected. The ultimate impact of the COVID-19 outbreak is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

We are also vulnerable to other types of natural disasters and other events that could disrupt our operations. We do not carry insurance for earthquakes or other natural disasters, and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. Recruiting and retaining qualified scientific, manufacturing, and commercial personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. In addition, failure to succeed in clinical trials, or delays in the regulatory approval process, may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive or key employee might impede the progress of our research, development and commercialization objectives.

We may acquire companies, product candidates or products or engage in strategic transactions, which could divert our management's attention and cause us to incur various costs and expenses.

We may acquire or invest in companies, product candidates or products that we believe could complement or expand our business or otherwise offer growth opportunities. The pursuit of potential acquisitions or investments may divert the attention of management and may cause us to incur various costs and expenses in identifying, investigating, and pursuing them, whether or not they are consummated. We may not be able to identify desirable acquisitions or investments or be successful in completing or realizing anticipated benefits from such transactions.

In addition, we may receive inquiries relating to potential strategic transactions, including collaborations, licenses, and acquisitions. Such potential transactions may divert the attention of management and may cause us to incur various costs and expenses in investigating and evaluating such transactions, whether or not they are consummated.

We face potential product liability claims, and, if such claims are successful, we may incur substantial liability.

Commercial sales of DSUVIA and Zalviso expose us to the risk of product liability claims. Product liability claims might be brought against us by patients, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our products; and,
- decreased demand for our products.

Our current product liability insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. In addition, our current product liability insurance contains an exclusion related to any claims related to our products from a governmental body, or payer, or those claims arising from a multi-plaintiff action for bodily injury or property damage. Multi-plaintiff claims caused by product defects are covered. This exclusion does not apply to any bodily injury claim related to our products made by an individual. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments are excluded from our insurance coverage or exceed our insurance coverage, could adversely affect our results of operations and business. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability.

Our insurance coverage includes the sale of Zalviso to our commercial partner, Grünenthal. We intend to commercialize and promote DZUVEO in Europe with a strategic partner which may result in further expansion of our insurance coverage to include sales of DZUVEO in Europe. There can be no assurance that such coverage will be adequate to protect us against any future losses due to liability.

Our employees, independent contractors, principal investigators, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, investigators, consultants, commercial partners and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct that violates (1) regulations implemented by the FDA and similar foreign regulatory bodies; (2) laws requiring the reporting of true, complete and accurate information to such regulatory bodies; (3) healthcare fraud and abuse laws of the United States and similar foreign fraudulent misconduct laws; and (4) laws requiring the reporting of financial information or data accurately. The promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry are subject to extensive laws designed to prevent misconduct, including fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of pricing, discounting, marketing, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. It is not always possible to identify and deter employee and other third-party misconduct. The precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws. If any such actions are instituted against us, and we are not successful in defending ourselves, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, imprisonment, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar agreements to resolve allegations of non-compliance with these laws, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Our Intellectual Property

If we cannot defend our issued patents from third party claims or if our pending patent applications fail to issue, our business could be adversely affected.

To protect our proprietary technology, we rely on patents as well as other intellectual property protections including trade secrets, nondisclosure agreements, and confidentiality provisions. As of December 31, 2019, we are the owner of record of 76 issued patents worldwide. These issued patents cover AcelRx's sufentanil sublingual tablet, medication delivery devices and other platform technology. These issued patents, inclusive of the patents we have listed in the FDA's Orange Book for DSUVIA, are expected to provide coverage until at least 2027 – 2031.

Because sufentanil is not a new chemical entity, its regulatory exclusivity period in the United States is limited to three years under the Hatch-Waxman Act. While the FDA may not approve a 505(b)(2) NDA or abbreviated new drug application, or ANDA, using DSUVIA as its reference listed drug prior to November 2, 2021, we may be subject to certification based on the patents we have listed in the FDA's Orange Book for DSUVIA and engage in litigation against such a 505(b)(2) or ANDA applicant at any time.

In addition, we are pursuing a number of U.S. non-provisional patent applications and foreign national applications directed to DSUVIA and Zalviso. The patent applications that we have filed and have not yet been granted may fail to result in issued patents in the United States or in foreign countries. Even if the patents do successfully issue, third parties may challenge the patents.

Our commercial success will depend in part on successfully defending our current patents against third party challenges and expanding our existing patent portfolio to provide additional layers of patent protection, as well as extending patent protection. There can be no assurance that we will be successful in defending our existing and future patents against third party challenges, or that our pending patent applications will result in additional issued patents.

The patent positions of pharmaceutical companies, including ours, can be highly uncertain and involve complex and evolving legal and factual questions. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. Legal developments may preclude or limit the scope of available patent protection.

There is also no assurance that any patents issued to us will not become the subject of adversarial proceedings such as opposition, inter partes review, post-grant review, reissue, supplemental examination, re-examination or other post-issuance proceedings. In addition, there is no assurance that the respective court or agency in such adversarial proceedings would not make unfavorable decisions, such as reducing the scope of a patent of ours or determining that a patent of ours is invalid or unenforceable. There is also no assurance that any patents issued to us will provide us with competitive advantages, will not be challenged by any third parties, or that the patents of others will not prevent the commercialization of products incorporating our technology. Furthermore, there can be no guarantee that others will not independently develop similar products, duplicate any of our products, or design around our patents.

Litigation involving patents, patent applications and other proprietary rights is expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing our products to market and interfere with our business.

Our commercial success depends in part on not infringing patents and proprietary rights of third parties. Although we are not currently aware of litigation or other proceedings or third-party claims of intellectual property infringement related to DSUVIA or Zalviso, the pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights.

As we enter our target markets, it is possible that competitors or other third parties will claim that our products and/or processes infringe on their intellectual property rights. These third parties may have obtained and may in the future obtain patents covering products or processes that are similar to, or may include compositions or methods that encompass our technology, allowing them to claim that the use of our technologies infringes on these patents.

In a patent infringement claim against us, we may assert, as a defense, that we do not infringe the relevant patent claims, that the patent is invalid or both. The strength of our defenses will depend on the patents asserted, the interpretation of these patents, and our ability to invalidate the asserted patents. However, we could be unsuccessful in advancing non-infringement and invalidity arguments in our defense. In the United States, issued patents enjoy a presumption of validity, and the party challenging the validity of a patent claim must present clear and convincing evidence of invalidity, which is a high burden of proof. Conversely, the patent owner need only prove infringement by a preponderance of the evidence, which is a lower burden of proof.

If we were found by a court to have infringed a valid patent claim, we could be prevented from using the patented technology and be required to pay the owner of the patent for damages for past sales and for the right to license the patented technology for future sales. If we decide to pursue a license to one or more of these patents, we may not be able to obtain a license on commercially reasonable terms, if at all, or the license we obtain may require us to pay substantial royalties or grant cross licenses to our patent rights. For example, if the relevant patent is owned by a competitor, that competitor may choose not to license patent rights to us. If we decide to develop alternative technology, we may not be able to do so in a timely or cost-effective manner, if at all.

In addition, because patent applications can take years to issue and are often afforded confidentiality for some period of time there may currently be pending applications, unknown to us, that later result in issued patents that could cover one or more of our products.

It is possible that we may in the future receive communications from competitors and other companies alleging that we may be infringing their patents, trade secrets or other intellectual property rights, offering licenses to such intellectual property or threatening litigation. In addition to patent infringement claims, third parties may assert copyright, trademark or other proprietary rights against us. We may need to expend considerable resources to counter such claims and may not be successful in our defense. Our business may suffer if a finding of infringement is established.

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.

The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. The pharmaceutical patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property.

We cannot predict the breadth of claims that may be allowed or enforced in the patents that may be issued from the applications we currently, or may in the future, own or license from third parties. Claims could be brought regarding the validity of our patents by third parties and regulatory agencies. Further, if any patent license we obtain is deemed invalid and/or unenforceable, it could impact our ability to commercialize or partner our technology.

Competitors or third parties may infringe our patents. We may decide it is necessary to file patent infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or that the third party's technology does not in fact infringe upon our patents. An adverse determination of any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our related pending patent applications at risk of not issuing. Litigation may fail and, even if successful, may result in substantial costs and be a distraction to our management. We may not be able to prevent misappropriation of our proprietary rights, particularly in countries outside the United States where patent rights may be more difficult to enforce. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential or sensitive information could be compromised by disclosure in the event of litigation. In addition, during the course of litigation there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- we were the first to make the inventions covered by each of our pending patent applications or issued patents;
- our patent applications were filed before the inventions covered by each patent or patent application was published by a third party;
- we were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents issued to us or our collaborators will provide a basis for commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties; or,
- the patents of others will not have an adverse effect on our business.

If we do not adequately protect our proprietary rights, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could materially harm our business, negatively affect our position in the marketplace, limit our ability to commercialize DSUVIA and Zalviso, if approved, and delay or render impossible our achievement of profitability.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary know-how and technological advances, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. Failure to obtain or maintain trade secret protection could enable competitors to use our proprietary information to develop products that compete with our products or cause additional, material adverse effects upon our competitive business position.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications will be due to be paid to the United States Patent and Trademark Office and various foreign governmental patent agencies in several stages over the lifetime of the patents and/or applications.

We have systems in place, including use of third party vendors, to manage payment of periodic maintenance fees, renewal fees, annuity fees and various other patent and application fees. The United States Patent and Trademark Office, or the USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. There are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If this occurs, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may not be able to enforce our intellectual property rights throughout the world.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. Additionally, claims may be brought regarding the validity of our patents by third parties and regulatory agencies in the United States and foreign countries. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of intellectual property.

We have not yet registered our trademarks in all our potential markets, and failure to secure those registrations could adversely affect our business.

We have registered our ACELRX mark in the United States, Canada, the EU and India. In early 2014, the FDA accepted the Zalviso mark and, in November 2018, the FDA accepted the DSUVIA mark. Although we are not currently aware of any oppositions to or cancellations of our registered trademarks or pending applications, it is possible that one or more of the applications could be subject to opposition or cancellation after the marks are registered. The registrations will be subject to use and maintenance requirements. It is also possible that we have not yet registered all of our trademarks in all of our potential markets, such as securing the registration of DSUVIA in Canada, and that there are names or symbols other than “ACELRX” that may be protectable marks for which we have not sought registration, and failure to secure those registrations could adversely affect our business. Opposition or cancellation proceedings may be filed against our trademarks and our trademarks may not survive such proceedings.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may be highly volatile.

The trading price of our common stock has experienced significant volatility and is likely to be volatile in the future. For example, the closing price or our common stock ranged between $3.93 and $1.66 during 2019. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- failure to successfully commercialize DSUVIA in the United States or to successfully develop and commercialize Zalviso in the United States;
- inability to obtain additional funding;
- the integration and performance of any businesses we acquire;
- the perception of limited market sizes or pricing for our products;

- further delays in resubmitting the NDA for Zalviso, and any additional adverse developments or perceived adverse developments with respect to the FDA's review of the Zalviso NDA, upon resubmission;
- safety issues;
- adverse results or delays in future clinical trials;
- changes in laws or regulations applicable to our products;
- inability to obtain adequate product supply for our products, or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- changes in the structure of the healthcare payment systems;
- inability to maintain ISO 13485 certification and CE Mark approval for Zalviso;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- decisions by our collaboration partners regarding market access, pricing, and commercialization efforts in countries where they have the right to commercialize our products;
- failure to maintain our existing collaborations or enter into new collaborations;
- the perception of the pharmaceutical industry generally, and of opioid manufacturers more specifically, by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or other significant transactions, including disposition transactions, or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key management or scientific personnel;
- costs associated with potential governmental investigations, inquiries, regulatory actions or lawsuits that may be brought against us as a result of us being an opioid manufacturer;
- other types of significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, the stock market in general, and The Nasdaq Global Market, or Nasdaq, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Sales of a substantial number of shares of our common stock in the public market by our stockholders could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. Our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants under our equity incentive plans. Grants under our equity incentive plans may also cause our stockholders to experience additional dilution, which could cause our stock price to fall. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. All of our shares of common stock outstanding are eligible for sale in the public market, subject in some cases to the volume limitations and manner of sale requirements of Rule 144 under the Securities Act. Sales of stock by our stockholders could have a material adverse effect on the trading price of our common stock.

Our involvement in securities-related class action litigation could divert our resources and management's attention and harm our business.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In addition, the market price of our common stock may vary significantly based on AcelRx-specific events, such as receipt of future complete response letters, negative clinical results, a negative vote or decision by an FDA advisory committee, or other negative feedback from the FDA, EMA, or other regulatory agencies. In the past, securities-related class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies often experience significant stock price volatility in connection with their investigational drug candidate development programs and the FDA's review of their NDAs.

If AcelRx experiences a decline in its stock price, we could face additional securities class action lawsuits. Securities class actions are often expensive and can divert management’s attention and our financial resources, which could adversely affect our business.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2019, we had federal net operating loss carryforwards of $212.4 million, of which $114.9 million federal net operating losses generated before January 1, 2018 will begin to expire in 2029. Federal net operating losses of $97.5 million generated in 2019 and 2018 will carryforward indefinitely but are subject to the 80% taxable income limitation. As of December 31, 2019, we had state net operating loss carryforwards of $113.5 million, which begin to expire in 2028.

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. Federal net operating losses generated prior to 2018 will continue to be governed by the net operating loss tax rules as they existed prior to the adoption of the new Tax Cuts and Jobs Act of 2017, or Tax Act, which means that generally they will expire 20 years after they were generated if not used prior thereto. Many states have similar laws. Accordingly, our federal and state net operating losses could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted Tax Act, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited to 80% of current year taxable income.

In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, 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 loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. The completion of the July 2013 public equity offering, together with our public equity offering in December 2012, our initial public offering, private placements and other transactions that have occurred, have triggered such an ownership change. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo further ownership changes in the future. In the future, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset United States federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our capital stock, and we are prohibited from doing so under the terms of the Loan Agreement. Regardless of the restrictions in the Loan Agreement or the terms of any potential future indebtedness, we anticipate that we will retain all available funds and any future earnings to support our operations and finance the growth and development of our business and, therefore, we do not expect to pay cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our Board of Directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our Board of Directors may deem relevant.

Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- a staggered Board of Directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to our Board of Directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board of Directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our Board of Directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease approximately 25,893 square feet of office and laboratory space in Redwood City, California under an agreement that expires on January 31, 2024, with an option to extend for an additional period of six years. On January 2, 2019, we entered into an agreement to sublease 12,106 square feet of this space commencing on February 16, 2019 and expiring on January 31, 2024. We believe that our facilities are adequate to meet our current needs.

Item 3. Legal Proceedings

From time to time we may be involved in legal proceedings arising in the ordinary course of business. We are not currently involved in any material legal proceedings. We may, however, be involved in material legal proceedings in the future. Such matters are subject to uncertainty and there can be no assurance that such legal proceedings will not have a material adverse effect on our business, results of operations, financial position or cash flows.

Item 4. Mine Safety Disclosures

Not Applicable.

PART II

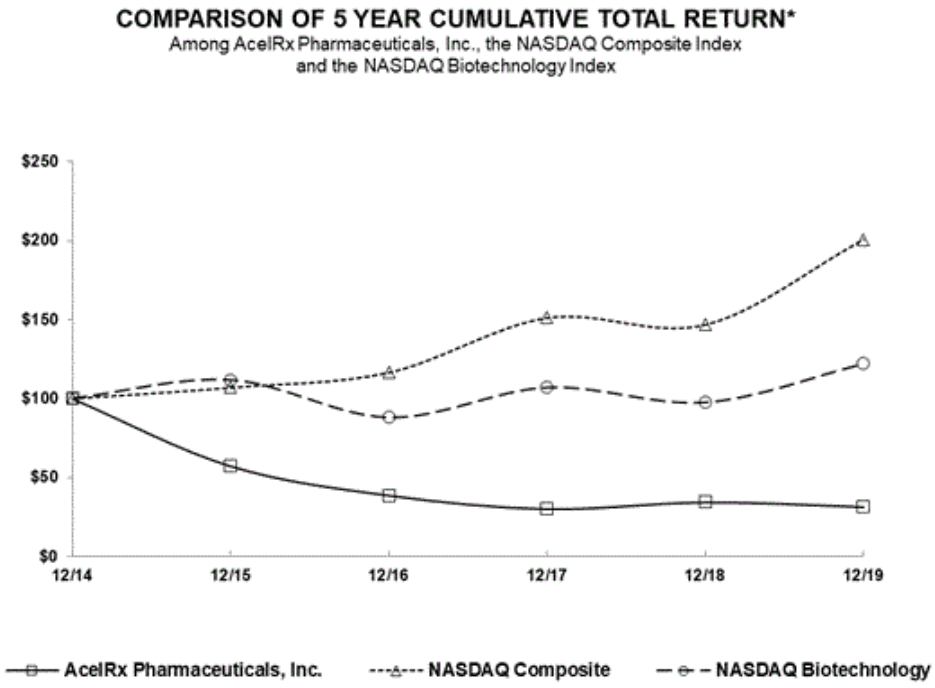
Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock has been traded on The Nasdaq Global Market since February 11, 2011 under the symbol "ACRX". As of March 5, 2020, there were 12 holders of record of our common stock. This number does not include "street name" or beneficial holders, whose shares are held of record by banks, brokers, financial institutions and other nominees.

Stock Price Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since December 31, 2014, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



The above Stock Price Performance Graph and related information shall not be deemed "soliciting material" or to be "filed" with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock, and we are prohibited from doing so under the terms of our Loan Agreement. Regardless of the restrictions in our Loan Agreement or the terms of any potential future indebtedness, we anticipate that we will retain all available funds and any future earnings to support our operations and finance the growth and development of our business and, therefore, we do not expect to pay cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our Board of Directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our Board of Directors may deem relevant.

Recent Sales of Unregistered Securities

None.

Item 6. Selected Financial Data

The selected financial data set forth below should be read together with the Consolidated Financial Statements and related notes, "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations," and the other information contained in this Form 10-K. The selected financial data is not intended to replace our audited financial statements and the accompanying notes. Our historical results are not necessarily indicative of our future results.

	Year Ended December 31,				
	2019	2018	2017	2016	2015
	(in thousands, except share and per share data)				
Consolidated Statements of Operations Data:					
Total revenue	$ 2,289	$ 2,151	$ 7,995	$ 17,357	$ 19,263
Costs and Operating Expenses:					
Cost of goods sold	$ 6,806	$ 3,976	$ 10,659	$ 12,315	$ 1,770
Research and development	4,661	13,137	19,409	21,402	22,488
General and administrative	45,027	20,765	16,609	15,597	14,203
Restructuring costs	—	—	—	—	756
Total costs and operating expenses	56,494	37,878	46,677	49,314	39,217
Loss from operations	(54,205)	(35,727)	(38,682)	(31,957)	(19,954)
Interest expense	(2,535)	(2,217)	(3,316)	(2,770)	(2,977)
Interest income and other income, net	2,166	1,138	510	918	1,720
Non-cash interest income (expense) on liability related to sale of future royalties	1,337	(10,341)	(10,721)	(9,382)	(2,428)
Net loss before income taxes	$ (53,237)	$ (47,147)	$ (52,209)	$ (43,191)	$ (23,639)
Provision (benefit) for income taxes	3	2	(701)	(34)	760
Net loss	$ (53,240)	$ (47,149)	$ (51,508)	$ (43,157)	$ (24,399)
Net loss per share of common stock, basic	$ (0.67)	$ (0.81)	$ (1.10)	$ (0.95)	$ (0.55)
Shares used in computing net loss per share of common stock, basic	79,184,266	58,408,548	46,883,535	45,313,118	44,300,099
Net loss per share of common stock, diluted	$ (0.67)	$ (0.81)	$ (1.10)	$ (0.95)	$ (0.60)
Shares used in computing net loss per share of common stock, diluted	79,184,266	58,408,548	46,883,535	45,313,118	44,468,440

	As of December 31,				
	2019	2018	2017	2016	2015
			(in thousands)		
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 66,137	$ 105,715	$ 60,469	$ 80,310	$ 113,464
Working capital	58,077	92,066	49,753	78,862	106,167
Total assets	91,356	120,533	75,552	99,993	127,785
Long-term debt	25,147	11,991	19,096	21,549	20,922
Liability related to sale of future royalties	92,035	93,679	83,588	72,987	63,612
Accumulated deficit	(398,106)	(345,019)	(297,870)	(246,362)	(203,205)
Total stockholders' (deficit) equity	(41,418)	4,253	(36,509)	(5,337)	33,113

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

The following discussion and analysis should be read in conjunction with our audited financial statements and the related notes that appear elsewhere in this Annual Report on Form 10-K.

This discussion and analysis generally covers our financial condition and results of operations for the year ended December 31, 2019, including year-over-year comparisons versus the year ended December 31, 2018. Our Annual Report on Form 10-K for the year ended December 31, 2018 includes a discussion and analysis of our financial condition and results of operations for the year ended December 31, 2017 in Item 7 of Part II, "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings. DSUVIA® (known as DZUVEO in Europe) and Zalviso, are both focused on the treatment of acute pain, and each utilize sufentanil, delivered via a non-invasive route of sublingual administration, exclusively for use in medically supervised settings. On November 2, 2018, the U.S. Food and Drug Administration, or FDA, approved our resubmitted NDA for DSUVIA for use in adults in certified medically supervised healthcare settings, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. In June 2018, the European Commission, or EC, granted marketing approval of DZUVEO for the treatment of patients with moderate-to-severe acute pain in medically monitored settings. We are further developing a distribution capability and commercial organization to continue to market and sell DSUVIA in the United States. The commercial launch of DSUVIA in the United States occurred in the first quarter of 2019. In geographies where we decide not to commercialize ourselves, including for DZUVEO in Europe, we may seek to out-license commercialization rights. We currently intend to commercialize and promote DSUVIA/DZUVEO outside the United States with one or more strategic partners, although we have not yet entered into any such arrangement. The timing of the resubmission of the Zalviso NDA is dependent upon the finalization of the FDA's new opioid approval guidelines and process. If we are successful in obtaining approval of Zalviso in the United States, we plan to potentially promote Zalviso either by ourselves or with strategic partners. Zalviso is approved in Europe and is currently being commercialized by Grünenthal GmbH, or Grünenthal.

Product Development Programs

Our product development portfolio features two innovative therapies for the treatment of acute pain. Please refer to "Part I. Item 1. Business—Product Development Programs" for a detailed discussion of DSUVIA and Zalviso.

Acquisition

On March 15, 2020, we entered into the Agreement and Plan of Merger with Tetraphase Pharmaceuticals, Inc., or Tetraphase, and Consolidated Merger Sub, Inc., a Delaware corporation and indirect wholly owned subsidiary of the Company, or Merger Sub, pursuant to which we will acquire Tetraphase. Pursuant to the merger agreement, each share of Tetraphase common stock issued and outstanding immediately prior to the effective time of the merger will automatically be converted into the right to receive 0.6303 shares of the Company's common stock, subject to certain adjustments pursuant to the terms of the merger agreement, and a contingent value right for additional consideration to be paid to the then former securityholders of Tetraphase upon the achievement of certain sales milestones. The closing of the merger is expected in the second quarter of 2020 subject to customary closing conditions. For additional information regarding the merger, see Note 17 "Subsequent Events" in the accompanying notes to the Consolidated Financial Statements.

Co-Promotion Agreement

On March 15, 2020, we entered into the Co-Promotion Agreement with Tetraphase to co-promote DSUVIA and Tetraphases's XERAVA™ (eravacycline), which is FDA approved for the treatment of complicated intra-abdominal infections. Under the terms of this agreement, each company is responsible for maintaining compliance under the agreed marketing and promotion plan and achieving a minimum number of sales calls for each product. On March 16, 2020, in connection with entering into the Co-Promotion Agreement, we initiated a reduction in headcount, designed to eliminate the overlap with the Tetraphase commercial team to more efficiently commercialize DSUVIA in connection with the Tetraphase commercial team. We have eliminated 30 positions, mainly within the commercial organization. For additional information regarding the Co-Promotion Agreement, see Note 17 "Subsequent Events" in the accompanying notes to the Consolidated Financial Statements.

Collaborative Arrangements

Our collaborative arrangements allow us to commercialize Zalviso in the EU, Switzerland, Liechtenstein, Iceland, Norway and Australia. Please refer to "Part I. Item 1. Business— Collaborative Arrangements" for a detailed discussion of our collaborative arrangements.

Financial Overview

We have incurred net losses and generated negative cash flows from operations since inception and expect to incur losses in the future as we continue commercialization activities to support the U.S. launch of DSUVIA, continue our research and development activities and support Grünenthal's European sales of Zalviso. As a result, we expect to continue to incur operating losses and negative cash flows until such time as DSUVIA has gained market acceptance and generated significant revenues.

Although Zalviso has been approved for sale in Europe, we sold the majority of the royalty rights and certain commercial sales milestones we are entitled to receive under the Grünenthal Agreements to PDL BioPharma, Inc., or PDL, in September 2015.

We launched the commercialization of DSUVIA in the United States in the first quarter of 2019. We will incur capital expenditures related to the installation of our high-volume automated packaging line for DSUVIA, from which we expect to have qualified product being packaged beginning in 2021. We anticipate that the high-volume line for DSUVIA will contribute to a significant decrease in costs of goods sold in 2021 and beyond.

To date, we have funded our operations primarily through the issuance of equity securities, borrowings, payments from our commercial partner, Grünenthal, monetization of certain future royalties and commercial sales milestones from the European sales of Zalviso by Grünenthal, funding from the Department of Defense, or DoD, and more recently with revenues from sales of DSUVIA since the commercial launch in the first quarter of 2019. The contract with the DoD was substantially completed in 2018.

Our revenues since inception have consisted primarily of revenues from our Amended Agreements with Grünenthal and our research contracts with the DoD. There can be no assurance that our relationship with Grünenthal will continue beyond the initial term or that we will be able to meet the milestones specified in the Amended Agreements. Under the terms of the DoD contract, the DoD reimbursed us for certain costs incurred for development, manufacturing, regulatory and clinical costs outlined in the DoD contract, including reimbursement for certain personnel and overhead expenses.

We have not yet entered into a collaboration agreement with a strategic partner for the commercialization of DZUVEO in Europe. There can be no assurance that we will enter into a collaborative agreement for DZUVEO, or any other collaborative agreements, or receive research-related contract awards in the future. Accordingly, we expect revenues to continue to fluctuate from period-to-period. Although we have received approval of DSUVIA in the U.S., and Zalviso and DZUVEO in Europe, the launch of DSUVIA in the U.S. is still early, and we cannot provide assurance that we will generate revenue from those products in excess of our operating expenses, nor that we will obtain marketing approval for Zalviso in the United States and subsequently generate revenue from Zalviso in excess of our operating expenses.

Our net losses were $53.2 million, $47.1 million and $51.5 million during the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had an accumulated deficit of $398.1 million. As of December 31, 2019, we had cash, cash equivalents and short-term investments totaling $66.1 million compared to $105.7 million as of December 31, 2018.

Critical Accounting Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our Consolidated Financial Statements and the related disclosures, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts in our Consolidated Financial Statements and accompanying notes. We base our estimates on historical experience and on various other assumptions that we 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 may differ from these estimates under different assumptions or conditions. To the extent that there are material differences between these estimates and actual results, our future financial statement presentation, financial condition, results of operations and cash flows will be affected. Note 1 "Organization and Summary of Significant Accounting Policies" in the accompanying Notes to Consolidated Financial Statements describes the significant accounting policies used in the preparation of the financial statements. Certain of these significant accounting policies are considered to be critical accounting policies, as defined below.

A critical accounting policy is defined as one that is both material to the presentation of our financial statements and requires management to make difficult, subjective or complex judgments that could have a material effect on our financial condition and results of operations. Specifically, critical accounting estimates have the following attributes: (i) we are required to make assumptions about matters that are highly uncertain at the time of the estimate; and (ii) different estimates we could reasonably have used, or changes in the estimate that are reasonably likely to occur, would have a material effect on our financial condition or results of operations.

We believe the following policies to be the most critical to an understanding of our financial condition and results of operations because they require us to make estimates, assumptions and judgments about matters that are inherently uncertain. Management has discussed the development, selection and disclosure of the following estimates with the Audit Committee.

Revenue from Contracts with Customers

Beginning January 1, 2018, we have followed the provisions of ASC Topic 606, *Revenue from Contracts with Customer*s. The guidance provides a unified model to determine how revenue is recognized. We recognize revenue upon transfer of control of promised products or services to customers in an amount that reflects the consideration we expect to receive in exchange for those products or services. We sell our products primarily through wholesale distributors.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under 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 based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

Product sales revenue

Revenues from product sales are recognized when distributors obtain control of our product, which occurs at a point in time, upon delivery to such distributors. These distributors subsequently resell the product to certified medically supervised healthcare settings. In addition to distribution agreements with these customers, we enter into arrangements with group purchasing organizations, or GPOs, and other certified medically supervised healthcare settings that provide for privately negotiated discounts with respect to the purchase of our products. Revenue from product sales is recorded at the transaction price, net of estimates for variable consideration consisting of distributor fees, GPO discounts, GPO administrative fees and returns. Variable consideration is recorded at the time product sales are recognized resulting in a reduction in product revenue. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Variable consideration is estimated using the most-likely amount method, which is the single-most likely outcome under a contract and is typically at the stated contractual rate. Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted in accordance with the expected value method under ASC Topic 606 for relevant factors. These factors include current contractual and statutory requirements, specific known market events and trends, industry data, and/or forecasted customer buying and payment patterns. Actual amounts of consideration ultimately received may differ from our estimates. If actual results vary materially from our estimates, we will adjust these estimates, which will affect revenue from product sales and earnings in the period such estimates are adjusted. These estimates include:

- Distributor Fees – We offer contractually determined fees to our distributors.
- GPO Discounts - We offer discounts to GPO members. These discounts are taken when the GPO members purchase DSUVIA from our distributors, who then charge the discount amount back to us.
- GPO Administrative Fees - We pay administrative fees to GPOs for services and access to data. These fees are based on contracted terms and are paid after the quarter in which the product was purchased by the GPOs' members.
- Returns – We allow our distributors to return product for credit up to 12 months after the product expiration date. As such, there may be a significant period of time between the time the product is shipped and the time the credit is issued on returned product.
- Prompt Pay Discounts – We offer cash discounts to our distributors, generally 2% of the sales price, as an incentive for prompt payment. We account for cash discounts by reducing accounts receivable by the prompt pay discount amount and recognize the discount as a reduction of revenue in the same period the related revenue is recognized.

We believe our estimated allowance for product returns requires a high degree of judgment and is subject to change based on our limited experience and certain quantitative and qualitative factors. We believe our estimated allowances for distributor fees, GPO discounts, GPO administrative fees and prompt pay discounts do not require a high degree of judgment because the amounts are settled within a relatively short period of time.

Amounts accrued for product revenue allowances and related accruals are evaluated each reporting period and adjusted when trends or significant events indicate that a change in estimate is appropriate and to reflect actual experience. Product revenue-related liabilities are recorded in our Consolidated Balance Sheets as accrued liabilities, while prompt pay discounts are recorded in our Consolidated Balance Sheets as a reduction in accounts receivable. We will continue to assess our estimates of variable consideration as we accumulate additional historical data and will adjust these estimates accordingly. Changes in product revenue allowance estimates could materially affect our results of operations and financial position.

Contract and other collaboration revenue

We entered into award contracts with the DoD to support the development of DSUVIA. These contracts provided for the reimbursement of qualified expenses for research and development activities. Revenue under these arrangements was recognized when the related qualified research expenses were incurred. We were entitled to reimbursement of overhead costs associated with the study costs under the DoD arrangements. We estimated this overhead rate by utilizing forecasted expenditures. Final reimbursable overhead expenses were dependent on direct labor and direct reimbursable expenses throughout the life of each contract, which increased or decreased based on actual expenses incurred.

We also generate revenue from collaboration agreements. These agreements typically include payments for upfront signing or license fees, cost reimbursements for development and manufacturing services, milestone payments, product sales, and royalties on licensee's future product sales. Product sales related revenue under these collaboration agreements is classified as product sales revenue, while other revenue generated from collaboration agreements is classified as contract and other collaboration revenue.

Performance Obligations

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC Topic 606. Our performance obligations include delivering product to our distributors, commercialization license rights, development services, services associated with the regulatory approval process, joint steering committee services, demonstration devices, manufacturing services, material rights for discounts on manufacturing services, and product supply.

We have optional additional items in contracts, which are considered marketing offers and are accounted for as separate contracts when the customer elects such options. Arrangements that include a promise for future commercial product supply and optional research and development services at the customer's or our discretion are generally considered as options. We assess if these options provide a material right to the licensee and if so, such material rights 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 revenue when the customer obtains control of the goods or services.

Transaction Price

We have both fixed and variable consideration. Non-refundable upfront fees and product supply selling prices are considered fixed, while milestone payments are identified as variable consideration when determining the transaction price. Funding of research and development activities is considered variable until such costs are reimbursed at which point, they are considered fixed. We allocate the total transaction price to each performance obligation based on the relative estimated standalone selling prices of the promised goods or services for each performance obligation.

At the inception of each arrangement that includes milestone payments, we evaluate whether the milestones are considered probable of being achieved 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 value of the associated milestone (such as a regulatory submission by us) is included in the transaction price. Milestone payments that are not within our control, such as approvals from regulators, are not considered probable of being achieved until those approvals are received.

For arrangements that include sales-based royalties, 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 (a) when the related sales occur, or (b) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Allocation of Consideration

As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price of each performance obligation identified in the contract. Estimated selling prices for license rights and material rights for discounts on manufacturing services are calculated using an income approach model and can include the following key assumptions: the development timeline, sales forecasts, costs of product sales, commercialization expenses, discount rate, the time which the manufacturing services are expected to be performed, and probabilities of technical and regulatory success. For all other performance obligations, we use a cost-plus margin approach.

Timing of Recognition

Significant management judgment is required to determine the level of effort required under an arrangement and the period over which we expect to complete our performance obligations under the arrangement. We estimate the performance period or measure of progress at the inception of the arrangement and re-evaluate it each reporting period. This re-evaluation may shorten or lengthen the period over which revenue is recognized. Changes to these estimates are recorded on a cumulative catch-up basis. If we cannot reasonably estimate when our performance obligations either are completed or become inconsequential, then revenue recognition is deferred until we can reasonably make such estimates. Revenue is then recognized over the remaining estimated period of performance using the cumulative catch-up method. Revenue is recognized for products at a point in time when control of the product is transferred to the customer in an amount that reflects the consideration we expect to be entitled to in exchange for those product sales, which is typically once the product physically arrives at the customer, and for licenses of functional intellectual property at the point in time the customer can use and benefit from the license. For performance obligations that are services, revenue is recognized over time proportionate to the costs that we have incurred to perform the services using the cost-to-cost input method.

Inventories

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. Inventory includes the cost of the active pharmaceutical ingredients, or API, raw materials and third-party contract manufacturing and packaging services. Indirect overhead costs associated with production and distribution are allocated to the appropriate cost pool and then absorbed into inventory based on the units produced or distributed, assuming normal capacity, in the applicable period. Indirect overhead costs in excess of normal capacity are recorded as period costs in the period incurred. DSUVIA was approved by the FDA in November 2018. Prior to FDA approval, all manufacturing costs for DSUVIA were expensed to research and development. Upon FDA approval, manufacturing costs for DSUVIA manufactured for commercial sale have been capitalized.

Our policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. We periodically evaluate the carrying value of inventory on hand for potential excess amount over demand using the same lower of cost or net realizable value approach as that used to value the inventory. Because the predetermined, contractual transfer prices we are receiving from Grünenthal are less than the direct costs of manufacturing, all Zalviso inventories are carried at net realizable value.

Cost of Goods Sold

Cost of goods sold for product revenue includes third party manufacturing costs, shipping costs, and indirect overhead costs associated with production and distribution which are allocated to the appropriate cost pool and recognized when revenue is recognized. Indirect overhead costs in excess of normal capacity are recorded as period costs in the period incurred.

Under the Amended Agreements with Grünenthal, we sell Zalviso to Grünenthal at predetermined, contractual transfer prices that are less than the direct costs of manufacturing and recognize indirect costs as period costs where they are in excess of normal capacity and not recoverable on a lower of cost or net realizable value basis. Cost of goods sold for Zalviso shipped to Grünenthal includes the inventory costs of API, third-party contract manufacturing costs, packaging and distribution costs, shipping, handling and storage costs, depreciation and costs of the employees involved with production.

Leases

In February 2016, the FASB issued Accounting Standards Update, or ASU, No. 2016-02, *Leases (Topic 842)*, to enhance the transparency and comparability of financial reporting related to leasing arrangements. We adopted the standard effective January 1, 2019.

At the inception of an arrangement, we determine whether the arrangement is or contains a lease based on the unique facts and circumstances present. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable. As such, we utilize our incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received.

Lease expense is recognized over the expected term on a straight-line basis. Operating leases are recognized on the balance sheet as right-of-use assets, operating lease liabilities current and operating lease liabilities non-current. As a result, we no longer recognize deferred rent on the balance sheet.

Research and Development Expenses

We expense research and development expenses as incurred. Research and development expenses consist primarily of direct and research-related allocated overhead costs such as facilities costs, salaries and related personnel costs, and material and supply costs. In addition, research and development expenses include costs related to clinical trials to validate our testing processes and procedures and related overhead expenses. Expenses resulting from clinical trials are recorded when incurred based in part on factors such as estimates of work performed, patient enrollment, progress of patient studies and other events. We make good faith estimates that we believe to be accurate, but the actual costs and timing of clinical trials are highly uncertain, subject to risks and may change depending upon a number of factors, including our clinical development plan.

Stock-Based Compensation

We measure and recognize compensation expense for all stock-based payment awards made to our employees and directors, including employee stock options and employee stock purchases related to the Employee Share Purchase Plan, or ESPP, on estimated fair values. The fair value of equity-based awards is amortized over the vesting period of the award using a straight-line method.

The Black-Scholes option pricing model requires inputs such as expected term, expected volatility and risk-free interest rate. These inputs are subjective and generally require significant analysis and judgment to develop. During the year ended December 31, 2017, we determined that our historical data provided a reasonable basis for estimating future behavior in regard to expected term and volatility, and as a result, began using our own historical option exercise experience and the volatility of our own common stock as the basis for these assumptions. The risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption. Effective January 1, 2017, we adopted ASU 2016-09 and elected to recognize forfeitures when they occur using a modified retrospective approach, which did not have a material impact on our Consolidated Financial Statements.

Non-Cash Interest Expense on Liability Related to Sale of Future Royalties

In September 2015, we sold certain royalty and milestone payment rights from the sales of Zalviso in the European Union by our commercial partner, Grünenthal, pursuant to the Collaboration and License Agreement, dated as of December 16, 2013, as amended, to PDL for an upfront cash purchase price of $65.0 million. We continue to have significant continuing involvement in the Royalty Monetization primarily due to our obligation to act as the intermediary for the supply of Zalviso to Grünenthal. Under the relevant accounting guidance, because of our significant continuing involvement, the Royalty Monetization has been accounted for as a liability that will be amortized using the effective interest method over the life of the arrangement. In order to determine the amortization of the liability, we are required to estimate the total amount of future royalty and milestone payments to be received by ARPI LLC and paid to PDL, up to a capped amount of $195.0 million, over the life of the arrangement. The aggregate future estimated royalty and milestone payments (subject to the capped amount), less the $61.2 million of net proceeds we received, are recorded as interest expense over the life of the liability. Consequently, we impute interest on the unamortized portion of the liability and record interest expense related to the Royalty Monetization accordingly.

There are a number of factors that could materially affect the amount and timing of royalty payments from Zalviso in Europe, most of which are not within our control. Such factors include, but are not limited to, the success of Grünenthal’s sales and promotion of Zalviso, changing standards of care, the introduction of competing products, manufacturing or other delays, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of Zalviso, significant changes in foreign exchange rates as the royalties remitted to ARPI are made in U.S. dollars, and other events or circumstances that could result in reduced royalty payments from European sales of Zalviso, all of which may result in a reduction of non-cash royalty revenues and the non-cash interest expense over the life of the Royalty Monetization. Conversely, if sales of Zalviso in Europe are more than expected, the non-cash royalty revenues and the non-cash interest expense we record would be greater over the term of the Royalty Monetization. We periodically assess the expected royalty and milestone payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than our initial estimates or the timing of such payments is materially different than our original estimates, we will prospectively adjust the amortization of the liability and the interest rate. Because estimated sales forecasts and payments may vary over the life of the Royalty Monetization, we may be required to recognize interest income as the imputed interest rate is adjusted prospectively to reflect the revised effective interest rate over the term of the Royalty Monetization.

We will record non-cash royalty revenues and non-cash interest expense within our Consolidated Statements of Comprehensive Loss over the term of the Royalty Monetization.

When the expected payments under the Royalty Monetization are lower than the gross proceeds of $65.0 million received, we defer recognition of any probable contingent gain until the Royalty Monetization liability expires.

Results of Operations

Our results of operations have fluctuated from period to period and may continue to fluctuate in the future, based upon the progress of our commercial launch of DSUVIA, our research and development efforts, and variations in the level of expenditures related to commercial launch and development efforts during any given period. Results of operations for any period may be unrelated to results of operations for any other period. In addition, historical results should not be viewed as indicative of future operating results.

Years Ended December 31, 2019 and 2018

Revenue

Product Sales Revenue

The Company's product sales revenue consists of sales of DSUVIA in the U.S. and Zalviso in Europe. Our commercial partner, Grünenthal, commercially launched Zalviso in Europe, with the first commercial sale occurring in April 2016. We began commercial sales of DSUVIA in the United States in the first quarter of 2019.

Revenues from product sales are recognized when distributors obtain control of our product, which occurs at a point in time, upon delivery to such distributors. These distributors subsequently resell the products to certified medically supervised healthcare settings. In addition to distribution agreements with these customers, in the United States, we enter into arrangements with group purchasing organizations, or GPOs, and other certified medically supervised healthcare settings that provide for privately negotiated discounts with respect to the purchase of our products. Revenue from product sales is recorded at the transaction price, net of estimates for variable consideration consisting of distributor fees, GPO discounts, GPO administrative fees and returns. Variable consideration is recorded at the time product sales are recognized, resulting in a reduction in product revenue.

We believe our estimated allowance for product returns requires a high degree of judgment and is subject to change based on our limited experience and certain quantitative and qualitative factors. We believe our estimated allowances for distributor fees, GPO discounts, GPO administrative fees and prompt pay discounts do not require a high degree of judgment because the amounts are settled within a relatively short period of time. Amounts accrued for product revenue allowances and related accruals are evaluated each reporting period and adjusted when trends or significant events indicate that a change in estimate is appropriate and to reflect actual experience.

Product sales revenue by product for the years ended December 31, 2019 and 2018 was as follows:

	2019	2018
DSUVIA	$ 377	$ —
Zalviso	1,453	825
Total product sales revenue	$ 1,830	$ 825

The increase in DSUVIA product sales revenue for the year ended December 31, 2019, as compared to the prior year, is due to the approval of DSUVIA in November 2018. As mentioned above, we began the DSUVIA launch in the first quarter of 2019.

The increase in Zalviso product sales revenue for the year ended December 31, 2019, as compared to the prior year, was primarily the result of increased orders from Grünenthal.

As of December 31, 2019, we had current and non-current portions of the deferred revenue balance under the Amended Agreements with Grünenthal of $0.3 million and $2.8 million, respectively. The estimated margin we expect to receive on transfer prices under the Amended Agreements was deemed to be a significant and incremental discount on manufacturing services, as compared to market rates for contract manufacturing margin. The original value assigned to this portion of the total allocated consideration was $4.4 million. We anticipate that the deferred revenue balance will decline on a straight-line basis through 2029, as we recognize product sales revenue under the Amended Agreements.

Contract and Other Collaboration Revenue

Contract and other collaboration revenue includes revenue recognized for services performed under the DoD Contract for DSUVIA. Under the terms of the DoD Contract, the DoD reimbursed us for costs incurred for development, manufacturing, regulatory and clinical costs as outlined in the DoD Contract, including reimbursement for certain personnel and overhead expenses.

In addition, contract and other collaboration revenue includes revenue under the Amended Agreements related to the joint steering committee for Zalviso, research and development services, non-cash royalty revenue related to the Royalty Monetization and royalty revenue for sales of Zalviso in Europe.

Contract and other collaboration revenue for the years ended December 31, 2019 and 2018 was as follows (in thousands):

	Years Ended December 31,		$ Change	% Change
	2019	2018	2019 vs. 2018	2019 vs. 2018
DoD Contract	$ —	$ 838	$ (838)	(100)%
Non-cash royalty revenue related to Royalty Monetization (See Note 8)	312	289	23	8%
Royalty revenue	104	96	8	8%
Other revenue	43	103	(60)	(58)%
Total contract and other collaboration revenue	$ 459	$ 1,326	$ (867)	(65)%

The period of performance under the DoD Contract ended on February 28, 2019.

We estimate and recognize royalty revenue and non-cash royalty revenue on a quarterly basis. Adjustments to estimated revenue are recognized in the subsequent quarter based on actual revenue earned per the royalty reports received from Grünenthal. In addition, under the Royalty Monetization, we sold a portion of the expected royalty stream and commercial milestones from the European sales of Zalviso by Grünenthal to PDL. As a result, contract and other collaboration revenue is not expected to have a significant impact on our cash flows in the near-term since a significant portion of our European Zalviso royalties and milestones were already monetized with PDL in 2015.

Cost of goods sold

As mentioned above, we commenced commercial sales of DSUVIA in the first quarter of 2019. In October 2015, we initiated commercial production of Zalviso for Grünenthal.

Total costs of goods sold for the years ended December 31, 2019 and 2018 was as follows (in thousands):

	Years Ended December 31,		$ Change	% Change
	2019	2018	2019 vs. 2018	2019 vs. 2018
Direct costs	$ 2,525	$ 874	$ 1,651	189%
Indirect costs	4,281	3,102	1,179	38%
Total costs of goods sold	$ 6,806	$ 3,976	$ 2,830	71%

Direct costs from contract manufacturers for DSUVIA and Zalviso totaled $2.5 million and $0.9 million in the years ended December 31, 2019 and 2018, respectively. Direct cost of goods sold for DSUVIA and Zalviso includes the inventory costs of the active pharmaceutical ingredient, or API, third-party contract manufacturing costs, estimated warranty costs, packaging and distribution costs, shipping, handling and storage costs.

The indirect costs to manufacture DSUVIA and Zalviso totaled $4.3 million and $3.1 million in the years ended December 31, 2019 and 2018, respectively. Indirect costs include internal personnel and related costs for purchasing, supply chain, quality assurance, depreciation and related expenses. We expect these indirect costs to represent a smaller percentage of revenue as our product sales increase.

We periodically evaluate the carrying value of inventory on hand for potential excess amounts over demand using the same lower of cost or net realizable value approach as that used to value the inventory. During the year ended December 31, 2019, we recorded an inventory impairment reserve of approximately $1.0 million as a result of an analysis to estimate potential DSUVIA inventory that may expire before being sold. This represents initial DSUVIA batches produced for development and therefore represented shorter dated product than batches manufactured for commercial sale.

For the foreseeable future, we anticipate negative gross margins on Zalviso product delivered to Grünenthal. Under the Amended Agreements, we sell Zalviso to Grünenthal at a predetermined transfer price. We do not recover internal indirect costs as part of the transfer price. In addition, at current low volume levels, our direct costs are in excess of the transfer prices we are receiving from Grünenthal. Furthermore, the Amended Agreements include declining maximum transfer prices over the term of the contract with Grünenthal. These transfer prices were agreed to assuming economies of scale that would occur with increasing production volumes (from the potential approval of Zalviso in the U.S. and an increase in demand in Europe) and corresponding decreases in manufacturing costs. We do not have long-term supply agreements with our contract manufacturers and prices are subject to periodic changes. However, we continue to look for additional cost saving opportunities. For example, we are currently consolidating the production of some of the components of Zalviso which we expect will result in lower manufacturing costs. To date, we have not yet resubmitted the Zalviso NDA and sales by Grünenthal in Europe have not been substantial. If we do not timely resubmit the Zalviso NDA and then receive timely approval and are unable to successfully launch Zalviso in the U.S., or the volume of Grünenthal sales does not increase significantly, we will not achieve the manufacturing cost reductions required in order to accommodate these declining transfer prices without a corresponding decrease in our gross margin.

Research and Development Expenses

The majority of our operating expenses to date have been for research and development activities related to Zalviso and DSUVIA. Research and development expenses included the following:

- expenses incurred under agreements with contract research organizations and clinical trial sites;
- employee-related expenses, which include salaries, benefits and stock-based compensation;
- payments to third party pharmaceutical and engineering development contractors;
- payments to third party manufacturers;
- depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, and equipment and laboratory and other supply costs; and
- costs for equipment and laboratory and other supplies.

We expect to incur future research and development expenditures to support the FDA regulatory review of the Zalviso NDA, once it is resubmitted. The timing of the resubmission of the Zalviso NDA is dependent on the finalization of the FDA's new opioid approval guidelines and process.

We track external development expenses on a program-by-program basis. Our development resources are shared among all our programs. Compensation and benefits, facilities, depreciation, stock-based compensation, and development support services are not allocated specifically to projects and are considered research and development overhead.

Below is a summary of our research and development expenses during the years ended December 31, 2019 and 2018 (in thousands, except percentages):

	Years Ended December 31,		$ Change	% Change
	2019	2018	2019 vs. 2018	2019 vs. 2018
DSUVIA	$ 658	$ 2,613	$ (1,955)	(75)%
Zalviso	549	732	(183)	(25)%
Overhead	3,454	9,792	(6,338)	(65)%
Total research and development expenses	$ 4,661	$ 13,137	$ (8,476)	(65)%

Research and development expenses during the year ended December 31, 2019, as compared to the year ended December 31, 2018, decreased by $8.5 million primarily due to lower overhead-related research and development expenses as we shifted the majority of our research and development personnel to support our commercialization efforts following the FDA approval of DSUVIA. In addition, we substantially completed our DSUVIA and Zalviso development programs resulting in decreased DSUVIA- and Zalviso-related spending in the year ended December 31, 2019 as compared to the prior year.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consisted primarily of salaries, benefits and stock-based compensation for personnel engaged in commercialization, administration, finance and business development activities. Other significant expenses included allocated facility costs and professional fees for general legal, audit and consulting services.

Total selling, general and administrative expenses for the years ended December 31, 2019 and 2018, were as follows (in thousands, except percentages):

	Years Ended December 31,		$ Change	% Change
	2019	2018	2019 vs. 2018	2019 vs. 2018
Selling, general and administrative expenses	$ 45,027	$ 20,765	$ 24,262	117%

Selling, general and administrative expenses increased by $24.3 million during the year ended December 31, 2019, as compared to the year ended December 31, 2018. The increase is primarily due to increased personnel-related expenses and programs in support of the commercial launch of DSUVIA. We have increased our headcount for selling, general and administrative efforts in the year ended December 31, 2019 by an average of 47 employees as compared to the year ended December 31, 2018.

Other Income (Expense)

Total other income (expense) for the years ended December 31, 2019 and 2018, was as follows (in thousands, except percentages):

	Years Ended December 31,		$ Change	% Change
	2019	2018	2019 vs. 2018	2019 vs. 2018
Interest expense	$ (2,535)	$ (2,217)	$ (318)	14%
Interest income and other income (expense), net	2,166	1,138	1,028	90%
Non-cash interest income (expense) on liability related to sale of future royalties	1,337	(10,341)	11,678	(113)%
Total other income (expense)	$ 968	$ (11,420)	$ 12,388	(108)%

Interest expense consisted primarily of interest accrued or paid on our debt obligation agreements and amortization of debt discounts. On May 30, 2019, we entered into a Loan and Security Agreement, or the Loan Agreement, with Oxford Finance LLC, or Oxford. Under the Loan Agreement, we borrowed an aggregate principal amount of $25.0 million. We accounted for the termination of the loan agreement with Hercules Capital Funding Trust 2014-1 and Hercules Technology II, L.P., or the Prior Agreement, as a debt extinguishment and, accordingly, incurred a loss of $0.2 million associated with the unamortized end of term fee. Interest expense increased in the year ended December 31, 2019, as compared to the prior year, primarily as a result of a higher outstanding loan balance. As of December 31, 2019, the accrued balance due under the Loan Agreement with Oxford was $24.2 million. Refer to Note 6 “Long-Term Debt” in the accompanying notes to the Consolidated Financial Statements for additional information.

Interest income and other income (expense), net, for the years ended December 31, 2019 and 2018 primarily related to interest earned on our investments. The increase in interest income and other income (expense), net, in the year ended December 31, 2019 is primarily due to a larger average investment balance compared to the year ended December 31, 2018.

The increase in non-cash interest income on the liability related to the sale of future royalties for the year ended December 31, 2019 as compared to the year ended December 31, 2018, is attributable to the Royalty Monetization that we completed in September 2015. As described in Note 8 “Liability Related to Sale of Future Royalties”, the Royalty Monetization has been recorded as debt under the applicable accounting guidance. We periodically assess the expected royalty and milestone payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than our initial estimates or the timing of such payments is materially different than our original estimates, we will prospectively adjust the amortization of the liability and the interest rate. During the three months ended June 30, 2019, we made a material revision to our estimates as the expected payments under the Royalty Monetization are less than the $65.0 million in gross proceeds received. The change in estimate reduced the effective interest rate over the life of the liability to 0% by recording interest income over the remaining term of the arrangement, prospectively, as an offset to the interest expense that was recognized in prior periods, and resulted in a decrease of $8.1 million to the net loss for the year ended December 31, 2019. The effective interest income rate for the year ended December 31, 2019 was approximately 1.4%. During the three months ended December 31, 2018, we revised our estimates as a result of lower projected European royalties from sales of Zalviso over the life of the liability because the product launch was progressing more slowly than originally expected. The effective interest expense rate for the year ended December 31, 2018 was approximately 11.6%. We anticipate that we will record approximately $3 million in non-cash interest income related to the Royalty Monetization for the year ended December 31, 2020.

Liquidity and Capital Resources

Liquidity

We have incurred losses and generated negative cash flows from operations since inception. We expect to continue to incur significant losses in 2020 and may incur significant losses and negative cash flows from operations in the future. We have funded our operations primarily through issuance of equity securities, borrowings, payments from our commercial partner, Grünenthal, monetization of certain future royalties and commercial sales milestones from the European sales of Zalviso by Grünenthal, funding from the DoD, and more recently with revenues from sales of DSUVIA since the commercial launch in the first quarter of 2019.

As of December 31, 2019, we had cash, cash equivalents and investments totaling $66.1 million compared to $105.7 million as of December 31, 2018. The decrease was primarily due to cash required to fund our continuing operations, as we began our commercialization activities for DSUVIA and continued to support Grünenthal's European sales of Zalviso, partially offset by cash received in connection with our debt refinancing. We anticipate that our existing capital resources will permit us to meet our capital and operational requirements through the end of the first quarter of 2021. While we believe we have sufficient capital to meet our operational requirements through the end of the first quarter of 2021, our expectations may change depending on a number of factors including our expenditures related to the United States commercial launch of DSUVIA, any changes in the resubmission of the Zalviso NDA and/or delays in the FDA approval process for Zalviso. Our existing capital resources will not be sufficient to fund our operations until such time as we may be able to generate sufficient revenues to sustain our operations.

We have a Controlled Equity Offering[SM] Sales Agreement, or the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent, pursuant to which we may offer and sell, from time to time through Cantor, shares of our common stock. As of December 31, 2019, we had issued and sold an aggregate of approximately 10.3 million shares of common stock pursuant to the ATM Agreement, for which we had received net proceeds of approximately $33.7 million, after deducting commissions, fees and expenses of $1.0 million. As of December 31, 2019, approximately $45.3 million of our common stock remained to be sold under the ATM Agreement.

On May 30, 2019, we entered into the Loan Agreement with Oxford. Under the Loan Agreement, we borrowed an aggregate principal amount of $25.0 million under a term loan and used approximately $8.9 million of the proceeds from the Loan to repay our outstanding obligations under the Prior Agreement. After deducting all loan initiation costs and outstanding interest on the Prior Agreement, we received $15.9 million in net proceeds. As of December 31, 2019, the accrued balance under the Loan Agreement was $24.2 million. For more information, see Note 6 "Long-Term Debt" in the accompanying notes to the Consolidated Financial Statements.

The Royalty Monetization will be repaid to PDL over the life of the agreement through a portion of the European royalties and milestones received under the Amended License Agreement with Grünenthal. For more information, see Note 8 "Liability Related to the Sale of Future Royalties" in the accompanying notes to the Consolidated Financial Statements.

Our cash and investment balances are held in a variety of interest-bearing instruments, including obligations of commercial paper, corporate debt securities, U.S. government sponsored enterprise debt securities and money market funds. Cash in excess of immediate requirements is invested with a view toward capital preservation and liquidity.

Cash Flows

	Years Ended December 31,	
	2019	2018
	(in thousands)	
Net cash used in operating activities	$ (51,180)	$ (29,075)
Net cash used in investing activities	(36,563)	(10,877)
Net cash provided by financing activities	14,452	75,025

Cash Flows from Operating Activities

The primary use of cash for our operating activities during these periods was to fund commercial readiness activities for our approved product, DSUVIA, and our product candidate, Zalviso, in addition to the support of Grünenthal's European sales of Zalviso. Our cash used in operating activities also reflected changes in our working capital, net of adjustments for non-cash charges, such as depreciation and amortization of our fixed assets, stock-based compensation, non-cash interest income (expense) related to the sale of future royalties and interest expense related to our debt financings.

Cash used in operating activities of $51.2 million during the year ended December 31, 2019, reflected a net loss of $53.2 million, partially offset by aggregate non-cash charges of $6.0 million. Non-cash charges included $5.1 million in stock-based compensation expense, $1.7 million in depreciation expense, a $1.0 million inventory impairment charge and $0.7 million in non-cash interest income on the liability related to the Royalty Monetization. The net change in our operating assets and liabilities of $3.9 million included a $3.4 million increase in inventories.

Cash used in operating activities of $29.1 million during the year ended December 31, 2018, reflected a net loss of $47.1 million, partially offset by aggregate non-cash charges of $16.2 million. Non-cash charges included $10.3 million in non-cash interest expense on the liability related to the royalty monetization and $5.2 million for stock-based compensation expense. The net change in our operating assets and liabilities included a decrease in accounts receivable of $1.5 million.

Cash Flows from Investing Activities

Our investing activities have consisted primarily of our capital expenditures and purchases and sales and maturities of our available-for-sale investments.

During the year ended December 31, 2019, cash used in investing activities of $36.6 million was the net result of $100.1 million for purchases of investments and $3.5 million for purchases of property and equipment, offset by $67.0 million in proceeds from maturity of investments.

During the year ended December 31, 2018, cash used in investing activities of $10.9 million was the net result of $20.5 million in proceeds from maturity of investments, offset by $30.6 million for purchases of investments and purchases of property and equipment of $0.8 million.

Cash Flows from Financing Activities

Cash flows from financing activities primarily reflect proceeds from the sale of our securities and payments made on debt financings.

During the year ended December 31, 2019, cash provided by financing activities was primarily due to $24.8 million in net proceeds received in connection with the Loan Agreement with Oxford, offset by $8.9 million for the repayment of the Prior Agreement, $3.5 million in payments of long-term debt under the Prior Agreement, plus $1.2 million in net proceeds received under the Sales Agreement and $0.8 million in proceeds as a result of stock purchases made under our 2011 Employee Stock Purchase Plan, or ESPP, and stock option exercises.

During the year ended December 31, 2018, cash provided by financing activities of $75.0 million was primarily due to $64.7 million in net proceeds from our underwritten public offerings plus $16.8 million in net proceeds received under the Sales Agreement. In addition, we used $7.7 million during the year ended December 31, 2018 to repay our long-term debt with Hercules.

Operating Capital and Capital Expenditure Requirements

Our current operating plan includes expenditures related to the launch of DSUVIA in the United States, anticipated activities required to resubmit the Zalviso NDA. These assumptions may change as a result of many factors. We will continue to evaluate the work necessary to successfully launch DSUVIA and gain approval of Zalviso in the United States and intend to update our cash forecasts accordingly. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

Our future capital requirements may vary materially from our expectations based on numerous factors, including, but not limited to, the following:

- expenditures related to the launch of DSUVIA and potential commercialization of Zalviso;
- future manufacturing, selling and marketing costs related to DSUVIA and Zalviso, including our contractual obligations to Grünenthal for Zalviso;
- costs associated with business development activities and licensing transactions;
- the outcome, timing and cost of the regulatory resubmission of Zalviso and any approval for Zalviso;
- the initiation, progress, timing and completion of any post-approval clinical trials for DSUVIA, or Zalviso, if approved;
- changes in the focus and direction of our business strategy and/or research and development programs;

- milestone and royalty revenue we receive under our collaborative development and commercialization arrangements;
- delays that may be caused by changing regulatory requirements;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the timing and terms of future in-licensing and out-licensing transactions;
- the cost and timing of establishing sales, marketing, manufacturing and distribution capabilities;
- the cost of procuring clinical and commercial supplies of DSUVIA and Zalviso;
- the extent to which we acquire or invest in businesses, products or technologies; and
- the expenses associated with any possible litigation.

In the long-term, our existing capital resources will not be sufficient to fund our operations until such time as we may be able to generate sufficient revenues to sustain our operations. We will have to raise additional funds through the sale of our equity securities, monetization of current and future assets, issuance of debt or debt-like securities or from development and licensing arrangements to sustain our operations and continue our development programs.

Please see "Part I., Item 1A. Risk Factors—Risks Related to Our Financial Condition and Need for Additional Capital."

Contractual Obligations

The following table summarizes our long-term contractual obligations at December 31, 2019:

	Payments Due by Period				
Contractual obligations	**Total**	**2020**	**2021 - 2023**	**2024 - 2025**	**Thereafter**
			(in thousands)		
Operating leases[1]	$ 5,420	$ 1,268	$ 4,036	$ 116	$ —
Purchase obligations[2]	400	—	400	—	—
Long-term debt obligations (principal and interest) [3]	32,542	6,936	25,606	—	—
Repayment of liability related to the sale of future royalties[4]	19,605	352	2,045	2,166	15,042
Total contractual obligations	$ 57,967	$ 8,556	$ 32,087	$ 2,282	$ 15,042

(1) Operating lease includes base rent for facilities we occupy in Redwood City, California.

(2) We issue inventory and research and development program related purchase orders in the normal course of business. We do not consider purchase orders to be firm inventory or research and development program related commitments; therefore, they are excluded from the table above. If we choose to cancel a purchase order, we may be obligated to reimburse the vendor for unrecoverable outlays incurred prior to cancellation.

(3) The Loan Agreement dated as of May 30, 2019 includes a $1.3 million end of term payment due on maturity of the loan, in June 2023, which is included in the table above. See Note 6 "Long-Term Debt" for additional information.

(4) Liability related to sale of future royalties represents the carrying value at the latest balance sheet date of payments we would make to PDL under the Royalty Monetization, based on estimated future European sales of Zalviso. Actual payments may be significantly higher or lower based on actual future European sales of Zalviso. For further discussion regarding the liability related to the sale of future royalties, see Note 8 "Liability Related to Sale of Future Royalties".

Operating leases

Office Lease

In December 2011, we entered into a non-cancelable lease agreement, or the Existing Lease, for approximately 13,787 square feet of office and laboratory facilities in Redwood City, California, or the Current Premises, which serve as our headquarters, effective April 2012. Rent expense from the facility lease is recognized on a straight-line basis from the inception of the lease in December 2011, the early access date, through the end of the lease.

In May 2014, we entered into an amendment, or the First Amendment, to the Existing Lease. Pursuant to the First Amendment, the term of the Existing Lease was extended for a period of twenty (20) months and twenty-two (22) days to January 31, 2018, unless sooner terminated pursuant to the terms of the Existing Lease. In addition, the First Amendment included a new lease on an additional approximate 12,106 square feet of office space, or the Expansion Space, which is adjacent to the Current Premises. The new lease for the Expansion Space had a term of 42 months commencing on August 1, 2014 and expiring on January 31, 2018.

In October 2015, we executed an agreement to sublease 11,871 square feet of the Expansion Space for a term of 26 months commencing on December 1, 2015. The sublessee was entitled to abatement of the first two monthly installments of rent. Subsequent monthly installments of rent started at a rental rate of $2.05 per square foot (subject to agreed nominal increases).

In June 2017, we entered into an amendment, or the Second Amendment, to the Existing Lease, and as amended by the First and Second Amendments, the Lease, with Metropolitan Life Insurance Company, or the Landlord, for the Current Premises and the Expansion Space. Pursuant to the Second Amendment, the term of the Lease was extended for a period of seventy-two (72) months to January 31, 2024, or the Expiration Date, unless sooner terminated pursuant to the terms of the Lease.

Pursuant to the Second Amendment, we will pay on a monthly basis annual rent of approximately $1.3 million in 2020, with annual increases each 12-month period beginning February 1st. In addition, we will pay the Landlord specified percentages of certain operating expenses related to the leased facility incurred by the Landlord.

On January 2, 2019, we entered into an agreement to sublease the Expansion Space commencing on February 16, 2019 and expiring on January 31, 2024. Rent installments from the sublessee are approximately $48,000 per month (subject to agreed nominal increases).

Contract Manufacturing Lease

On December 12, 2012, we entered into a Capital Expenditure and Equipment Agreement, or the Capital Agreement, with Patheon Pharmaceuticals, Inc., or Patheon, as amended in January 2014, or the Amended Capital Agreement for commercial supply manufacturing services related to our Zalviso drug product. The initial term of the agreement was through December 31, 2017, which term automatically renews in two-year increments unless earlier terminated by either party by giving eighteen months' notice. The Amended Capital Agreement requires that we pay a maximum "overhead fee" of $0.2 million annually during the term of the Amended Services Agreement with Patheon (see Purchase obligations below), which amount may be reduced to $0 based on the amount of annual revenues earned by Patheon under the Amended Services Agreement. No fee was due in 2017 or 2018 based on the amount of revenues earned by Patheon from AcelRx in 2016 and 2017, respectively. We paid $34,000 to Patheon in 2019, as we did not meet the annual revenue threshold in 2018. There will be no fee due in 2020 based on the amount of revenues earned by Patheon from AcelRx in 2019. The potential maximum "overhead fee" due in 2021 and 2022 is reflected in the contractual obligations table above, as the agreement has been automatically renewed through December 31, 2021.

Purchase obligations

In January 2013, we entered into a Manufacturing Services Agreement, or the Services Agreement, with Patheon relating to the manufacture of sufentanil sublingual tablets, for use with Zalviso. On August 22, 2017, we amended the Services Agreement with Patheon effective as of August 4, 2017, or the Amended Services Agreement, to include the manufacture of sufentanil sublingual tablets for use with DSUVIA.

Under the terms of the Amended Services Agreement, we have agreed to purchase, subject to Patheon's continued material compliance with the terms of the Amended Services Agreement, at least eighty percent (80%) of our sufentanil sublingual tablet requirements for Zalviso in the United States, Canada and Mexico from Patheon. Also, under the terms of the Amended Services Agreement, Patheon will manufacture, supply, and provide certain validation and stability services for DSUVIA intended for marketing and sale in the United States, Canada and Mexico, and their respective territories, the European Union, Switzerland, Liechtenstein, Norway, Iceland and Australia. The term of the Amended Services Agreement has been extended until December 31, 2021 and will automatically renew thereafter for periods of two years, unless terminated by either party upon eighteen months' prior written notice.

Long-term debt

Loan Agreement with Oxford

On May 30, 2019, we entered into the Loan Agreement with Oxford as the Lender. Under the Loan Agreement, the Lender made a term loan to us in an aggregate principal amount of $25.0 million, or the Loan, which was funded on May 30, 2019. We used approximately $8.9 million of the proceeds from the Loan to repay our outstanding obligations under the Prior Agreement. After deducting all loan initiation costs and outstanding interest on the Prior Agreement, we received $15.9 million in net proceeds. Refer to Note 6 "Long-Term Debt" for additional information.

The interest rate is calculated at a rate equal to the sum of (a) the greater of (i) the 30-day U.S. LIBOR rate reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue and (ii) 2.50%, plus (b) 6.75%. On July 27, 2017, the Financial Conduct Authority, or FCA, in the U.K. announced that it would phase out LIBOR as a benchmark by the end of 2021. It is unclear whether new methods of calculating LIBOR will be established such that it continues to exist after 2021 or if LIBOR will be replaced with an alternative reference rate; however, we do not believe such changes would have a material adverse effect on our financing costs. Payments on the Loan are interest-only until July 1, 2020 followed by equal principal payments and monthly accrued interest payments through the scheduled maturity date of June 1, 2023. At our election, the interest-only period may be extended to July 1, 2021, if prior to June 30, 2020, we receive unrestricted net cash proceeds of at least $45.0 million from either (i) the issuance and sale of equity securities, or (ii) “up front” payments in connection with a joint venture, collaboration or other partnering transaction, both of which are on terms and conditions acceptable to the Lender. A final payment equal to 5% of the aggregate principal amount of the Loan, or EOT Fee, will be due at the earlier of the maturity date, acceleration of the Loan, or prepayment of the Loan. The Company’s obligations under the Loan Agreement are secured by a security interest in all of the assets of the Company, other than the Company’s intellectual property which is subject to a negative pledge.

Non-Interest Bearing Payments for the Construction of Leasehold Improvements

In August 2019, we entered into a Site Readiness Agreement, or SRA, with a potential Contract Manufacturing Organization, or CMO, in contemplation of entering into a commercial supply agreement for DSUVIA at a future date. The total obligation under the SRA is $2.0 million of which $1.5 million has been incurred as of December 31, 2019. Refer to Note 6 “Long-Term Debt” for additional information.

Liability related to the sale of future royalties

Royalty Monetization with PDL

In September 2015, we sold certain royalty and milestone payment rights from the sales of Zalviso in the European Union by our commercial partner, Grünenthal, pursuant to the Collaboration and License Agreement, dated as of December 16, 2013, as amended, to PDL for an upfront cash purchase price of $65.0 million. PDL will receive 75% of the European royalties under the Amended Agreements with Grünenthal, as well as 80% of the first four commercial milestones worth $35.6 million (or 80% of $44.5 million), subject to the capped amount of $195.0 million. The Royalty Monetization has been accounted for as a liability that will be amortized using the interest method over the life of the arrangement. The timing and the amount of the repayment of this liability is contingent upon the receipt of the related royalty and milestone payments from Grünenthal. Upon receipt of these royalty and milestone payments from Grünenthal, we will remit the applicable portion to PDL. Refer to Note 8 “Liability Related to Sale of Future Royalties” for additional information.

Off-Balance Sheet Arrangements

Through December 31, 2019, we have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Our cash, cash equivalents and short-term investments as of December 31, 2019, were held in a variety of interest-bearing instruments, including obligations of commercial paper, corporate debt securities, U.S. government sponsored enterprise debt securities and money market funds. We do not have any auction rate securities on our Consolidated Balance Sheets, as they are not permitted by our investment policy. Our cash is invested in accordance with an investment policy approved by our Board of Directors which specifies the categories, allocations, and ratings of securities we may consider for investment. We do not believe our cash, cash equivalents and short-term investments have significant risk of default or illiquidity.

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. In an attempt to limit interest rate risk, we follow guidelines to limit the average and longest single maturity dates, place our investments with high quality issuers and follow internally developed guidelines to limit the amount of credit exposure to any one issuer. As of December 31, 2019, we had cash, cash equivalents and short-term investments of $66.1 million. In general, money market funds are not subject to market risk because the interest paid on such funds fluctuates with the prevailing interest rate, although some of the securities that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the value of the investment to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of our investment may decline. However, because our investments are primarily short-term in duration and our holdings in commercial paper, U.S. government bonds and corporate debt securities mature prior to our expected need for liquidity, we believe that our exposure to interest rate risk is not significant and, as a consequence, a 1% movement in market interest rates would not have a significant impact on the total value of our portfolio. We actively monitor changes in interest rates.

Domestic and international equity markets have experienced and may continue to experience heightened volatility and turmoil based on domestic and international economic conditions and concerns. In the event these economic conditions and concerns continue, and the markets continue to remain volatile, our results of operations could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary and our stock price may further decline. In addition, we maintain significant amounts of cash and cash equivalents that are not federally insured. We cannot provide assurance that we will not experience losses on these investments.

Item 8. Financial Statements and Supplementary Data

The financial statements required by this item are attached to this Form 10-K beginning with page F-1.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We have carried out an evaluation, under the supervision, and with the participation, of management including our principal executive officer and principal financial officer, of our disclosure controls and procedures (as defined in Rule 13a-15(e)) of the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of the end of the period covered by this Annual Report on Form 10–K. Based on their evaluation, our principal executive officer and principal financial officer concluded that, subject to the limitations described below, our disclosure controls and procedures were effective as of December 31, 2019.

Management's Annual Report on Internal Control over Financial Reporting

The following report is provided by management in respect of AcelRx Pharmaceuticals' internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act):

1. AcelRx Pharmaceuticals' management is responsible for establishing and maintaining adequate internal control over financial reporting.

2. AcelRx Pharmaceuticals management has used the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, framework (2013 framework) to evaluate the effectiveness of internal control over financial reporting. Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of AcelRx Pharmaceuticals' internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of AcelRx Pharmaceuticals' internal control over financial reporting are not omitted and is relevant to an evaluation of internal control over financial reporting.

3. Management has assessed the effectiveness of AcelRx Pharmaceuticals' internal control over financial reporting as of December 31, 2019 and has concluded that such internal control over financial reporting was effective.

OUM & Co. LLP, our independent registered public accounting firm, has attested to and issued a report on the effectiveness of our internal control over financial reporting, which is included herein.

Changes in Internal Control over Financial Reporting

There have been no significant changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, internal control over financial reporting during the fiscal quarter ended
December 31, 2019.

Limitations on the Effectiveness of Controls.

A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within an organization have been detected. Accordingly, our disclosure controls and procedures and our internal control over financial reporting are designed to provide reasonable, not absolute, assurance that the objectives of the control system are met. We continue to implement, improve and refine our disclosure controls and procedures and our internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Stockholders and Board of Directors
AcelRx Pharmaceuticals, Inc.
Redwood City, California

Opinion on Internal Control over Financial Reporting

We have audited AcelRx Pharmaceutical, Inc.'s (the "Company's") internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "COSO criteria"). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, 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 consolidated balance sheets of the Company as of December 31, 2019 and 2018, the related consolidated statements of comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2019, and the related notes, and our report dated March 16, 2020 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 Item 9A, *Management Report on Internal Control over Financial Reporting*. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of internal control over financial reporting 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, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included 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/ OUM & CO. LLP

San Francisco, California
March 16, 2020

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is hereby incorporated by reference from the information under the captions "Proposal No. 1: Election of Directors," "Information Regarding the Board of Directors and Corporate Governance—Information Regarding Committees of the Board of Directors" and "Executive Officers of the Registrant" contained in the Company's definitive Proxy Statement, to be filed with the Securities and Exchange Commission no later than 120 days from the end of the Company's last fiscal year in connection with the solicitation of proxies for its 2020 Annual Meeting of Stockholders. The information required by Section 16(a) is incorporated by reference from the information under the caption "Delinquent Section 16(a) Reports" in the Proxy Statement.

The Company has adopted a code of ethics that applies to its Chief Executive Officer, Chief Financial Officer, and to all of its other officers, directors, employees and agents. The code of ethics is available at the Corporate Governance section of the Investor Relations page on the Company's website at *www.acelrx.com*. The Company intends to disclose future amendments to, or waivers from, certain provisions of its code of ethics on the above website within five business days following the date of such amendment or waiver.

Item 11. Executive Compensation

The information required by this item is incorporated by reference from the information under the caption "Information Regarding the Board of Directors and Corporate Governance—Compensation Committee Interlocks and Insider Participation," "Executive Compensation" and "Executive Compensation—Compensation Committee Report" in the Company's Proxy Statement referred to in Item 10 above.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Equity Compensation Plan Information

The information required by this item is incorporated by reference from the information under the caption "Security Ownership of Certain Beneficial Owners and Management" in the Company's Proxy Statement referred to in Item 10 above.

Item 13. Certain Relationships and Related Transactions and Director Independence

The information required by this item is incorporated by reference from the information under the caption "Related Person Transactions and Indemnification—Certain Relationships and Related Transactions," "Information Regarding the Board of Directors and Corporate Governance—Independence of the Board of Directors" and "—Information Regarding Committees of the Board of Directors" in the Company's Proxy Statement referred to in Item 10 above.

Item 14. Principal Accounting Fees and Services

The information required by this item is incorporated by reference from the information under the caption "Proposal No. 2: Ratification of Appointment of Independent Registered Public Accounting Firm" in the Company's Proxy Statement referred to in Item 10 above.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are filed as part of this Form 10-K:

1. Financial Statements:

See Index to Financial Statements in Item 8 of this Form 10-K.

2. Financial Statement Schedules:

No schedules are provided because they are not applicable, not required under the instructions, or the requested information is shown in the financial statements or related notes thereto.

(b) Exhibits

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
2.1§	Agreement and Plan of Merger among the Registrant, Tetraphase Pharmaceuticals, Inc. and Consolidation Merger Sub, Inc., dated March 15, 2020	8-K	001-35068	2.1	3/16/2020
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-35068	3.1	2/18/2011
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-35068	3.1	6/25/2019
3.3	Amended and Restated Bylaws of the Registrant.	S-1	333-170594	3.4	1/7/2011

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
4.1	Description of Capital Stock.				
4.2	Reference is made to Exhibits 3.1 through 3.3.				
4.3	Specimen Common Stock Certificate of the Registrant.	S-1	333-170594	4.2	1/31/2011
4.4	Form of Warrant to Purchase Common Stock of the Registrant, dated as of May 30, 2019.	10-Q	001-35068	4.1	8/6/2019
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1	333-170594	10.1	1/7/2011
10.2+	2006 Stock Plan, as amended.	S-1	333-170594	10.2	11/12/2010
10.3+	Forms of Notice of Grant of Stock Option, Stock Option Agreement and Stock Option Exercise Notice under 2006 Stock Plan.	10-K	001-35068	10.3	3/30/2011
10.4+	2011 Equity Incentive Plan.	S-8	333-172409	99.3	2/24/2011
10.5+	Forms of Stock Option Grant Notice, Notice of Exercise and Option Agreement under 2011 Equity Incentive Plan.	10-K	001-35068	10.5	3/30/2011
10.6+	Forms of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement under 2011 Equity Incentive Plan.	10-K	001-35068	10.6	3/30/2011
10.7+	2011 Employee Stock Purchase Plan.	S-8	333-172409	99.6	2/24/2011
10.8	Lease between Metropolitan Life Insurance Company and the Registrant, dated December 15, 2011.	10-K	001-35068	10.9	3/23/2012
10.9	First Amendment to Lease between Metropolitan Life Insurance and the Registrant, dated May 2, 2014	8-K	001-35068	10.1	5/7/2014
10.10	Second Amendment to Lease between Metropolitan Life Insurance and the Registrant, dated June 14, 2017	8-K	001-35068	10.1	6/20/2017
10.11+	Amended and Restated Offer Letter between the Registrant and Larry Hamel, dated December 31, 2010.	S-1	333-170594	10.14	1/7/2011
10.12+	Amended and Restated Offer Letter between the Registrant and Badri (Anil) Dasu, dated December 30, 2010.	S-1	333-170594	10.15	1/7/2011
10.13+	Amended and Restated Offer Letter between the Registrant and Pamela Palmer, dated December 29, 2010.	S-1	333-170594	10.16	1/7/2011
10.14+	Offer Letter between the Registrant and Vincent J. Angotti, effective as of March 6, 2017.	10-Q	001-35068	10.4	5/8/2017
10.15+	Offer Letter between the Registrant and Raffi Asadorian, dated July 18, 2017.	8-K	001-35068	10.1	7/19/2017
10.16+	Non-Employee Director Compensation Policy.				
10.17+	2020 Cash Bonus Plan Summary.				
10.18+	Amended and Restated Severance Benefit Plan effective as of February 7, 2017.	8-K	001-35068	10.2	2/9/2017
10.19#	Manufacture and Supply Agreement between the Registrant and Grünenthal GmbH, effective as of December 16, 2013.	10-K	001-35068	10.28	3/17/2014
10.20#	Collaboration and License Agreement between the Registrant and Grünenthal GmbH, effective as of December 16, 2013.	10-K	001-35068	10.29	3/17/2014

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
10.21#	First Amendment to the Manufacture and Supply Agreement between the Registrant and Grünenthal GmbH, effective as of July 17, 2015.	10-Q	001-35068	10.2	11/3/2015
10.22#	First Amendment to the Collaboration and License Agreement between the Registrant and Grünenthal GmbH, effective as of July 17, 2015.	10-Q	001-35068	10.1	11/3/2015
10.23	Second Amendment to the Collaboration and License Agreement between the Registrant and Grünenthal GmbH, effective as of September 20, 2016.	10-Q	001-35068	10.1	11/2/2016
10.24	Manufacturing Services Agreement between Registrant and Patheon Pharmaceuticals, Inc., dated as of January 18, 2013	10-Q	001-35068	10.1	5/8/2013
10.25	Amended and Restated Capital Expenditure Agreement between Registrant and Patheon Pharmaceuticals, Inc., dated as of January 18, 2013	10-Q	001-35068	10.2	5/8/2013
10.26	Second Amendment to Amended and Restated Capital Expenditure and Equipment Agreement, between the Registrant and Patheon Pharmaceuticals, Inc. effective as of January 30, 2014.	10-Q	001-35068	10.4	5/8/2014
10.27#	Amendment #1 to Manufacturing Services Agreement between the Registrant and Patheon Pharmaceuticals, Inc., effective as of January 19, 2016.	10-Q	001-35068	10.6	5/2/2016
10.28#	Amendment #2 to Manufacturing Services Agreement between the Registrant and Patheon Pharmaceuticals, Inc., effective as of August 4, 2017.	10-Q	001-35068	10.1	11/9/2017
10.29#	Purchase and Sale Agreement between Registrant and ARPI LLC, dated as of September 18, 2015.	10-Q	001-35068	10.6	11/3/2015
10.30#	Subsequent Purchase and Sale Agreement between ARPI LLC (a wholly owned subsidiary of the Registrant) and PDL BioPharma, Inc., dated as of September 18, 2015.	10-Q	001-35068	10.7	11/3/2015
10.31	Controlled Equity Offering℠ Sales Agreement between the Registrant and Cantor Fitzgerald & Co., dated as of June 21, 2016.	8-K	001-35068	10.1	6/21/2016
10.32+	Form of Performance-Based Stock Option Award under 2011 Equity Incentive Plan.	10-Q	001-35068	10.2	5/10/2018
10.33	Sublease by and between Registrant and Genomic Health, Inc. dated as of November 30, 2018.	10-K	001-35068	10.44	3/7/2019
10.34	Loan and Security Agreement between the Registrant and Oxford Finance, LLC, dated as of May 30, 2019	8-K	001-35068	10.1	6/3/2019
10.35#	Agreement between the Registrant and SpecGX, LLC, dated June 16, 2017.	10-Q	001-35068	10.1	11/7/2019
10.36	Amendment to Agreement between the Registrant and SpecGX, LLC, dated September 23, 2019.	10-Q	001-35068	10.2	11/7/2019
10.37	Form of Contingent Value Rights Agreement to be entered into between the Registrant and a rights agent for the benefit of the securityholders of Tetraphase Pharmaceuticals, Inc.	8-K	001-35068	10.1	3/16/2020
10.38§	Form of Voting Agreement between the Registrant and certain Tetraphase Pharmaceuticals, Inc. securityholders, dated March 15, 2020.	8-K	001-35068	10.2	3/16/2020
10.39§	Form of Exchange Agreement between the Registrant and a Tetraphase Pharmaceuticals, Inc. securityholder, dated March 15, 2020.	8-K	001-35068	10.3	3/16/2020

10.40§	Co-Promotion Agreement between the Registrant and Tetraphase Pharmaceuticals, Inc., dated March 15, 2020.	8-K	001-35068	10.4	3/16/2020

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
21.2	Subsidiaries of the Registrant.				
23.1	Consent of OUM & Co. LLP, Independent Registered Public Accounting Firm.				
24.1	Power of Attorney (included in signature page).				
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.				
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.				
32.1	Certifications of Chief Executive Officer and Chief Financial Officer 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 Label Linkbase Document				
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document				

§ Schedules omitted pursuant to Item 601(a)(5) of Regulation S-K. The Registrant agrees to furnish supplementally a copy of any omitted schedule upon request by the SEC.

+ Indicates management contract or compensatory plan.

Material in the exhibit marked with am "[*]" has been omitted because it is confidential, not material, and would be competitively harmful if publicly disclosed.

The certifications attached as Exhibit 32.1 accompany this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

Date: March 16, 2020

AcelRx Pharmaceuticals, Inc.
(Registrant)

/s/ Vincent J. Angotti
Vincent J. Angotti
Chief Executive Officer and Director
(Principal Executive Officer)

/s/ Raffi Asadorian
Raffi Asadorian
Chief Financial Officer
(Principal Financial and Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Vincent J. Angotti and Raffi Asadorian, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual 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, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them, his or her substitute or substitutes, may lawfully 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/ Vincent J. Angotti **Vincent J. Angotti**	Chief Executive Officer and Director *(Principal Executive Officer)*	March 16, 2020
/s/ Raffi Asadorian **Raffi Asadorian**	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 16, 2020
/s/ Adrian Adams **Adrian Adams**	Chairman	March 16, 2020
/s/ Pamela P. Palmer, M.D., Ph.D. **Pamela P. Palmer, M.D., Ph.D.**	Director	March 16, 2020
/s/ Mark G. Edwards **Mark G. Edwards**	Director	March 16, 2020
/s/ Stephen J. Hoffman, Ph.D., M.D. **Stephen J. Hoffman, Ph.D., M.D.**	Director	March 16, 2020
/s/ Richard Afable, M.D. **Richard Afable, M.D.**	Director	March 16, 2020
/s/ Howard B. Rosen **Howard B. Rosen**	Director	March 16, 2020
/s/ Mark Wan **Mark Wan**	Director	March 16, 2020

ACELRX PHARMACEUTICALS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Stockholders and Board of Directors
AcelRx Pharmaceuticals, Inc.
Redwood City, California

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of AcelRx Pharmaceuticals, Inc. (the "Company") as of December 31, 2019 and 2018, the related consolidated statements of comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2019 and 2018, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2019**,** in conformity with accounting principles generally accepted in the United States of America.

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, 2019, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") and our report dated March 16, 2020 expressed an unqualified opinion thereon.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated 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 consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ OUM & CO. LLP

San Francisco, California
March 16, 2020
We have served as the Company's auditor since 2015.

AcelRx Pharmaceuticals, Inc.

Consolidated Balance Sheets
(in thousands, except share data)

	December 31, 2019	December 31, 2018
Assets		
Current Assets:		
Cash and cash equivalents	$ 14,684	$ 87,975
Short-term investments	51,453	17,740
Accounts receivable, net	432	49
Tax receivable	88	352
Inventories, net	3,295	854
Prepaid expenses and other current assets	1,736	1,024
Total current assets	71,688	107,994
Operating lease right-of-use assets	3,928	—
Property and equipment, net	14,552	11,483
Long-term tax receivable	263	351
Other assets	925	705
Total Assets	$ 91,356	$ 120,533
Liabilities and Stockholders' Equity (Deficit)		
Current Liabilities:		
Accounts payable	$ 1,720	$ 2,070
Accrued liabilities	5,528	4,540
Long-term debt, current portion	4,630	8,611
Deferred revenue, current portion	411	315
Operating lease liabilities, current portion	970	—
Liability related to the sale of future royalties, current portion	352	392
Total current liabilities	13,611	15,928
Long-term debt, net of current portion	20,517	3,380
Deferred revenue, net of current portion	2,833	3,148
Operating lease liabilities, net of current portion	3,640	—
Liability related to the sale of future royalties, net of current portion	91,683	93,287
Other long-term liabilities	490	537
Total liabilities	132,774	116,280
Commitments and Contingencies		
Stockholders' (Deficit) Equity:		
Common stock, $0.001 par value—200,000,000 shares authorized as of December 31, 2019 and 100,000,000 shares authorized as of December 31, 2018; 79,573,101 and 78,757,930 shares issued and outstanding as of December 31, 2019 and December 31, 2018, respectively	79	78
Additional paid-in capital	356,609	349,194
Accumulated deficit	(398,106)	(345,019)
Total stockholders' (deficit) equity	(41,418)	4,253
Total Liabilities and Stockholders' (Deficit) Equity	$ 91,356	$ 120,533

See notes to consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Consolidated Statements of Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,		
	2019	**2018**	**2017**
Revenue:			
Product sales	$ 1,830	$ 825	$ 6,673
Contract and other collaboration	459	1,326	1,322
Total revenue	2,289	2,151	7,995
Operating costs and expenses:			
Cost of goods sold	6,806	3,976	10,659
Research and development	4,661	13,137	19,409
Selling, general and administrative	45,027	20,765	16,609
Total operating costs and expenses	56,494	37,878	46,677
Loss from operations	(54,205)	(35,727)	(38,682)
Other income (expense):			
Interest expense	(2,535)	(2,217)	(3,316)
Interest income and other income (expense), net	2,166	1,138	510
Non-cash interest income (expense) on liability related to sale of future royalties	1,337	(10,341)	(10,721)
Total other income (expense)	968	(11,420)	(13,527)
Net loss before income taxes	(53,237)	(47,147)	(52,209)
Provision (benefit) for income taxes	3	2	(701)
Net loss	(53,240)	(47,149)	(51,508)
Other comprehensive loss:			
Unrealized losses on available for sale securities	—	—	(3)
Comprehensive loss	$ (53,240)	$ (47,149)	$ (51,511)
Net loss per share of common stock, basic and diluted	$ (0.67)	$ (0.81)	$ (1.10)
Shares used in computing net loss per share of common stock, basic and diluted –see Note 13	79,184,266	58,408,548	46,883,535

See notes to consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity (Deficit)
(in thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Other Comprehensive Income (loss)	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance as of December 31, 2016	45,333,790	$ 45	$ 240,977	$ (246,362)	$ 3	$ (5,337)
Stock-based compensation	—	—	4,294	—	—	4,294
Net proceeds from issuance of common stock in connection with equity financings	5,401,099	6	15,688	—	—	15,694
Issuance of common stock upon exercise of stock options	69,372	—	105	—	—	105
Issuance of common stock upon ESPP purchase	94,893	—	246	—	—	246
Change in unrealized gains and losses on investments	—	—	—	—	(3)	(3)
Net loss	—	—	—	(51,508)	—	(51,508)
Balance as of December 31, 2017	50,899,154	51	261,310	(297,870)	—	$ (36,509)
Stock-based compensation	—	—	5,168	—	—	5,168
Net proceeds from issuance of common stock in connection with equity financings	27,364,301	27	81,498	—	—	81,525
Issuance of common stock upon exercise of stock options	135,385	—	401	—	—	401
Issuance of common stock upon exercise of warrants	176,730	—	542	—	—	542
Issuance of common stock upon ESPP purchase	182,360	—	275	—	—	275
Net loss	—	—	—	(47,149)	—	(47,149)
Balance as of December 31, 2018	78,757,930	78	349,194	(345,019)	—	4,253
Cumulative effect adjustment for adoption of ASU No. 2016-02	—	—	—	153	—	153
Stock-based compensation	—	—	5,057	—	—	5,057
Net proceeds from issuance of common stock in connection with equity financings	500,000	—	1,233	—	—	1,233
Issuance of common stock upon exercise of stock options	111,702	—	270	—	—	270
Issuance of common stock upon ESPP purchase	203,469	1	472	—	—	473
Issuance of warrants related to debt financing	—	—	383	—	—	383
Net loss	—	—	—	(53,240)	—	(53,240)
Balance as of December 31, 2019	79,573,101	$ 79	$ 356,609	$ (398,106)	$ —	$ (41,418)

See notes to consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (53,240)	$ (47,149)	$ (51,508)
Adjustments to reconcile net loss to net cash used in operating activities:			
Non-cash royalty revenue related to royalty monetization	(312)	(289)	(151)
Non-cash interest (income) expense on liability related to royalty monetization	(1,337)	10,341	10,721
Depreciation and amortization	1,668	575	1,744
Non-cash interest expense related to debt financing	712	613	1,265
Stock-based compensation	5,057	5,168	4,294
Inventory impairment charge	951	—	369
Other	(773)	(201)	(198)
Changes in operating assets and liabilities:			
Accounts receivable	(383)	1,484	4,300
Inventories	(3,392)	102	920
Prepaid expenses and other assets	(465)	(850)	175
Tax receivable	352	—	(703)
Other assets	(220)	—	—
Accounts payable	(19)	458	309
Accrued liabilities	1,141	922	(1,301)
Operating lease liabilities	(701)	—	—
Deferred revenue	(219)	(362)	(361)
Deferred rent	—	113	360
Net cash used in operating activities	(51,180)	(29,075)	(29,765)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property and equipment	(3,470)	(819)	(2,405)
Purchase of investments	(100,068)	(30,558)	(7,565)
Proceeds from maturities of investments	66,975	20,500	—
Net cash used in investing activities	(36,563)	(10,877)	(9,970)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of long-term debt	25,000	—	—
Payment of costs in connection with refinancing of long-term debt	(190)	—	—
Payment of long-term debt	(3,470)	(7,718)	(3,514)
Extinguishment of debt	(8,864)	—	—
Payment of debt modification transaction costs	—	—	(204)
Net proceeds from issuance of common stock in connection with equity financings	1,233	81,525	15,694
Net proceeds from issuance of common stock through equity plans	743	1,218	351
Net cash provided by financing activities	14,452	75,025	12,327
NET (DECREASE) INCREASE IN CASH, CASH EQUIVALENTS	(73,291)	35,073	(27,408)
CASH, CASH EQUIVALENTS —Beginning of period	87,975	52,902	80,310
CASH, CASH EQUIVALENTS —End of period	$ 14,684	$ 87,975	$ 52,902
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Cash paid for interest	$ 1,712	$ 1,667	$ 2,043
Income taxes (refunded) paid	$ (350)	$ 2	$ 2
NONCASH INVESTING AND FINANCING ACTIVITIES:			
Purchases of property and equipment in accounts payable	$ —	$ 410	$ 222
Leasehold paid with note payable	$ 899	$ —	$ —
Transfer of tenant improvement allowance to sublease	$ 242	$ —	$ —
Establishment of right-of-use asset due to the adoption of ASU 2016-02	$ 4,730	$ —	$ —

See notes to consolidated financial statements.

1. Organization and Summary of Significant Accounting Policies

The Company

AcelRx Pharmaceuticals, Inc., or the Company or AcelRx, was incorporated in Delaware on July 13, 2005 as SuRx, Inc., and in January 2006, the Company changed its name to AcelRx Pharmaceuticals, Inc. The Company's operations are based in Redwood City, California.

AcelRx is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings. DSUVIA® (known as DZUVEO in Europe) and Zalviso®, are both focused on the treatment of acute pain, and each utilize sufentanil, delivered via a non-invasive route of sublingual administration, exclusively for use in medically supervised settings. On November 2, 2018, the U.S. Food and Drug Administration, or FDA, approved DSUVIA for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. In June 2018, the European Commission, or EC, granted marketing approval of DZUVEO for the treatment of patients with moderate-to-severe acute pain in medically monitored settings. AcelRx is further developing a distribution capability and commercial organization to continue to market and sell DSUVIA in the United States. The commercial launch of DSUVIA in the United States occurred in the first quarter of 2019. In geographies where AcelRx decides not to commercialize products by itself, including for DZUVEO in Europe, the Company may seek to out-license commercialization rights. The Company currently intends to commercialize and promote DSUVIA/DZUVEO outside the United States with one or more strategic partners, although it has not yet entered into any such arrangement. The timing of the resubmission of the Zalviso new drug application, or NDA, is dependent upon the finalization of the FDA's new opioid approval guidelines and process. AcelRx intends to seek regulatory approval for Zalviso in the United States and, if successful, potentially promote Zalviso either by itself or with strategic partners. Zalviso is approved in Europe and is currently being commercialized by Grünenthal GmbH, or Grünenthal.

DSUVIA/DZUVEO

DSUVIA, known as DZUVEO in Europe, approved by the FDA in November 2018 and approved by the EC in June 2018, is indicated for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. DSUVIA was designed to provide rapid analgesia via a non-invasive route and to eliminate dosing errors associated with IV administration. DSUVIA is a single-strength solid dosage form administered sublingually via a single-dose applicator, or SDA, by healthcare professionals. Sufentanil is an opioid analgesic currently marketed for intravenous, or IV, and epidural anesthesia and analgesia. The sufentanil pharmacokinetic profile when delivered sublingually avoids the high peak plasma levels and short duration of action observed with IV administration.

DSUVIA was approved with a Risk Evaluation and Mitigation Strategy, or REMS, which restricts distribution to certified medically supervised healthcare settings in order to prevent respiratory depression resulting from accidental exposure. DSUVIA is only distributed to facilities certified in the DSUVIA REMS program following attestation by an authorized representative to comply with appropriate dispensing and use restrictions of DSUVIA. To become certified, a healthcare setting is required to train their healthcare professionals on the proper use of DSUVIA and have the ability to manage respiratory depression. DSUVIA is not available in retail pharmacies or for outpatient use. As part of the REMS program, the Company monitors distribution and audits wholesalers' data, evaluates proper usage within the healthcare settings and monitors for any diversion and abuse. AcelRx will de-certify healthcare settings that are non-compliant with the REMS program.

Zalviso

Zalviso delivers 15 mcg sufentanil sublingually through a non-invasive delivery route via a pre-programmed, patient-controlled analgesia, or PCA, system. Zalviso is approved in Europe and is in late-stage development in the United States. The Company had initially submitted to the FDA an NDA seeking approval for Zalviso in September 2013 but received a complete response letter, or CRL, on July 25, 2014. Subsequently, the FDA requested an additional clinical study, IAP312, designed to evaluate the effectiveness of changes made to the functionality and usability of the Zalviso device and to take into account comments from the FDA on the study protocol. In the IAP312 study, for which top-line results were announced in August 2017, Zalviso met safety, satisfaction and device usability expectations. These results will supplement the three Phase 3 trials already completed in the Zalviso NDA resubmission.

On December 16, 2013, AcelRx and Grünenthal entered into a Collaboration and License Agreement, or the License Agreement, which was amended effective July 17, 2015 and September 20, 2016, or the Amended License Agreement, which grants Grünenthal rights to commercialize the Zalviso PCA system, or the Product, in the 28 European Union, or EU, member states, at the time of the agreement, plus Switzerland, Liechtenstein, Iceland, Norway and Australia (collectively, the Territory) for human use in pain treatment within, or dispensed by, hospitals, hospices, nursing homes and other medically supervised settings, (collectively, the Field). In September 2015, the EC approved the marketing authorization application, or MAA, previously submitted to the EMA, for Zalviso for the management of acute moderate-to-severe post-operative pain in adult patients. On December 16, 2013, AcelRx and Grünenthal, entered into a Manufacture and Supply Agreement, or the MSA, and together with the License Agreement, the Agreements. Under the MSA, the Company will exclusively manufacture and supply the Product to Grünenthal for the Field in the Territory. On July 22, 2015, the Company and Grünenthal amended the MSA, or the Amended MSA, effective as of July 17, 2015. The Amended MSA and the Amended License Agreement are referred to as the Amended Agreements.

The Company has incurred recurring operating losses and negative cash flows from operating activities since inception. Although Zalviso was approved for sale in Europe on September 18, 2015, the Company sold the majority of the royalty rights and certain commercial sales milestones it is entitled to receive under the Amended License Agreement with Grünenthal to PDL BioPharma, Inc., or PDL, in a transaction referred to as the Royalty Monetization. The FDA approved DSUVIA in November 2018 and the Company began its commercial launch of DSUVIA in the first quarter of 2019. As a result, the Company expects to continue to incur operating losses and negative cash flows until such time as DSUVIA has gained market acceptance and generated significant revenues.

Except as the context otherwise requires, when we refer to "we," "our," "us," the "Company" or "AcelRx" in this document, we mean AcelRx Pharmaceuticals, Inc., and its consolidated subsidiary. “DZUVEO” is a trademark, and “ACELRX”, “DSUVIA” and “Zalviso” are registered trademarks, all owned by AcelRx Pharmaceuticals, Inc. This report also contains trademarks and trade names that are the property of their respective owners.

Basis of Presentation

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the Consolidated Financial Statements and the accompanying notes. Actual results could differ from those estimates.

Reclassifications

Certain prior year amounts in the Consolidated Financial Statements have been reclassified to conform to the current year's presentation. In particular, the amount reported in the Consolidated Balance Sheets as restricted cash has been reclassified to other assets at December 31, 2018, the amounts reported in the Consolidated Balance Sheets as deferred rent and contingent put option liability have been reclassified to other long-term liabilities at December 31, 2018, and Zalviso product sales revenue has been reclassified to product sales from contract and other collaboration in the Consolidated Statements of Comprehensive Loss.

Principles of Consolidation

The Consolidated Financial Statements include the accounts of the Company and its wholly owned subsidiary, ARPI LLC, which was formed in September 2015 for the sole purpose of facilitating the Royalty Monetization with PDL of the expected royalty stream and milestone payments due from the sales of Zalviso in the European Union by its commercial partner, Grünenthal, pursuant to the Amended License Agreement. All intercompany accounts and transactions have been eliminated in consolidation. Refer to Note 8 “Liability Related to Sale of Future Royalties” for additional information.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the Consolidated Financial Statements and accompanying notes. Management evaluates its estimates on an ongoing basis including critical accounting policies. Estimates are based on historical experience and on various other market-specific and other relevant assumptions that the Company believes 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 from those estimates.

Cash, Cash Equivalents and Short-Term Investments

The Company considers all highly liquid investments with an original maturity (at date of purchase) of three months or less to be cash equivalents. Cash and cash equivalents consist of cash on deposit with banks.

All marketable securities are classified as available-for-sale and consist of commercial paper, U.S. government sponsored enterprise debt securities and corporate debt securities. These securities are carried at estimated fair value, which is based on quoted market prices or observable market inputs of almost identical assets, with unrealized gains and losses included in accumulated other comprehensive income (loss). The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion is included in interest income or expense. The cost of securities sold is based on specific identification. The Company's investments are subject to a periodic impairment review for other-than-temporary declines in fair value. The Company's review includes the consideration of the cause of the impairment including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in the market value. When the Company determines that the decline in fair value of an investment is below its accounting basis and this decline is other-than-temporary, it reduces the carrying value of the security it holds and records a loss in the amount of such decline.

Fair Value of Financial Instruments

The Company measures and reports its cash equivalents, investments and financial liabilities at fair value. Fair value is defined as the exchange price that would be received for an asset or an exit price paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The fair value hierarchy defines a three-level valuation hierarchy for disclosure of fair value measurements as follows:

Level I—Unadjusted quoted prices in active markets for identical assets or liabilities;

Level II—Inputs other than quoted prices included within Level I that are observable, unadjusted 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 related assets or liabilities; and

Level III—Unobservable inputs that are supported by little or no market activity for the related assets or liabilities.

The categorization of a financial instrument within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement.

Segment Information

The Company operates in a single segment, the development and commercialization of product candidates and products for the treatment of pain. The Company's net product sales revenue relates to sales in the United States. The Company's collaboration revenue relates to the Amended License Agreement with Grünenthal to commercialize Zalviso in the countries of the European Union, Switzerland, Liechtenstein, Iceland, Norway and Australia. The Company's contract and other revenue relates to the U.S. Department of Defense funding that supported the development of DSUVIA in the United States.

Concentration of Risk

The Company invests cash that is currently not being used for operational purposes in accordance with its investment policy in debt securities of U.S. government sponsored agencies and overnight deposits. The Company is exposed to credit risk in the event of default by the institutions holding the cash equivalents and available-for-sale securities to the extent recorded on the Consolidated Balance Sheets.

The Company relies on a single third-party supplier for the supply of sufentanil, the active pharmaceutical ingredient in DSUVIA and Zalviso, and various sole-source third-party contract manufacturer organizations to manufacture the DSUVIA SDA and Zalviso drug cartridge and device components, including the controller, the dispenser kit and the accessories.

DSUVIA is available in the U.S. for distribution primarily through a limited number of wholesalers and is not available in retail pharmacies. Zalviso is sold in Europe by the Company's collaboration partner, Grünenthal. Revenue and accounts receivable are concentrated with these customers.

Accounts Receivable, net

The Company has receivables from its distributors and collaboration partner, Grünenthal. To date, the Company has not had a bad debt allowance because of the limited number of financially sound customers who have historically paid their balances timely. The need for a bad debt allowance is evaluated each reporting period based on the Company's assessment of the credit worthiness of its customers or any other potential circumstances that could result in bad debt.

The Company has not experienced any losses with respect to the collection of its accounts receivable and believes that the entire accounts receivable balance as of December 31, 2019 is collectible.

Inventories, net

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. Inventory includes the cost of the active pharmaceutical ingredients, or API, raw materials and third-party contract manufacturing and packaging services. Indirect overhead costs associated with production and distribution are allocated to the appropriate cost pool and then absorbed into inventory based on the units produced or distributed, assuming normal capacity, in the applicable period. Indirect overhead costs in excess of normal capacity are recorded as period costs in the period incurred. DSUVIA was approved by the FDA in November 2018. Prior to FDA approval, all manufacturing costs for DSUVIA were expensed to research and development. Upon FDA approval, manufacturing costs for DSUVIA manufactured for commercial sale have been capitalized.

The Company's policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. The Company periodically evaluates the carrying value of inventory on hand for potential excess amount over demand using the same lower of cost or net realizable value approach as that used to value the inventory. Because the predetermined, contractual transfer prices the Company is receiving from Grünenthal are less than the direct costs of manufacturing, all Zalviso inventories are carried at net realizable value.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, generally three to five years. Leasehold improvements are amortized over the shorter of the estimated useful life of the improvements or the remaining lease term. Expenditures for repairs and maintenance, which do not extend the useful life of the property and equipment, are expensed as incurred. Upon retirement, the asset cost and related accumulated depreciation are relieved from the accompanying Consolidated Balance Sheets. Gains and losses associated with dispositions are reflected as a component of other expense in the accompanying Consolidated Statements of Comprehensive Loss.

Impairment of Long-Lived Assets

The Company periodically assesses the impairment of long-lived assets and, if indicators of asset impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through an analysis of the undiscounted future expected operating cash flows. If impairment is indicated, the Company records the amount of such impairment for the excess of the carrying value of the asset over its estimated fair value. For example, if the Company is not successful in its commercialization of DSUVIA, and if approved, Zalviso, purchased equipment and manufacturing-related facility improvements the Company has made at its contract manufacturers could become impaired. The Company may determine that it is no longer probable that the Company will realize the future economic benefit associated with the costs of these assets through future manufacturing activities, and if so, the Company would record an impairment charge associated with these assets.

Contingent put option

The contingent put option associated with the Company’s Loan Agreement with Oxford is recorded as a liability. Changes in the fair value of the contingent put option are recognized as interest income and other income (expense), net in the Consolidated Statements of Comprehensive Loss. For further discussion, see Note 6 “Long-Term Debt”.

Leases

In February 2016, the FASB issued Accounting Standards Update, or ASU, No. 2016-02, *Leases (Topic 842)*, to enhance the transparency and comparability of financial reporting related to leasing arrangements. The Company adopted the standard effective January 1, 2019.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable. As such, the Company utilizes its incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received.

Lease expense is recognized over the expected term on a straight-line basis. Operating leases are recognized on the balance sheet as right-of-use assets, operating lease liabilities current and operating lease liabilities non-current. As a result, the Company no longer recognizes deferred rent on the balance sheet.

Revenue from Contracts with Customers

Beginning January 1, 2018, the Company has followed the provisions of Accounting Standards Codification, or ASC, Topic 606, *Revenue from Contracts with Customers*. This guidance provides a unified model to determine how revenue is recognized. The Company recognizes revenue upon transfer of control of promised products or services to customers in an amount that reflects the consideration the Company expects to receive in exchange for those products or services. The Company sells its products primarily through wholesale distributors.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under 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 based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

Product sales revenue

Revenues from product sales are recognized when distributors obtain control of the Company's product, which occurs at a point in time, upon delivery to such distributors. These distributors subsequently resell the product to certified medically supervised healthcare settings. In addition to distribution agreements with these customers, the Company enters into arrangements with group purchasing organizations, or GPOs, and other certified medically supervised healthcare settings that provide for privately negotiated discounts with respect to the purchase of its products. Revenue from product sales is recorded at the transaction price, net of estimates for variable consideration consisting of distributor fees, GPO discounts, GPO administrative fees and returns. Variable consideration is recorded at the time product sales are recognized resulting in a reduction in product revenue. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Variable consideration is estimated using the most-likely amount method, which is the single-most likely outcome under a contract and is typically at the stated contractual rate. Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted in accordance with the expected value method under ASC Topic 606 for relevant factors. These factors include current contractual and statutory requirements, specific known market events and trends, industry data, and/or forecasted customer buying and payment patterns. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results vary materially from the Company's estimates, the Company will adjust these estimates, which will affect revenue from product sales and earnings in the period such estimates are adjusted. These estimates include:

- Distributor Fees – The Company offers contractually determined fees to its distributors.
- GPO Discounts - The Company offers discounts to GPO members. These discounts are taken when the GPO members purchase DSUVIA from the Company's distributors, who then charge the discount amount back to the Company.
- GPO Administrative Fees - The Company pays administrative fees to GPOs for services and access to data. These fees are based on contracted terms and are paid after the quarter in which the product was purchased by the GPOs' members.
- Returns – The Company allows its distributors to return product for credit up to 12 months after its product expiration date. As such, there may be a significant period of time between the time the product is shipped and the time the credit is issued on returned product.
- Prompt Pay Discounts – The Company offers cash discounts to its distributors, generally 2% of the sales price, as an incentive for prompt payment. The Company accounts for cash discounts by reducing accounts receivable by the prompt pay discount amount and recognizes the discount as a reduction of revenue in the same period the related revenue is recognized.

The Company believes its estimated allowance for product returns requires a high degree of judgment and is subject to change based on its limited experience and certain quantitative and qualitative factors. The Company believes its estimated allowances for distributor fees, GPO discounts and GPO administrative fees and prompt pay discounts do not require a high degree of judgment because the amounts are settled within a relatively short period of time.

Amounts accrued for product revenue allowances and related accruals are evaluated each reporting period and adjusted when trends or significant events indicate that a change in estimate is appropriate and to reflect actual experience. Product revenue-related liabilities are recorded in the Company's Consolidated Balance Sheets as accrued liabilities, while prompt pay discounts are recorded in the Company's Consolidated Balance Sheets as a reduction in accounts receivable. The Company will continue to assess its estimates of variable consideration as it accumulates additional historical data and will adjust these estimates accordingly. Changes in product revenue allowance estimates could materially affect the Company's results of operations and financial position.

Contract and other collaboration revenue

The Company entered into award contracts with U.S. Department of Defense, or the DoD, to support the development of DSUVIA. These contracts provided for the reimbursement of qualified expenses for research and development activities. Revenue under these arrangements was recognized when the related qualified research expenses were incurred. The Company was entitled to reimbursement of overhead costs associated with the study costs under the DoD arrangements. The Company estimated this overhead rate by utilizing forecasted expenditures. Final reimbursable overhead expenses were dependent on direct labor and direct reimbursable expenses throughout the life of each contract, which increased or decreased based on actual expenses incurred.

The Company generates revenue from collaboration agreements. These agreements typically include payments for upfront signing or license fees, cost reimbursements for development and manufacturing services, milestone payments, product sales, and royalties on licensee's future product sales. Product sales related revenue under these collaboration agreements is classified as product sales revenue, while other revenue generated from collaboration agreements is classified as contract and other collaboration revenue.

Performance Obligations

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC Topic 606. The Company's performance obligations include delivering product to its distributors, commercialization license rights, development services, services associated with the regulatory approval process, joint steering committee services, demonstration devices, manufacturing services, material rights for discounts on manufacturing services, and product supply.

The Company has optional additional items in contracts, which are considered marketing offers and are accounted for as separate contracts when the customer elects such options. Arrangements that include a promise for future commercial product supply and optional research and development services at the customer's or the Company's discretion are generally considered as options. The Company assesses if these options provide a material right to the licensee and if so, such material rights 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 revenue when the customer obtains control of the goods or services.

Transaction Price

The Company has both fixed and variable consideration. Variable consideration for product revenue is described as Net product sales in the Consolidated Statements of Comprehensive Loss. For collaboration agreements, non-refundable upfront fees and product supply selling prices are considered fixed, while milestone payments are identified as variable consideration when determining the transaction price. Funding of research and development activities is considered variable until such costs are reimbursed at which point, they are considered fixed. The Company allocates the total transaction price to each performance obligation based on the relative estimated standalone selling prices of the promised goods or services for each performance obligation.

At the inception of each arrangement that includes milestone payments, the Company evaluates whether the milestones are considered probable of being achieved 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 value of the associated milestone (such as a regulatory submission by the Company) is included in the transaction price. Milestone payments that are not within the control of the Company, such as approvals from regulators, are not considered probable of being achieved until those approvals are received.

For arrangements that include sales-based royalties, 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 (a) when the related sales occur, or (b) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Allocation of Consideration

As part of the accounting for collaboration arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price of each performance obligation identified in the contract. Estimated selling prices for license rights and material rights for discounts on manufacturing services are calculated using an income approach model and can include the following key assumptions: the development timeline, sales forecasts, costs of product sales, commercialization expenses, discount rate, the time which the manufacturing services are expected to be performed, and probabilities of technical and regulatory success. For all other performance obligations, the Company uses a cost- plus margin approach.

Timing of Recognition

Significant management judgment is required to determine the level of effort required under collaboration arrangements and the period over which the Company expects to complete its performance obligations under the arrangement. The Company estimates the performance period or measure of progress at the inception of the arrangement and re-evaluates it each reporting period. This re-evaluation may shorten or lengthen the period over which revenue is recognized. Changes to these estimates are recorded on a cumulative catch up basis. If the Company cannot reasonably estimate when its performance obligations either are completed or become inconsequential, then revenue recognition is deferred until the Company can reasonably make such estimates. Revenue is then recognized over the remaining estimated period of performance using the cumulative catch-up method. Revenue is recognized for products at a point in time when control of the product is transferred to the customer in an amount that reflects the consideration the Company expects to be entitled to in exchange for those product sales, which is typically once the product physically arrives at the customer, and for licenses of functional intellectual property at the point in time the customer can use and benefit from the license. For performance obligations that are services, revenue is recognized over time proportionate to the costs that the Company has incurred to perform the services using the cost-to-cost input method.

Cost of Goods Sold

Cost of goods sold for product revenue includes third party manufacturing costs, shipping and handling costs, and indirect overhead costs associated with production and distribution which are allocated to the appropriate cost pool and recognized when revenue is recognized. Indirect overhead costs in excess of normal capacity are recorded as period costs in the period incurred.

Under the Amended Agreements with Grünenthal, the Company sells Zalviso to Grünenthal at predetermined, contractual transfer prices that are less than the direct costs of manufacturing and recognizes indirect costs as period costs where they are in excess of normal capacity and not recoverable on a lower of cost or net realizable value basis. Cost of goods sold for Zalviso shipped to Grünenthal includes the inventory costs of API, third-party contract manufacturing costs, packaging and distribution costs, shipping, handling and storage costs, depreciation and costs of the employees involved with production.

Research and Development Expenses

Research and development costs are charged to expense when incurred. Research and development expenses include salaries, employee benefits, including stock-based compensation, consultant fees, laboratory supplies, costs associated with clinical trials and manufacturing, including contract research organization fees, other professional services and allocations of corporate costs. The Company reviews and accrues clinical trial expenses based on work performed, which relies on estimates of total costs incurred based on patient enrollment, completion of patient studies and other events.

Advertising Expenses

Advertising costs are expensed as incurred. Advertising expenses were $1.1 million, $0.5 million and $0.0 million for the years ended December 31, 2019, 2018 and 2017, respectively, and are included in selling, general and administrative expenses in the Consolidated Statements of Comprehensive Loss.

Stock-Based Compensation

Compensation expense for all stock-based payment awards made to employees and directors, including employee stock options and restricted stock units related to the 2011 Equity Incentive Plan, or 2011 EIP, and employee share purchases related to the 2011 Employee Stock Purchase Plan, or ESPP, is based on estimated fair values at grant date. The Company determines the grant date fair value of the awards using the Black-Scholes option-pricing model and generally recognizes the fair value as stock-based compensation expense on a straight-line basis over the vesting period of the respective awards.

The Black-Scholes option pricing model requires inputs such as expected term, expected volatility and risk-free interest rate. These inputs are subjective and generally require significant analysis and judgment to develop. The Company uses its historical option exercise experience and the volatility of its common stock as the basis for its assumptions regarding expected term and volatility. The risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption. Effective January 1, 2017, the Company adopted ASU 2016-09 and elected to recognize forfeitures when they occur using a modified retrospective approach, which did not have a material impact on its Consolidated Financial Statements.

Non-Cash Interest Income (Expense) on Liability Related to Sale of Future Royalties

In September 2015, the Company sold certain royalty and milestone payment rights from the sales of Zalviso in the European Union by its commercial partner, Grünenthal, pursuant to the License Agreement, as then amended, to PDL for gross proceeds of $65.0 million. The Company continues to have significant continuing involvement in the Royalty Monetization primarily due to an obligation to supply Zalviso to Grünenthal. Under the relevant accounting guidance, because of the Company's significant continuing involvement, the Royalty Monetization is accounted for as a liability that is being amortized using the effective interest method over the life of the arrangement. In order to determine the amortization of the liability, the Company is required to estimate the total amount of future royalty and milestone payments to be received by ARPI LLC and payments made to PDL, up to a capped amount of $195.0 million, over the life of the arrangement. The aggregate future estimated royalty and milestone payments (subject to the capped amount), less the $61.2 million of net proceeds the Company received, are amortized as interest expense over the life of the liability. Consequently, the Company imputes interest on the unamortized portion of the liability and records interest expense, or interest income, as these estimates are updated.

There are a number of factors that could materially affect the amount and timing of royalty and milestone payments from Zalviso in Europe, most of which are not within the Company's control. Such factors include, but are not limited to, the success of Grünenthal's sales and promotion of Zalviso, changing standards of care, the introduction of competing products, manufacturing or other delays, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of Zalviso, significant changes in foreign exchange rates as the royalties remitted to ARPI LLC are made in U.S. dollars, and other events or circumstances that could result in reduced royalty payments from European sales of Zalviso, all of which may result in a reduction of non-cash royalty revenues and the non-cash interest expense over the life of the Royalty Monetization. Conversely, if sales of Zalviso in Europe are more than expected, the non-cash royalty revenues and the non-cash interest expense recorded by the Company would be greater over the term of the Royalty Monetization. The Company periodically assesses the expected royalty and milestone payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than the Company's initial estimates or the timing of such payments is materially different than its original estimates, the Company will prospectively adjust the amortization of the liability and the interest rate. Because estimated sales forecasts and payments may vary over the life of the Royalty Monetization, the Company may be required to recognize interest income as the imputed interest rate is adjusted prospectively to reflect the revised effective interest rate over the term of the Royalty Monetization.

The Company records non-cash royalty revenues and non-cash interest income (expense), net, within its Consolidated Statements of Comprehensive Loss over the term of the Royalty Monetization.

When the expected payments under the Royalty Monetization are lower than the gross proceeds of $65.0 million received, the Company defers recognition of any probable contingent gain until the Royalty Monetization liability expires.

Comprehensive Loss

Comprehensive loss is comprised of net loss and other comprehensive income (loss) and is disclosed in the Consolidated Statements of Comprehensive Loss. For the Company, other comprehensive income (loss) consists of changes in unrealized gains and losses on the Company's investments.

Income Taxes

Deferred tax assets and liabilities are measured based on differences between the financial reporting and tax basis of assets and liabilities using enacted rates and laws that are expected to be in effect when the differences are expected to reverse. The Company records a valuation allowance for the full amount of deferred assets, which would otherwise be recorded for tax benefits relating to operating loss and tax credit carryforwards, as realization of such deferred tax assets cannot be determined to be more likely than not.

Net Loss per Share of Common Stock

The Company's basic net loss per share of common stock is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period. The diluted net loss per share of common stock is computed by giving effect to all potential common stock equivalents outstanding for the period determined using the treasury stock method. For purposes of this calculation, convertible preferred stock, options to purchase common stock, restricted stock subject to repurchase, restricted stock units, warrants to purchase convertible preferred stock and warrants to purchase common stock were considered to be common stock equivalents. In periods with a reported net loss, such common stock equivalents are excluded from the calculation of diluted net loss per share of common stock if their effect is antidilutive. For additional information regarding the net loss per share, see Note 13 "Net Loss per Share of Common Stock".

Recently Adopted Accounting Pronouncements

On August 29, 2018, the Financial Accounting Standards Board, or FASB, issued ASU No. 2018-15, *"Intangibles – Goodwill and Other – Internal Use Software (Subtopic 350-40)"*. The FASB's new guidance aligns the requirements for capitalizing implementation costs in a Cloud Computing Arrangement, or CCA, service contract with the requirements for capitalizing implementation costs incurred for an internal-use software license.

The amendments in ASU No. 2018-15 require the entity to present the expense related to the capitalized implementation costs in the same line item in the statement of income as the fees associated with the hosting element (service) of the arrangement and classify payments for capitalized implementation costs in the statement of cash flows in the same manner as payments made for fees associated with the hosting element. The entity is also required to present the capitalized implementation costs in the statement of financial position in the same line item that a prepayment for the fees of the associated hosting arrangement would be presented.

ASU No. 2018-15 is effective for public business entities for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted, including adoption in any interim period for which financial statements have not been issued. Entities can choose to adopt the new guidance (1) prospectively to eligible costs incurred on or after the date this guidance is first applied or (2) retrospectively. The Company early adopted ASU No. 2018-15 effective January 1, 2019 under the prospective method, which did not have a material effect on the Company's results of operations, financial condition or cash flows.

In August 2018, the U.S. Securities and Exchange Commission, or SEC, published Release No. 33-10532, *Disclosure Update and Simplification*, or DUSTR, which adopted amendments to certain disclosure requirements that have become redundant, duplicative, overlapping, outdated or superseded, in light of other SEC disclosure requirements, U.S. Generally Accepted Accounting Principles, or GAAP, or changes in the information environment. While most of the DUSTR amendments eliminate outdated or duplicative disclosure requirements, the final rule amends the interim financial statement requirements to include a reconciliation of changes in stockholders' (deficit) equity in the notes or as a separate statement for each period for which a statement of comprehensive loss is required to be filed. The new interim reconciliation of changes in stockholders' (deficit) equity has been included in the Company's interim financial statements effective January 1, 2019.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which establishes a new lease accounting model for lessees. In January, July and December 2018, the FASB issued additional amendments to the new lease guidance relating to, transition, and clarification. The July 2018 amendment, ASU No. 2018-11, *Leases (Topic 842): Targeted Improvements*, provided an optional transition method that allows entities to elect to apply the standard prospectively at its effective date, versus recasting the prior periods presented. The new standard establishes a right-of-use, or ROU, model that requires a lessee to record an ROU asset and a lease liability on the balance sheet for all leases with terms longer than 12 months. Disclosure requirements have been enhanced with the objective of enabling financial statement users to assess the amount, timing, and uncertainty of cash flows arising from leases. ASU No. 2016-02 became effective for the Company on January 1, 2019. The Company has implemented the standard using an optional transition method that allows the Company to initially apply the new leases standard as of the adoption date and recognize a cumulative-effect adjustment to the opening balance of accumulated deficit in the period of adoption. In connection with the adoption, the Company has elected to utilize the package of practical expedients, including: (1) not reassess the lease classification for any expired or existing leases, (2) not reassess the treatment of initial direct costs as they related to existing leases, and (3) not reassess whether expired or existing contracts are or contain leases. In addition, the Company elected the hindsight practical expedient to determine the lease term for existing leases. The election of the hindsight practical expedient resulted in the extension of the lease term for the Company's embedded lease.

The adoption of the new leases standard resulted in the following adjustments to the Consolidated Balance Sheets as of January 1, 2019 (in thousands):

	Increase/(Decrease)
Operating lease right-of-use assets	$ 4,730
Accrued liabilities [(a)]	$ (100)
Operating lease liabilities	$ 484
Operating lease liabilities, net of current portion	$ 4,610
Deferred rent, net of current portion	$ (416)
Accumulated deficit [(b)]	$ (153)

(a) Represents current portion of Deferred rent reclassified to Operating lease liabilities.

(b) Represents cumulative-effect adjustment upon adoption of ASU No. 2016-02.

The adoption of ASU No. 2016-02, the new leases standard, did not impact previously reported financial results because the impact to prior periods was reflected as a cumulative-effect adjustment to the accumulated deficit under the optional transition method.

Recently Issued Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, "*Financial Instruments – Credit Losses: Measurement of Credit Losses on Financial Instruments*," or ASU 2016-13. ASU 2016-13 replaces the incurred loss impairment methodology in current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU 2016-13 is effective for the Company beginning January 1, 2023, with early adoption allowed beginning January 1, 2020. In May 2019, the FASB issued ASU 2019-05, "*Financial Instruments – Credit Losses*", or ASU 2019-05, to allow entities to irrevocably elect the fair value option for certain financial assets previously measured at amortized cost upon adoption of the new credit losses standard. The new effective dates and transition align with those of ASU 2016-13. Management is currently assessing the date of adoption and the impact ASU 2016-13 and ASU 2019-05 will have on the Company, but it does not anticipate adoption of these new standards to have a material impact on the Company's financial position, results of operations and cash flows.

2. Investments and Fair Value Measurement

Investments

The Company classifies its marketable securities as available-for-sale and records its investments at fair value. Available-for-sale securities are carried at estimated fair value based on quoted market prices or observable market inputs of almost identical assets, with the unrealized holding gains and losses included in accumulated other comprehensive income. Marketable securities which have maturities beyond one year as of the end of the reporting period are classified as non-current.

The table below summarizes the Company's cash, cash equivalents and investments (in thousands):

	As of December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 1,957	$ —	$ —	$ 1,957
Money market funds	598	—	—	598
Commercial paper	12,129	—	—	12,129
Total cash and cash equivalents	14,684	—	—	14,684
Short-term investments:				
U.S. government agency securities	14,268	—	—	14,268
Commercial paper	27,131	—	—	27,131
Corporate debt securities	10,054	—	—	10,054
Total short-term investments	51,453	—	—	51,453
Total cash, cash equivalents and short-term investments	$ 66,137	$ —	$ —	$ 66,137

	As of December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 2,037	$ —	$ —	$ 2,037
Money market funds	1,436	—	—	1,436
U.S. government agency securities	10,181	—	—	10,181
Commercial paper	74,321	—	—	74,321
Total cash and cash equivalents	87,975	—	—	87,975
Short-term investments:				
U.S. government agency securities	1,497	—	—	1,497
Commercial paper	16,243	—	—	16,243
Total short-term investments	17,740	—	—	17,740
Total cash, cash equivalents and short-term investments	$ 105,715	$ —	$ —	$ 105,715

None of the available-for-sale securities held by the Company had material unrealized losses and there were no realized losses for the years ended December 31, 2019 and 2018. There were no other-than-temporary impairments for these securities as of December 31, 2019 or 2018. No gross realized gains or losses were recognized on the available-for-sale securities and, accordingly, there were no amounts reclassified out of accumulated other comprehensive income to earnings during the years ended December 31, 2019 and 2018.

As of December 31, 2019 and 2018, the contractual maturity of all investments held was less than one year.

Fair Value Measurement

The Company's financial instruments consist of Level I and II assets and Level III liabilities. Money market funds are highly liquid investments and are actively traded. The pricing information on these investment instruments are readily available and can be independently validated as of the measurement date. This approach results in the classification of these securities as Level 1 of the fair value hierarchy. For Level II instruments, the Company estimates fair value by utilizing third party pricing services in developing fair value measurements where fair value is based on valuation methodologies such as models using observable market inputs, including benchmark yields, reported trades, broker/dealer quotes, bids, offers and other reference data. Such Level II instruments typically include U.S. treasury, U.S. government agency securities and commercial paper. As of December 31, 2019, the Company held, in addition to Level II assets, a contingent put option liability associated with the Loan Agreement with Oxford. Similarly, as of December 31, 2018, the Company held a contingent put option liability associated with the Amended and Restated Loan and Security Agreement, or the Amended Loan Agreement, or Prior Agreement, with Hercules Capital Funding Trust 2014-1 and Hercules Technology II, L.P., together, Hercules. See Note 6 "Long-Term Debt" for further description. The Company's estimate of fair value of each of the contingent put option liabilities was determined by using a risk-neutral valuation model, wherein the fair value of the underlying debt facility is estimated both with and without the presence of the default provisions, holding all other assumptions constant. The resulting difference between the two estimated fair values is the estimated fair value of the default provisions, or the contingent put option, which is included under other long-term liabilities on the Consolidated Balance Sheets. Changes to the estimated fair value of these liabilities are recorded in interest income and other income (expense), net in the Consolidated Statements of Comprehensive Loss. The fair value of the underlying debt facility is estimated by calculating the expected cash flows in consideration of an estimated probability of default and expected recovery rate in default and discounting such cash flows back to the reporting date using a risk-free rate.

The following table sets forth the fair value of the Company's financial assets and liabilities by level within the fair value hierarchy (in thousands):

	As of December 31, 2019			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$ 598	$ 598	$ —	$ —
U.S. government agency securities	14,268	—	14,268	—
Commercial paper	39,260	—	39,260	—
Corporate debt securities	10,054	—	10,054	—
Total assets measured at fair value	$ 64,180	$ 598	$ 63,582	$ —
Liabilities				
Contingent put option liability	$ 437	$ —	$ —	$ 437
Total liabilities measured at fair value	$ 437	$ —	$ —	$ 437

	As of December 31, 2018			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$ 1,436	$ 1,436	$ —	$ —
U.S. government agency securities	11,678	—	11,678	—
Commercial paper	90,564	—	90,564	—
Total assets measured at fair value	$ 103,678	$ 1,436	$ 102,242	$ —
Liabilities				
Contingent put option liability	$ 121	$ —	$ —	$ 121
Total liabilities measured at fair value	$ 121	$ —	$ —	$ 121

The following table sets forth a summary of the changes in the fair value of the Company's Level III financial liabilities for the years ended December 31, 2019 and 2018 (in thousands):

	Year Ended December 31, 2019
Fair value—beginning of period	$ 121
Change in fair value of contingent put option associated with the Loan Agreement	437
Change in fair value of contingent put option associated with the Prior Agreement	(121)
Fair value—end of period	$ 437

	Year Ended December 31, 2018
Fair value—beginning of period	$ 207
Change in fair value of contingent put option associated with Amended Loan Agreement	(86)
Fair value—end of period	$ 121

3. Inventories

Inventories consist of finished goods, raw materials and work in process and are stated at the lower of cost or net realizable value and consist of the following (in thousands):

	As of December 31,	
	2019	2018
Raw materials	$ 1,153	$ 694
Work-in-process	593	160
Finished goods	1,549	—
Inventories	$ 3,295	$ 854

During the year ended December 31, 2019, the Company recorded a write-down of inventory of approximately $1.0 million as a result of an analysis to estimate potential DSUVIA inventory that may expire before being sold. This represents initial DSUVIA batches produced for development and therefore represented shorter dated product than batches manufactured for commercial sale. During the year ended December 31, 2017, the Company recorded an inventory impairment charge of $0.4 million, primarily for Zalviso raw materials inventory on hand, plus related purchase commitments. Inventory that has been impaired is recorded in cost of goods sold in the accompanying Consolidated Statements of Comprehensive Loss.

4. Property and Equipment

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

	As of December 31,	
	2019	2018
Laboratory equipment	$ 4,389	$ 3,972
Leasehold improvements	4,616	4,469
Computer equipment and software	1,749	237
Construction in process	11,949	10,593
Tooling	1,109	1,109
Furniture and fixtures	292	47
	24,104	20,427
Less accumulated depreciation and amortization	(9,552)	(8,944)
Property and equipment, net	$ 14,552	$ 11,483

Depreciation and amortization expense was $0.9 million, $0.5 million and $1.7 million during the years ended December 31, 2019, 2018 and 2017, respectively.

5. Revenue from Contracts with Customers

The following table summarizes revenue from contracts with customers for the years ended December 31, 2019, 2018 and 2017 into categories that depict how the nature, amount, timing and uncertainty of revenue and cash flows are affected by economic factors (in thousands):

	December 31,		
	2019	2018	2017
Product sales:			
DSUVIA	$ 377	$ —	$ —
Zalviso	1,453	825	6,673
Total product sales	1,830	825	6,673
Contract and other collaboration:			
DoD Contract revenue	—	838	852
Non-cash royalty revenue related to Royalty Monetization (See Note 8)	312	289	151
Royalty revenue	104	96	50
Other revenue	43	103	269
Total revenues from contract and other collaboration	459	1,326	1,322
Total revenue	$ 2,289	$ 2,151	$ 7,995

For additional detail on the Company's accounting policy regarding revenue recognition, refer to Note 1 "Organization and Summary of Significant Accounting Policies - Revenue from Contracts with Customers."

Product Sales

The Company's commercial launch of DSUVIA in the United States occurred in the first quarter of 2019. Zalviso is sold in Europe by the Company's collaboration partner, Grünenthal.

Contract and Other Collaboration

Amended License Agreement

Under the Amended License Agreement with Grünenthal, the Company is eligible to receive approximately $194.5 million in additional milestone payments, based upon successful regulatory and product development efforts ($28.5 million) and net sales target achievements ($166.0 million). Grünenthal will also make tiered royalty and supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, depending on the level of sales achieved, on net sales of Zalviso. A portion of the tiered royalty payment, exclusive of the supply and trademark fee payments, will be paid to PDL in connection with the Royalty Monetization. For additional information on the Royalty Monetization with PDL, see Note 8 “Liability Related to Sale of Future Royalties”. Unless earlier terminated, the Amended License Agreement continues in effect until the expiration of the obligation of Grünenthal to make royalty and supply and trademark fee payments, which supply and trademark fee continues for so long as the Company continues to supply the Product to Grünenthal. The Amended License Agreement is subject to earlier termination in the event the parties mutually agree, by a party in the event of an uncured material breach by the other party, upon the bankruptcy or insolvency of either party, or by Grünenthal for convenience.

Amended MSA

Under the terms of the Amended MSA with Grünenthal, the Company will manufacture and supply the Product for use in the Field for the Territory exclusively for Grünenthal. The Product will be supplied at prices approximating the Company’s manufacturing cost, subject to certain caps, as defined in the MSA Amendment. The MSA Amendment requires the Company to use commercially reasonable efforts to enter stand-by contracts with third parties providing significant supply and manufacturing services and, under certain specified conditions, permits Grünenthal to use a third-party back-up manufacturer to manufacture the Product for Grünenthal’s commercial sale in the Territory.

The Amended Agreements entitle the Company to receive additional payments upon the achievement of certain development milestones which relate to post approval product enhancements, expanded market opportunities and manufacturing efficiencies for Zalviso and require future research, development and regulatory activities. These payments are excluded from the transaction price as they are considered payments for optional additional services that Grünenthal may elect in the future. When these services are elected, they will be considered as a new contract under ASC Topic 606 and will not impact the revenue recognition of the performance obligations identified under Amended Agreements.

The Amended Agreements also include milestone payments related to specified net sales targets, totaling $166.0 million. These payments are considered sales-based license royalties under ASC Topic 606 and will be recognized apart from the other contract consideration when the related sales occur.

The Company recognizes revenue from license rights when the customer can use and benefit from the license rights. The Company recognizes revenue from its services performance obligations over time using a cost-to-cost input method which best represents the incremental benefit that the customer receives as control is transferred.

DoD Contract

On May 11, 2015, the Company entered into an award contract (referred to as the DoD Contract) supported by the Clinical and Rehabilitative Medicine Research Program, or CRMRP, of the United States Army Medical Research and Materiel Command, or the USAMRMC, within the U.S. Department of Defense, or the DoD, in which the DoD agreed to provide up to $17.0 million to the Company in order to support the development of DSUVIA. The DoD contract period of performance ended on February 28, 2019.

Contract Liability

The Company has entered into the Amended Agreements with Grünenthal related to Zalviso. At December 31, 2019, approximately $3.1 million of deferred revenue, $0.3 million of which represented the current portion, was attributable to the significant and incremental discount on Zalviso manufacturing services for Grünenthal. This deferred revenue is being recognized on a straight-line basis over the period such discount is made available to Grünenthal, which is estimated to continue through 2029.

The following table presents changes in the Company's contract liability for the year ended December 31, 2019:

	Balance at Beginning of the Period	Additions	Deductions	Balance at the end of the Period
		(in thousands)		
Contract liability:				
Deferred revenue – Amended Agreements	$ 3,463	$ —	$ (315)	$ 3,148
Deferred revenue – Other	—	96	—	96
Deferred revenue	$ 3,463	$ 96	$ (315)	$ 3,244

For the years ended December 31, 2019 and 2018, the Company recognized the following revenue from performance obligations satisfied (in thousands):

	Year ended December 31, 2019	Year ended December 31, 2018
Amounts included in contract liabilities at the beginning of the period:		
Performance obligations satisfied – Amended Agreements	$ 315	$ 362
New activities in the period from performance obligations satisfied:		
Performance obligations satisfied – Amended Agreements	1,181	566
Total revenue from performance obligations satisfied	$ 1,496	$ 928

6. Long-Term Debt

Prior Agreement with Hercules

On December 16, 2013, AcelRx entered into an Amended and Restated Loan and Security Agreement, or the Original Loan Agreement. with Hercules Technology II, L.P. and Hercules Capital, Inc., formerly known as Hercules Technology Growth Capital, Inc., together, the Lenders. In connection with the Original Loan Agreement, the Company issued a warrant to each Lender which, collectively, were exercisable for an aggregate of 176,730 shares of common stock and each carried an exercise price of $6.79 per share. See Note 9 "Warrants" for further description.

On March 2, 2017, the Company entered into the Amended Loan Agreement, which amended and restated the Original Loan Agreement. Pursuant to the Amended Loan Agreement, the Company borrowed the first tranche of approximately $20.5 million upon closing of the transaction on March 2, 2017, which was represented by secured term promissory notes, or the Notes. The Company used all of the proceeds from the first tranche to repay its obligations under the Original Loan Agreement, including a final payment of $1.7 million made on October 1, 2017. The interest rate was calculated at a rate equal to the greater of either (i) 9.55% plus the prime rate as reported from time to time in The Wall Street Journal minus 3.50%, and (ii) 9.55%. Payments under the Prior Agreement were interest-only until October 1, 2017 followed by equal monthly payments of principal and interest through the scheduled maturity date of March 1, 2020. In addition, the Prior Agreement required a final payment equal to 6.5% of the aggregate principal amount of $20.5 million in loans, or the End of Term Fee, owed upon full repayment of the loan. On May 30, 2019, the Company used approximately $8.9 million of the proceeds from the Loan Agreement with Oxford (described below) to repay its outstanding obligations under the Prior Agreement, including the outstanding principal plus accrued interest of $7.4 million, and the End of Term Fee of $1.3 million. The Company accounted for the termination of the Prior Agreement as a debt extinguishment and, accordingly, incurred a loss of approximately $0.2 million associated with the unamortized End of Term Fee.

The Company's obligations under the Prior Agreement were secured by a security interest in substantially all of its assets, other than its intellectual property. In addition, upon an event of default, including a change of control, Hercules had the option to accelerate repayment of the Amended Loan Agreement, including payment of any applicable prepayment charges. This option was considered a contingent put option liability, as the holder of the loan has the ability to exercise the option in the event of default, and is considered an embedded derivative, which must be valued and separately accounted for in the Company's consolidated financial statements. As of December 31, 2018, the estimated fair value of the contingent put option liability was $0.1 million, which was determined by using a risk-neutral valuation model, wherein the fair value of the underlying debt facility is estimated both with and without the presence of the default provisions, holding all other assumptions constant. See Note 2 "Investments and Fair Value Measurement" for further description.

The accrued balance due under the Prior Agreement was $12.0 million at December 31, 2018. Interest expense related to the Prior Agreement was $0.6 million, $2.2 million and $3.3 million for the years ended December 31, 2019, 2018 and 2017, respectively.

Loan Agreement with Oxford

On May 30, 2019, the Company entered into the Loan Agreement with Oxford as the Lender. Under the Loan Agreement, the Lender made a term loan to the Company in an aggregate principal amount of $25.0 million, or the Loan, which was funded on May 30, 2019. The Company used approximately $8.9 million of the proceeds from the Loan to repay its outstanding obligations under the Prior Agreement. After deducting all loan initiation costs and outstanding interest on the Prior Agreement, the Company received $15.9 million in net proceeds.

The interest rate is calculated at a rate equal to the sum of (a) the greater of (i) the 30-day U.S. LIBOR rate reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue and (ii) 2.50%, plus (b) 6.75%. On July 27, 2017, the Financial Conduct Authority, or FCA, in the U.K. announced that it would phase out LIBOR as a benchmark by the end of 2021. It is unclear whether new methods of calculating LIBOR will be established such that it continues to exist after 2021 or if LIBOR will be replaced with an alternative reference rate; however, the Company does not believe such changes would have a material adverse effect on its financing costs. Payments on the Loan are interest-only until July 1, 2020 followed by equal principal payments and monthly accrued interest payments through the scheduled maturity date of June 1, 2023. At the Company's election, the interest-only period may be extended to July 1, 2021, if prior to June 30, 2020, the Company receives unrestricted net cash proceeds of at least $45.0 million from either (i) the issuance and sale of equity securities, or (ii) "up front" payments in connection with a joint venture, collaboration or other partnering transaction, both of which are on terms and conditions acceptable to the Lender. A final payment equal to 5% of the aggregate principal amount of the Loan, or EOT Fee, will be due at the earlier of the maturity date, acceleration of the Loan, or prepayment of the Loan. The Company's obligations under the Loan Agreement are secured by a security interest in all the assets of the Company, other than the Company's intellectual property which is subject to a negative pledge.

The Company may prepay the Loan at any time. If the Loan is paid prior to the maturity date, the Company will pay the Lender a prepayment charge, based on a percentage of the then outstanding principal balance, equal to 2% if the prepayment occurs before May 30, 2020, 1.5% if the prepayment occurs after May 30, 2020, but on or before May 30, 2021 or 1% if the prepayment occurs after May 30, 2021. Upon voluntary or mandatory prepayment, in addition to the prepayment charge, the Company is required to pay the EOT Fee, Lender's expenses and all outstanding principal and accrued interest through the prepayment date.

The Loan Agreement includes customary representations and covenants that, subject to exceptions, will restrict the Company's ability to do the following things: declare dividends or redeem or repurchase equity interests; incur additional liens; make loans and investments; incur additional indebtedness; engage in mergers, acquisitions, and asset sales; transact with affiliates; undergo a change in control; add or change business locations; and engage in businesses that are not related to its existing business. The Loan Agreement requires that the Company always maintain unrestricted cash of not less than $5.0 million in accounts subject to control agreements in favor of Lender, tested monthly as of the last day of the month.

The Loan Agreement also includes standard events of default, including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of the Lender's security interest or in the value of the collateral, a material adverse change in business, operations or the prospect of repayment, events relating to bankruptcy or insolvency. The Loan also contains a cross default provision, under which if a third party (under any agreement) has the right to accelerate indebtedness greater than $250,000, the Loan would also be considered in default. In addition, the Loan defines events which negatively impact government approvals, judgements in excess of $500,000 and the delisting of the Company's shares of common stock on the Nasdaq Global Market, or Nasdaq, as events of default. Upon the occurrence of an event of default, a default interest rate of an additional 5% may be applied to the outstanding loan balances, and the Lender may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Loan Agreement. Acceleration would result in the payment of any applicable prepayment charges and application of the default interest rate to the outstanding balance until payment is made if full. The Company bifurcated a compound derivative liability related to a contingent interest feature and acceleration upon default provision (contingent put option) provided to the Lender. The bifurcated embedded derivative must be valued and separately accounted for in the Company's consolidated financial statements. The contingent put option liability is classified as a component of other long-term liabilities. As of December 31, 2019, the estimated fair value of the contingent put option liability was $0.4 million which was determined by using a risk-neutral valuation model, wherein the fair value of the underlying debt facility is estimated, both with and without the presence of the default provisions, holding all other assumptions constant. See Note 2 "Investments and Fair Value Measurement" for further description.

In connection with the Loan Agreement, on May 30, 2019, the Company issued warrants to the Lender and its affiliates, which are exercisable for an aggregate of 176,679 shares of the Company's common stock with a per share exercise price of $2.83, or the Warrants. The Warrants have been classified within stockholders' (deficit) equity and accounted for as a discount to the loan by allocating the gross proceeds on a relative fair value basis. For further discussion, see Note 9 "Warrants".

The accrued balance due under the Loan Agreement was $24.2 million at December 31, 2019. Interest expense related to the Loan Agreement was $1.9 million, $0.6 million of which represented amortization of the debt discount, for the year ended December 31, 2019.

Non-Interest Bearing Payments for the Construction of Leasehold Improvements

In August 2019, the Company entered into a Site Readiness Agreement, or SRA, with a potential Contract Manufacturing Organization, or CMO, in contemplation of entering into a commercial supply agreement for its product DSUVIA® at a future date. Under the SRA, the Company is building out a suite within the CMO's production facility. If additional equipment and facility modifications are required to meet the Company's Product needs, the Company may be required to contribute to the cost of such additional equipment and facility modifications. The Company has determined that it is the owner of the leasehold improvements related to the build-out which will be paid for in four annual installments of $0.5 million through July 2022. The total obligation under the SRA is $2.0 million of which $1.5 million has been incurred as of December 31, 2019. The effective interest rate related to the payments at December 31, 2019 was 13.61%.

The following table summarizes the balance of the future payments at December 31, 2019 (in thousands):

	As of December 31, 2019
Present value of the face amount of $1.0 million	$ 899
Less: current portion	463
Long-term debt, net of current portion	$ 436

Future Payments on Long-Term Debt

The following table summarizes the outstanding future payments associated with the Company's long-term debt as of December 31, 2019 (in thousands):

2020	$ 6,936
2021	10,429
2022	9,187
2023	5,530
Total payments	32,082
Less amount representing interest	(4,792)
Notes payable, gross	27,290
Less: Unamortized portion of EOT Fee	(978)
Less: Unamortized discount on notes payable	(1,165)
Long-term debt	25,147
Less current portion	(4,630)
Long-term debt, net of current portion	$ 20,517

7. Leases

Office Lease

The Company leases office and laboratory space for its corporate headquarters, located at 351 Galveston Drive, Redwood City, California. In June 2017, the Company renegotiated the Lease with its Landlord, or the New Lease. The New Lease is effective from February 1, 2018 through January 31, 2024 and contains a renewal option for a six-year extension after the current expiration date. The Company does not expect that the renewal option will be exercised and has therefore excluded the option from the calculation of the right of use asset and lease liability. The initial monthly rent is approximately $0.1 million with annual increases of 3% commencing on February 1st. The lease includes non-lease components (i.e. property management costs) that are paid separately from rent based on actual costs incurred and therefore were not included in the right-of-use asset and liability but are reflected as an expense in the period incurred. In calculating the present value of the lease payments, the Company has elected to utilize its incremental borrowing rate based on the remaining lease term.

On January 2, 2019, the Company entered into an agreement to sublease approximately 47% of its office and laboratory space effective February 16, 2019 and expiring on January 31, 2024, or the Sublease. The initial monthly rent from the sublessee is approximately $48,000 per month with annual increases of 3% commencing on February 1, 2019. Under the Sublease agreement, the sublessee was granted early access to the facility on January 2, 2019, which is deemed the lease commencement date and rent was abated for 45 days until the effective date of the lease. The sublessee is obligated to pay its proportionate share of property management costs on a pass-through basis. The Company incurred a total of $0.4 million in initial direct costs in entering the sublease, of which approximately $0.2 million is related to the tenant improvement allowance transferred to the sublessee. Initial direct costs are being amortized over the term of the sublease.

The transfer of the tenant improvement allowance to the sublessee resulted in a change in cash flows for the New Lease and was accounted for as a modification with changes in lease term and consideration. As a result, the Company remeasured the lease liability with the revised lease payments and recognized approximately $24,000 as a decrease to the lease liability, with a corresponding adjustment to the right-of-use asset.

Contract Manufacturing Lease

On December 12, 2012, the Company entered into an agreement for commercial supply manufacturing services related to the Company's Zalviso drug product with a contract manufacturing organization. The initial term of the agreement was through December 31, 2017, which term automatically renews in two-year increments unless earlier terminated by either party by giving eighteen months' notice. Commencing in 2013, the Company is required to make overhead fee payments each year of $0.2 million, prorated based on aggregate revenues. The Company has determined that this fee is an in-substance fixed lease payment as it represents the minimum annual payment under the contract. The Company concluded that this agreement contains an embedded lease as the clean rooms have been built specifically for production of the Company's product and their use is effectively controlled by the Company as it has priority over the space during the term of the agreement. The Company accounts for the agreement as an operating lease and has evaluated the non-cancelable term to be through the binding commitment date of December 31, 2021.

The components of lease expense are presented in the following table (in thousands):

	Year Ended December 31, 2019
Operating lease costs	$ 1,360
Sublease income	(596)
Net lease costs	$ 764

Other information related to the operating leases is presented in the following table (in thousands, except years and percentages):

	Year Ended December 31, 2019
Cash paid for amounts included in the measurement of lease liabilities	
Operating cash flows used for operating leases	$ 1,084
Supplemental non-cash disclosures of lease activities	
Transfer of tenant improvement allowance to sublease	$ 242
Right-of-use assets obtained in exchange for new operating lease liabilities	$ 4,730

The weighted average remaining lease term and discount rate related to the operating leases are presented in the following table:

	December 31, 2019
Weighted-average remaining term – operating lease (in years)	4.08
Weighted-average discount rate – operating lease	11.72%

Maturities of lease liabilities as of December 31, 2019 are presented in the following table (in thousands):

Year:		
2020	$	1,268
2021		1,305
2022		1,345
2023		1,386
2024		116
Total future minimum lease payments		5,420
Less imputed interest		(810)
Total	$	4,610
Reported as:		
Operating lease liabilities	$	970
Operating lease liabilities, net of current portion		3,640
Total lease liability	$	4,610

Future minimum sublease payments as of December 31, 2019 are presented in the following table (in thousands):

Year:		
2020	$	593
2021		610
2022		629
2023		648
2024		54
Total future minimum sublease payments	$	2,534

The rent receivable balance is reported in the Consolidated Balance Sheets as follows (in thousands):

Reported as:		
Prepaid expenses and other current assets	$	78
Other assets		354
Total rent receivable	$	432

8. Liability Related to Sale of Future Royalties

On September 18, 2015, the Company consummated the Royalty Monetization, in which it sold certain royalty and milestone payment rights to its newly formed wholly owned subsidiary, ARPI LLC, pursuant to a Purchase and Sale Agreement, or PSA. Subsequently, ARPI LLC sold the royalty and milestone payment rights to PDL for an upfront cash purchase price of $65.0 million, subject to a capped amount of $195.0 million pursuant to the Subsequent Purchase and Sale Agreement, or SPSA. Under the SPSA, PDL will receive 75% of the European royalties under the Amended License Agreement as well as 80% of the first four commercial milestones, worth $35.6 million (or 80% of $44.5 million), subject to the capped amount. The Company is entitled to receive 25% of the royalties, 20% of the first four commercial milestones, 100% of the remaining commercial milestones and all remaining development milestones of $43.5 million, including the $15.0 million payment for the EC approval of the MAA for Zalviso.

The Company and ARPI LLC continue to retain certain duties and obligations under the Amended License Agreement. These include the collection of the royalty and milestones amounts due and enforcement of related provisions under the Amended License Agreement, among others. In addition, the Company must prepare a quarterly distribution report relating to the Amended License Agreement, containing among other items, the amount of royalty and milestone payments received, reimbursable expenses and set-offs. The Company and ARPI LLC must also provide PDL with notice of certain communications, events or actions with respect to the Amended License Agreement and infringement of any underlying intellectual property.

The Company has significant continuing involvement in the Royalty Monetization primarily due to an obligation to act as the intermediary for the supply of Zalviso to Grünenthal. Under the relevant accounting guidance, because of its significant continuing involvement, the Royalty Monetization has been accounted for as a liability that will be amortized using the effective interest method over the life of the arrangement. In order to determine the amortization of the liability, the Company is required to estimate the total amount of future royalty and milestone payments to be received by ARPI LLC and paid to PDL, up to a capped amount of $195.0 million, over the life of the arrangement. The aggregate future estimated royalty and milestone payments (subject to the capped amount), less the $61.2 million of net proceeds the Company received will be recorded as interest expense over the life of the liability. Consequently, the Company imputes interest on the unamortized portion of the liability and records interest expense relating to the Royalty Monetization accordingly.

The Company periodically assesses the expected royalty and milestone payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than the Company's prior estimates or the timing of such payments is materially different than its prior estimates, the Company prospectively adjusts the amortization of the liability and the effective interest rate. During the three months ended June 30, 2019, the Company made a material revision to its estimates which resulted in an interest income rate on the Royalty Monetization liability balance at a prospective average rate of approximately 4.2%, which will be applied over the remaining term of the agreement. The change in estimate of future payments to PDL was a result of lower projected European royalties and milestones from sales of Zalviso over the life of the liability. The change in estimate results in interest income being recognized prospectively, over the remaining term of the agreement, as the estimated expected payments are less than the $65.0 million in gross proceeds received. The Company currently estimates that future payments to PDL over the remaining life of the arrangement will be approximately $20 million, therefore, a contingent gain of approximately $45 million may be recognized when it is realized upon expiration of the liability at the end of the Royalty Monetization term. Due to the significant judgments and factors related to the estimates of future payments under the Royalty Monetization arrangement, there are significant uncertainties surrounding the amount and timing of payments and the probability of realization of the estimated contingent gain.

The change in estimate reduced the effective interest rate over the life of the liability to 0% by recording interest income over the remaining term of the arrangement as an offset to the interest expense that was recognized in prior periods and resulted in a decrease of $8.1 million to the net loss, or $0.10 per share of common stock, basic and diluted, for the year ended December 31, 2019. The effective interest income rate for the year ended December 31, 2019 was approximately 1.4%. During the three months ended December 31, 2018, the Company revised its estimates as a result of lower projected European royalties from sales of Zalviso over the life of the liability because the product launch was progressing more slowly than originally expected. The effective interest expense rate for the years ended December 31, 2018 and December 31, 2017 was approximately 11.6% and 13.6%, respectively.

The following table shows the activity within the liability account during the year ended December 31, 2019 (in thousands):

	Year ended December 31, 2019	Period from inception to December 31, 2019
Liability related to sale of future royalties — beginning balance	$ 93,679	$ —
Proceeds from sale of future royalties	—	61,184
Non-cash royalty revenue	(307)	(684)
Non-cash interest (income) expense recognized	(1,337)	31,535
Liability related to sale of future royalties as of December 31, 2019	92,035	92,035
Less: current portion	(352)	(352)
Liability related to sale of future royalties — net of current portion	$ 91,683	$ 91,683

As royalties are remitted to PDL from ARPI LLC, as described in Note 1 "Organization and Summary of Significant Accounting Policies," the balance of the liability will be effectively repaid over the life of the agreement. The Company will record non-cash royalty revenues and non-cash interest expense within its Consolidated Statements of Comprehensive Loss over the term of the Royalty Monetization.

9. Warrants

Loan Agreement Warrants

In connection with the Loan Agreement, on May 30, 2019, the Company issued warrants to the Lender and its affiliates, which are exercisable for an aggregate of 176,679 shares of the Company's common stock with a per share exercise price of $2.83, or the Warrants. The Warrants may be exercised on a cashless basis. The Warrants are exercisable for a term beginning on the date of issuance and ending on the earlier to occur of ten years from the date of issuance or the consummation of certain acquisitions of the Company as set forth in the Warrants. The number of shares for which the Warrants are exercisable and the associated exercise price are subject to certain proportional adjustments as set forth in the Warrants.

The Company estimated the fair value of these Warrants as of the issuance date to be $0.4 million, which was used in estimating the fair value of the debt instrument and was recorded as equity. The fair value of the Warrants was calculated using the Black-Scholes option-valuation model, and was based on the strike price of $2.83, the stock price at issuance of $2.66, the ten-year contractual term of the warrants, a risk-free interest rate of 2.22%, expected volatility of 80.22% and 0% expected dividend yield.

As of December 31, 2019, warrants to purchase 176,679 shares of common stock issued to the Lender and its affiliates had not been exercised and were still outstanding. These warrants expire in May 2029.

Original Loan Agreement Warrants

In connection with the Original Loan Agreement, the Company issued warrants to the Lenders which were exercisable for an aggregate of 176,730 shares of common stock with an exercise price of $6.79 per share, or the Warrants. In connection with Amendment No. 2 to the Original Loan Agreement, the Company reduced the exercise price of the warrants already held by the Lenders from the previous exercise price of $6.79 per share to $3.88 per share, or the First Warrant Amendments. In connection with Amendment No. 3 to the Original Loan Agreement, the Company reduced the exercise price of the warrants already held by the Lenders from the previous exercise price of $3.88 per share to $3.07 per share, or the Second Warrant Amendments.

In December 2018, all of the outstanding warrants were exercised to purchase 176,730 shares of common stock which were issued to the Lenders.

2012 Private Placement Warrants

In connection with the Private Placement, completed in June 2012, the Company issued PIPE warrants to purchase up to 2,630,103 shares of common stock. The per share exercise price of the PIPE warrants was $3.40 which equals the closing consolidated bid price of the Company's common stock on May 29, 2012, the effective date of the Purchase Agreement. The PIPE warrants issued in the Private Placement became exercisable six months after the issuance date and expire on the five-year anniversary of the initial exercisability date. Under the terms of the PIPE warrants, upon certain transactions, including a merger, tender offer, sale of all or substantially all of the assets of the Company or if a person or group shall become the owner of 50% of the Company's issued and outstanding common stock, which is outside of the Company's control, each PIPE warrant holder may elect to receive a cash payment in exchange for the warrant, in an amount determined by application of the Black-Scholes option-pricing model. Accordingly, the PIPE warrants were recorded as a liability at fair value and then marked to fair value each reporting period, with changes in estimated fair value recorded through the Consolidated Statements of Comprehensive Loss in interest income and other income (expense), net. The PIPE warrants were valued using the Black-Scholes option-pricing model, the inputs for which included exercise price of the PIPE warrants, market price of the underlying common shares, expected term, volatility based on a group of the Company's peers and the risk-free rate corresponding to the expected term of the PIPE warrants.

Upon execution of the Purchase Agreement, the fair value of the PIPE warrants was estimated to be $5.8 million, which was recorded as a liability. The change in fair value for the year ended December 31, 2017, which was recorded as other income, was $0.3 million.

During the year ended December 31, 2017, 512,456 warrants expired unexercised and there are no remaining PIPE warrants outstanding.

10. Commitments and Contingencies

Litigation

From time to time the Company may be involved in legal proceedings arising in the ordinary course of business. The Company does not have contingent liabilities established for any litigation matters.

11. Stockholders' Equity

Common Stock

2018 Underwritten Public Offerings

On November 14, 2018, the Company completed an underwritten public offering of 14,603,173 shares of common stock, at a price of $3.15 per share to the public. The total gross proceeds from this offering were approximately $46.0 million with net proceeds to the Company of $43.1 million after deducting the underwriting discounts and commissions and other offering expenses payable by us.

On July 16, 2018, the Company completed an underwritten public offering of 7,272,727 shares of common stock, at a price of $2.75 per share to the public. On August 7, 2018, the underwriters exercised in full their option to purchase an additional 1,090,909 shares of common stock at the public offering price of $2.75 per share, less underwriting discounts and commissions. The total gross proceeds from this offering of an aggregate 8,363,636 shares were approximately $23.0 million with net proceeds to the Company of $21.7 million after deducting the underwriting discounts and commissions and other offering expenses payable by the Company.

ATM Agreement

On June 21, 2016, the Company entered into a Controlled Equity Offering℠ Sales Agreement, or the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent, pursuant to which the Company may offer and sell, from time to time through Cantor, shares of the Company's common stock, or the Common Stock having an aggregate offering price of up to $40.0 million, or the Shares. On May 9, 2019, the Company increased the aggregate offering price of shares of the Company's common stock which may be offered and sold under the ATM Agreement by $40.0 million, for a total of $80.0 million, or the Shares. The offering of Shares pursuant to the ATM Agreement will terminate upon the earlier of (a) the sale of all of the Shares subject to the ATM Agreement or (b) the termination of the ATM Agreement by Cantor or the Company, as permitted therein. The Company will pay Cantor a commission rate in the low single digits on the aggregate gross proceeds from each sale of Shares and have agreed to provide Cantor with customary indemnification and contribution rights. During the year ended December 31, 2019, the Company issued and sold 500,000 shares of common stock pursuant to the ATM Agreement, for which the Company received net proceeds of approximately $1.2 million, after deducting commissions, fees and expenses of $32,000. During the year ended December 31, 2018, the Company issued and sold an aggregate of 4.4 million shares of common stock pursuant to the ATM Agreement, for which the Company received net proceeds of approximately $16.8 million, after deducting commissions, fees and expenses of $0.4 million. During the year ended December 31, 2017, the Company issued and sold 5.4 million shares of common stock pursuant to the ATM Agreement, for which the Company received net proceeds of approximately $15.7 million, after deducting commissions, fees and expenses of $0.5 million.

As of December 31, 2019, the Company may offer and sell shares of the Company's common stock having an aggregate offering price of up to $45.3 million.

Stock Plans

2006 Stock Plan

In August 2006, the Company established the 2006 Plan in which 342 shares of common stock were originally reserved for the issuance of incentive stock options, or ISOs, and nonstatutory stock options, or NSOs, to employees, directors or consultants of the Company. In February 2008, an additional 375 shares of common stock were reserved for issuance under the 2006 Plan and, in November 2009, an additional approximately 1.4 million shares of common stock were reserved for issuance under the 2006 Plan. Per the 2006 Plan, the exercise price of ISOs and NSOs granted to a stockholder who at the time of grant owns stock representing more than 10% of the voting power of all classes of the stock of the Company could not be less than 110% of the fair value per share of the underlying common stock on the date of grant. Effective upon the execution and delivery of the underwriting agreement for the Company's IPO, no additional stock options or other stock awards may be granted under the 2006 Plan.

2011 Equity Incentive Plan

In January 2011, the Board of Directors adopted, and the Company's stockholders approved, the 2011 Equity Incentive Plan, or 2011 Incentive Plan. As of February 10, 2011, no more awards may be granted under the 2006 Plan, although all outstanding stock options and other stock awards previously granted under the 2006 Plan will continue to remain subject to the terms of the 2006 Plan.

The initial aggregate number of shares of the Company's common stock that were issuable pursuant to stock awards under the 2011 Incentive Plan was approximately 1.9 million shares. The number of shares of common stock reserved for issuance under the 2011 Incentive Plan automatically increased on January 1 of each year, starting on January 1, 2012 and continuing through January 1, 2020, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or such lesser number of shares of common stock as determined by the Board of Directors. The term of any option granted under the 2011 Incentive Plan is determined by the Board of Directors on the date of grant but shall not be longer than 10 years. Options under the 2011 Equity Incentive Plan generally vest over four years, and all options expire after 10 years. The Company issues new shares for settlement of vested restricted stock units and exercises of stock options. The Company does not have a policy of purchasing its shares relating to its stock-based programs.

2011 Employee Stock Purchase Plan

Additionally, in January 2011, the Board of Directors adopted, and the Company's stockholders approved, the 2011 Employee Stock Purchase Plan, or the ESPP.

As of December 31, 2019, there were 655,420 shares available for issuance under the ESPP. In January 2020, an additional 1,591,462 shares were authorized for issuance under the 2011 Incentive Plan. The number of shares of the Company's common stock reserved for issuance under the ESPP automatically increased on January 1 of each year, starting January 1, 2012 and continuing through January 1, 2020, in an amount equal to the lower of (1) 2% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or (2) a number of shares of common stock as determined by the Board of Directors. If a purchase right granted under the ESPP terminates without having been exercised, the shares of the Company's common stock not purchased under such purchase right will be available for issuance under the ESPP.

In the year ended December 31, 2019, there were 203,469 shares issued under the ESPP. The weighted average fair value of shares issued under the ESPP in 2019, 2018 and 2017 was $2.33, $1.51 and $2.59 per share, respectively.

12. Stock-Based Compensation

The Company recorded total stock-based compensation expense for stock options, stock awards and the ESPP as follows (in thousands):

	December 31, 2019	December 31, 2018	December 31, 2017
Cost of goods sold	$ 260	$ 358	$ 324
Research and development	920	1,970	1,901
Selling, general and administrative	3,877	2,840	2,069
Total	$ 5,057	$ 5,168	$ 4,294

The following table summarizes restricted stock unit activity under the 2011 Incentive Plan:

	Number of Restricted Stock Units	Weighted Average Grant Date Fair Value
Restricted stock units outstanding, January 1, 2019	—	$ —
Granted	1,029,085	2.53
Vested	—	—
Forfeited	(40,440)	2.54
Restricted stock units outstanding, December 31, 2019	988,645	$ 2.53

The following table summarizes option activity under the 2011 Incentive Plan and 2006 Plan:

	Number of Stock Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value (in thousands)
December 31, 2018	11,422,705	$ 3.64		
Granted	2,058,128	2.53		
Forfeited	(442,979)	2.57		
Expired	(277,413)	5.31		
Exercised	(111,702)	2.41		
December 31, 2019	12,648,739	$ 3.47	6.5	$ 197
Vested and exercisable options—December 31, 2019	8,583,475	$ 3.90	5.6	$ 90
Vested and expected to vest—December 31, 2019	12,648,739	$ 3.47	6.5	$ 197

As of December 31, 2019, there were 1,950,652 shares available for future grant under the 2011 Incentive Plan. In January 2020, an additional 3,182,924 shares were authorized for issuance under the 2011 Incentive Plan.

Additional information regarding the Company's stock options outstanding and vested and exercisable as of December 31, 2019 is summarized below:

	Options Outstanding			Options Vested and Exercisable	
Exercise Prices	Number of Stock Options Outstanding	Weighted-Average Remaining Contractual Life (Years)	Weighted-Average Exercise Price per Share	Shares Subject to Stock Options	Weighted-Average Exercise Price per Share
$1.68 - $2.56	4,469,976	7.7	$ 2.24	2,308,859	$ 2.21
$2.57 - $3.92	5,946,276	6.5	$ 3.13	4,081,817	$ 3.23
$4.08 - $6.60	1,627,987	4.2	$ 5.58	1,588,299	$ 5.61
$8.18 - $10.55	604,500	4.0	$ 10.29	604,500	$ 10.29
	12,648,739	6.5	$ 3.47	8,583,475	$ 3.90

The weighted average grant-date fair value of options granted during the years ended December 31, 2019, 2018 and 2017 was $1.83, $1.62 and $1.91 per share, respectively. As of December 31, 2019, total stock-based compensation expense related to unvested options to be recognized in future periods was $6.4 million which is expected to be recognized over a weighted-average period of 2.4 years. The grant date fair value of shares vested during the years ended December 31, 2019, 2018 and 2017 was $4.4 million, $4.9 million and $3.5 million, respectively. The total intrinsic value of options exercised during the years ended December 31, 2019, 2018 and 2017 was $0.1 million, $0.2 million and $40 thousand, respectively.

The Company used the following assumptions to calculate the fair value of each employee stock option:

	Year Ended December 31,		
	2019	2018	2017
Expected term (in years)	6.0	5.9	5.7
Risk-free interest rate	1.5% - 2.5%	2.5% - 3.1%	1.82% - 2.09%
Expected volatility	85%	83%	73%
Expected dividend rate	0%	0%	0%

13. Net Loss per Share of Common Stock

The Company's basic net loss per share of common stock is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period. The diluted net loss per share of common stock is computed by giving effect to all potential common stock equivalents outstanding for the period determined using the treasury stock method. For purposes of this calculation, options to purchase common stock, restricted stock units and warrants to purchase common stock were considered to be common stock equivalents. In periods with a reported net loss, common stock equivalents are excluded from the calculation of diluted net loss per share of common stock if their effect is antidilutive.

The following outstanding shares of common stock equivalents were excluded from the computation of diluted net loss per share of common stock for the periods presented because including them would have been antidilutive:

	Year Ended December 31,		
	2019	2018	2017
ESPP, RSUs and stock options to purchase common stock	13,798,797	11,797,960	8,767,783
Common stock warrants	176,679	—	176,730

14. Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2019	2018
Accrued compensation and employee benefits	$ 3,796	$ 3,611
Inventory and other contract manufacturing accruals	752	234
Other accrued liabilities	980	695
Total accrued liabilities	$ 5,528	$ 4,540

15. 401(k) Plan

The Company sponsors a 401(k) plan that stipulates that eligible employees can elect to contribute to the 401(k) plan, subject to certain limitations. Pursuant to the 401(k) plan, the Company makes a matching contribution of up to 4% of the related compensation. Under the vesting schedule, employees have ownership in the matching employer contributions based on the number of years of vesting service completed. Company contributions were $0.5 million for the year ended December 31, 2019 and $0.3 million for each of the years ended December 31, 2018 and 2017.

16. Income Taxes

The Company recorded a provision for income taxes of $3.0 thousand and $2.0 thousand during the years ended December 31, 2019 and 2018, respectively, and a benefit for income taxes of $0.7 million during the year ended December 31, 2017.

Net deferred tax assets as of December 31, 2019 and 2018 consist of the following (in thousands):

	December 31, 2019	December 31, 2018
Deferred tax assets:		
Accruals and other	$ 3,672	$ 3,263
Research credits	7,275	7,275
Net operating loss carryforward	52,361	39,082
Section 59(e) R&D expenditures	8,933	10,387
Deferred revenue	21,324	20,689
Total deferred tax assets	93,565	80,696
Valuation allowance	(93,565)	(80,696)
Net deferred tax assets	$ —	$ —

Reconciliations of the statutory federal income tax to the Company's effective tax during the years ended December 31, 2019, 2018 and 2017 are as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Tax at statutory federal rate	$ (11,180)	$ (9,901)	$ (17,751)
State tax—net of federal benefit	(2,538)	(792)	350
General business credits	—	(500)	(316)
Stock options	800	1,048	42
Other	7	295	(19)
Change in valuation allowance	12,914	9,852	(17,110)
Tax reform – tax rate change	—	—	34,103
Provision (benefit) for income taxes	$ 3	$ 2	$ (701)

ASC 740 requires that the tax benefit of net operating losses, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is "more likely than not." Realization of deferred tax assets is dependent on future taxable income, if any, the timing and the amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $12.9 million and $9.9 million, and decreased by $17.1 million during the years ended December 31, 2019, 2018 and 2017, respectively.

As of December 31, 2019, the Company had federal net operating loss carryforwards of $212.4 million, of which $114.9 million federal net operating losses generated before January 1, 2018 will begin to expire in 2029. Federal net operating losses of $97.5 million generated in 2019 and 2018 will carryforward indefinitely but are subject to the 80% taxable income limitation. As of December 31, 2019, the Company had state net operating loss carryforwards of $113.5 million, which begin to expire in 2028.

As of December 31, 2017, the Company had a federal alternative minimum tax credit carryover of $0.7 million which was refundable under the tax reform enacted on December 22, 2017, $0.3 million of which was received during the year ended December 31, 2019, $0.1 million of which is now classified as Tax receivable on the Company's balance sheet and $0.3 million of which is classified as a Long-term tax receivable.

As of December 31, 2019, the Company had federal research credit carryovers of $6.5 million, which begin to expire in 2026. As of December 31, 2019, the Company had state research credit carryovers of $4.0 million, which will carryforward indefinitely.

Under Section 382 of the Internal Revenue Code of 1986, as amended, 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 loss carryforwards and other pre-change tax attributes, such as research credits, to offset its post-change income may be limited. Based on an analysis performed by the Company as of December 31, 2013, it was determined that two ownership changes have occurred since inception of the Company. The first ownership change occurred in 2006 at the time of the Series A financing and, as a result of the change, $1.4 million in federal and state net operating loss carryforwards will expire unutilized. In addition, $26 thousand in federal and state research and development credits will expire unutilized. The second ownership change occurred in July 2013 at the time of the underwritten public offering; however, the Company believes the resulting annual imposed limitation on use of pre-change tax attributes is sufficiently high that the limit itself will not result in unutilized pre-change tax attributes.

Uncertain Tax Positions

A reconciliation of the beginning and ending balances of the unrecognized tax benefits during the years ended December 31, 2019, 2018 and 2017 is as follows (in thousands):

	Year Ended December 31,		
	2019	**2018**	**2017**
Unrecognized benefit—beginning of period	$ 2,635	$ 2,365	$ 2,162
Gross increases—prior period tax positions	—	57	—
Gross increases—current period tax positions	—	213	203
Unrecognized benefit—end of period	$ 2,635	$ 2,635	$ 2,365

The entire amount of the unrecognized tax benefits would not impact the Company's effective tax rate if recognized.

There were no accrued interest or penalties related to unrecognized tax benefits in the years ended December 31, 2019, 2018 and 2017. The Company files income tax returns in the United States, California, and other states. The tax years 2005 through 2014, and 2016 through 2019, remain open in all jurisdictions. The Company is not currently under examination by income tax authorities in federal, state or other foreign jurisdictions. The Company does not anticipate any significant changes within 12 months of this reporting date of its uncertain tax positions.

17. Subsequent Event

Merger Agreement

On March 15, 2020, the Company entered into the Agreement and Plan of Merger with Tetraphase Pharmaceuticals, Inc., or Tetraphase, and Consolidated Merger Sub, Inc., a Delaware corporation and indirect wholly owned subsidiary of the Company, or Merger Sub. Pursuant to the merger agreement, (i) each share of Tetraphase common stock issued and outstanding immediately prior to the effective time of the merger will automatically be converted into the right to receive 0.6303 shares of the Company's common stock, subject to certain adjustments pursuant to the terms of the merger agreement, and a contingent value right, or CVR, that could provide up to an additional aggregate $12.5 million to Tetraphase stockholders upon the achievement of net sales of XERAVA™ of $20 million, $35 million and $55 million within the applicable timeframes, and as soon as year-end 2021; and (ii) Merger Sub will merge with and into Tetraphase, with Tetraphase continuing as the surviving entity and a wholly owned subsidiary of the Company. The merger agreement has been approved by the board of directors of the Company and Tetraphase. The closing of the merger is expected in the second quarter of 2020 subject to customary closing conditions, including, among others, (i) the adoption of the Agreement and Plan of Merger by a majority of the stockholders of Tetraphase; (ii) the absence of (A) any temporary restraining order, preliminary or permanent injunction or other order issued by any court of competent jurisdiction enjoining or otherwise preventing the consummation of the merger or (B) any applicable law that makes consummation of the merger illegal; (iii) the absence of certain legal proceedings to which a governmental body is a party relating to the merger; (iv) subject to certain qualifications, the accuracy of the representations and warranties of the parties and compliance by the parties with their respective obligations under the merger agreement; (v) the absence of any material adverse effect on Tetraphase or the Company since the date of the merger agreement; (vi) the registration statement on Form S-4 to register the Company's common stock to be issued in the merger being declared effective by the SEC; and (vii) a minimum Tetraphase net cash balance.

AcelRx shareholders will own approximately 85.4% of the combined company, and Tetraphase shareholders will own approximately 14.6% on a pro forma, fully diluted basis, giving effect to all dilutive securities at the time of announcement, and excluding any settlement of the CVR through issuance of AcelRx common stock.

Co-Promotion Agreement

On March 15, 2020, the Company entered into the Co-Promotion Agreement with Tetraphase to co-promote DSUVIA and Tetraphases's XERAVA™ (eravacycline), which is FDA approved for the treatment of complicated intra-abdominal infections. Under the terms of this agreement, each company is responsible for maintaining compliance under the agreed marketing and promotion plan and achieving a minimum number of sales calls for each product. Either party can terminate the agreement with 15 months written notice. In the event of a change of control, or CoC, of either party, the CoC party will be subject to meeting certain performance standards, and if these performance standards are not met, then a royalty of 10% of net sales on the CoC party's product will be payable to the non-CoC party until the end of the agreement. The non-CoC party will also be able to solicit the employees of CoC party in the event of a change of control and have the right to terminate the agreement with one month's written notice.

On March 16, 2020, in connection with entering into the Co-Promotion Agreement, the Company initiated a reduction in headcount, designed to eliminate the overlap with the Tetraphase commercial team to more efficiently commercialize DSUVIA in connection with the Tetraphase commercial team. The Company has eliminated 30 positions, mainly within the commercial organization. The headcount reduction will be completed in the first quarter of 2020. The Company estimates that it will incur aggregate severance and related charges of approximately $0.5 million in the first quarter of 2020. The Company expects that this headcount reduction will result in cost savings of approximately $8 million on an annualized basis. These estimates are subject to a number of assumptions, and actual results may differ. The Company may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the reduction.

18. Unaudited Quarterly Financial Data

The following table sets forth certain unaudited quarterly financial data for the eight quarters ended December 31, 2019. The unaudited information set forth below has been prepared on the same basis as the audited information and includes all adjustments necessary to present fairly the information set forth herein. The operating results for any quarter are not indicative of results for any future period. All data is in thousands except per share data.

	2019				2018			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Revenues	$ 265	$ 941	$ 608	$ 475	$ 343	$ 818	$ 377	$ 613
Operating costs and expenses	$ 12,583	$ 14,302	$ 14,142	$ 15,467	$ 8,612	$ 7,971	$ 9,705	$ 11,590
Net loss	$ (13,674)	$ (12,412)	$ (12,731)	$ (14,423)	$ (11,592)	$ (10,541)	$ (12,458)	$ (12,558)
Net loss per share (basic and diluted)	$ (0.17)	$ (0.16)	$ (0.16)	$ (0.18)	$ (0.23)	$ (0.20)	$ (0.21)	$ (0.18)

Exhibit 4.1

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following is a description of the common stock, $0.001 par value ("Common Stock") of AcelRx Pharmaceuticals, Inc. (the "Company"), which is the only security of the Company registered pursuant to Section 12 of the Securities Exchange Act of 1934, as amended. The following summary description is based on the provisions of our Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation"), our Amended and Restated Bylaws (the "Bylaws"), and the applicable provisions of the Delaware General Corporation Law (the "DGCL"). The description is intended as a summary and is qualified in its entirety by reference to our Certificate of Incorporation and Bylaws. Our Certificate of Incorporation and our Bylaws are filed as exhibits to this Annual Report on Form 10-K.

Authorized Capital Stock

Our authorized capital stock consists of 200,000,000 shares of Common Stock and 10,000,000 shares of preferred stock, $0.001 par value ("Preferred Stock"). The rights, preferences and privileges of the holders of our Common Stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our Preferred Stock that we may designate in the future. As of December 31, 2019, we have no shares of Preferred Stock issued and outstanding. For a complete description of the terms and provisions of the Company's Preferred Stock refer to our Certificate of Incorporation and Bylaws.

Common Stock

Voting Rights. Each holder of our Common Stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. In all matters other than the election of directors, the affirmative vote of the majority of shares present in person, by remote communication, or represented by proxy at a meeting of the stockholders and entitled to vote generally on the subject matter shall be the act of the stockholders. Directors shall be elected by a plurality of the votes of the shares present in person, by remote communication, or represented by proxy at a meeting of the stockholders and entitled to vote generally on the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors to be elected at any particular time.

Dividends. Subject to preferences that may be applicable to any then outstanding Preferred Stock, holders of our Common Stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine.

Liquidation. In the event of our liquidation, dissolution or winding up, holders of our Common Stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of Preferred Stock.

Rights. Holders of our Common Stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our Common Stock.

Fully Paid and Nonassessable. All of our outstanding shares of Common Stock are fully paid and nonassessable.

Anti-Takeover Effects of Provisions of our Certificate of Incorporation and Bylaws and Delaware Law

Certificate of Incorporation and Bylaws. Our Certificate of Incorporation and Bylaws include a number of provisions that may deter or impede hostile takeovers or changes of control or management. These provisions include:

- *Issuance of undesignated Preferred Stock*. Under our Certificate of Incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated Preferred Stock with rights and preferences, including voting rights, designated from time to time by the board of directors. The existence of authorized but unissued shares of Preferred Stock enables our board of directors to make it more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.

- *Classified board*. Our Certificate of Incorporation provides for a classified board of directors consisting of three classes of directors, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. This provision may have the effect of delaying a change in control of the board.

- *Board of directors vacancies*. Our Certificate of Incorporation and Bylaws authorize only our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors may be set only by resolution adopted by a majority vote of our entire board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominees.

- *Stockholder action; special meetings of stockholders*. Our Certificate of Incorporation provides that our stockholders may not take action by written consent and may only take action at annual or special meetings of our stockholders. Stockholders will not be permitted to cumulate their votes for the election of directors. Our Bylaws further provide that special meetings of our stockholders may be called only by a majority of our board of directors, the chairman of our board of directors, or our chief executive officer. These provisions may prevent stockholders from corporate actions as stockholders at times when they otherwise would like to do so.

- *Advance notice requirements for stockholder proposals and director nominations*. Our Bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders. Our Bylaws also specify certain requirements as to the form and content of a stockholder's notice. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at our annual meeting of stockholders.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage certain types of transactions that may involve an actual or threatened acquisition of us. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the DGCL ("Section 203") regulating corporate takeovers. This section prevents some Delaware corporations from engaging, under some circumstances, in a business combination, which includes a merger or sale of at least 10% of the corporation's assets with any interested stockholder, meaning a stockholder who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of the corporation's outstanding voting stock, unless:

- the transaction is approved by the board of directors prior to the time that the interested stockholder became an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder's becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced; or
- at or subsequent to such time that the stockholder became an interested stockholder the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders by at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

In general, Section 203 defines "business combination" to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or

- the receipt by the interested stockholder of the benefit of any loss, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an “interested stockholder” as an entity or person who, together with the person’s affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

A Delaware corporation may “opt out” of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders’ amendment approved by at least a majority of the outstanding voting shares. We have not “opted out” of these provisions and do not plan to do so. The statute could prohibit or delay mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire us.

Transfer Agent and Registrar

The transfer agent and registrar for our Common Stock is Computershare, Inc.: 1-800-736-3001. The transfer agent's address is 250 Royall Street, Canton, Massachusetts 02021.

Exhibit 10.16

Non-Employee Director Compensation Policy

Compensation for our non-employee directors consists of cash, restricted stock units and stock options. The Compensation Committee periodically reviews the compensation paid to non-employee directors for their service on the Board and its committees and recommends any changes considered appropriate to the full Board for its approval. In February 2020, the Board approved the recommendations of the Compensation Committee to align our non-employee director cash compensation with the 50th percentile of our peer group and equity compensation with the 25th percentile of our peer group. Accordingly, effective January 1, 2020, each member of our Board who is not our employee will receive an annual retainer of $40,000. In addition, our non-employee directors will receive the following cash compensation for Board services, as applicable:

- the Board Chair receives an additional annual retainer of $30,000;
- the Audit Committee Chair receives an additional annual retainer of $20,000;
- the Compensation Committee Chair receives an additional annual retainer of $15,000;
- the Nominating and Corporate Governance Committee Chair receives an additional annual retainer of $10,000;
- an Audit Committee member receives an additional annual retainer of $10,000;
- a Compensation Committee member receives an additional annual retainer of $7,500; and
- a Nominating and Corporate Governance Committee member receives an additional retainer of $5,000.

Beginning in February 2020, upon election or appointment to our Board, a new non-employee director will now receive an initial grant of a stock option to purchase 22,500 shares of our common stock, which will vest as to 1/36th of the shares subject to the option on an equal monthly basis over a three-year period, and 11,250 RSUs with vesting over three years with annual cliff vesting for each of the three years. Each non-employee director who is then serving as a director or who is elected to our Board on the date of an annual meeting will be eligible to receive a grant of a stock option to purchase 15,000 shares of our common stock, which would vest as to 1/12th of the shares subject to the option on an equal monthly basis over a one-year period, and 7,500 RSUs with cliff vesting in one year.

All Board and committee retainers accrue and are payable on a quarterly basis at the end of each calendar quarter of service. We continue to reimburse our non-employee directors for travel, lodging and other reasonable expenses incurred in connection with their attendance at Board or committee meetings.

Exhibit 10.17

2020 Cash Bonus Plan Summary

Target bonuses for named executive officers of AcelRx Pharmaceuticals, Inc. (the "Company") under the 2020 Cash Bonus Plan (the "**Plan**") will range from 35% to 60% of such executive's 2020 base salary. The amount of cash bonus, if any, for each named executive officer will be based on both the named executive officer achieving his or her individual performance goals and on the Company meeting the 2020 corporate objectives to be approved by the Board. The target bonuses for the Company's named executive officers for 2020 are as follows:

Name	Position	Bonus %
Vincent Angotti	Chief Executive Officer	60%
Pamela Palmer, M.D., Ph.D.	Chief Medical Officer	40%
Raffi Asadorian	Chief Financial Officer	40%
Badri Dasu	Chief Engineering Officer	35%
Lawrence Hamel	Chief Development Officer	35%

Mr. Angotti's cash bonus under the Plan shall be based 100% on the achievement of the 2020 corporate objectives. The cash bonuses under the Plan for all other named executive officers shall be based 40% on the achievement of his or her individual performance goals, as determined by the Board, and 60% on the achievement of the 2020 corporate objectives. The named executive officers' actual bonuses may exceed 100% of target in the event performance exceeds the predetermined goals.

Exhibit 21.2

SUBSIDIARIES OF THE REGISTRANT

ARPI LLC, duly formed under the laws of the State of Delaware, a wholly owned subsidiary of AcelRx Pharmaceuticals, Inc.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

(i) Registration Statements on Form S-8 (Nos. 333-230139, 333-223535, 333-216492, 333-202709, 333-194634 and 333-187206) pertaining to the 2011 Equity Incentive Plan,

(ii) Registration Statements on Form S-8 (Nos. 333-209998 and 333-180334) pertaining to the 2011 Equity Incentive Plan and 2011 Employee Stock Purchase Plan,

(iii) Registration Statement on Form S-8 (No. 333-172409) pertaining to the 2006 Stock Plan, 2011 Equity Incentive Plan and 2011 Employee Stock Purchase Plan, and

(iv) Registration Statement on Form S-3 (No. 333-218506)

of our reports dated March 16, 2020 with respect to the consolidated financial statements and the effectiveness of internal control over financial reporting of AcelRx Pharmaceuticals, Inc., which appear in this Annual Report on Form 10-K.

/s/ OUM & CO. LLP

San Francisco, California
March 16, 2020

Exhibit 31.1

CERTIFICATIONS

I, Vincent J. Angotti, certify that:

1. I have reviewed this annual report on Form 10-K of AcelRx Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's Board of Directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2020

/s/ Vincent J. Angotti
Vincent J. Angotti
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Raffi Asadorian, certify that:

1. I have reviewed this annual report on Form 10-K of AcelRx Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's Board of Directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2020

/s/ Raffi Asadorian

Raffi Asadorian
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Vincent J. Angotti, Chief Executive Officer of AcelRx Pharmaceuticals, Inc. (the "Company"), and Raffi Asadorian, Chief Financial Officer of the Company, each hereby certifies that, to the best of his or her knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2019, to which this Certification is attached as Exhibit 32.1 (the "Annual Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and

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

In Witness Whereof, the undersigned have set their hands hereto as of the 16th day of March 2020.

/s/ Vincent J. Angotti	/s/ Raffi Asadorian
Vincent J. Angotti	Raffi Asadorian
Chief Executive Officer	Chief Financial Officer

"This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of AcelRx Pharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing."