UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

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

For the quarterly period ended September 30, 2019

or

☐ **TRANSITION REPORTS 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 Global Market**

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 ☒

As of October 28, 2019, the number of outstanding shares of the registrant's common stock was 79,573,001.

ACELRX PHARMACEUTICALS, INC.

QUARTERLY REPORT ON FORM 10-Q FOR THE QUARTER ENDED SEPTEMBER 30, 2019

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Forward-Looking Statements

This Quarterly Report on Form 10-Q, or Form 10-Q, 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-Q are contained principally under "Part I. Financial Information - Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Part II. Other Information - Item 1A. Risk Factors". 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-Q, 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:

- 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;
- 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 “Part II. Other Information - Item 1A. Risk Factors” in this Form 10-Q 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-Q 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-Q. 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. FINANCIAL INFORMATION

Item 1. Financial Statements

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Balance Sheets
(In thousands, except share data)

	September 30, 2019 (Unaudited)	December 31, 2018[1]
Assets		
Current Assets:		
Cash and cash equivalents	$ 21,949	$ 87,975
Short-term investments	58,451	17,740
Accounts receivable, net	244	49
Tax receivable	352	352
Inventories, net	2,980	854
Prepaid expenses and other current assets	1,693	1,024
Total current assets	85,669	107,994
Operating lease right-of-use assets	4,130	—
Property and equipment, net	13,844	11,483
Long-term tax receivable	351	351
Other assets	984	705
Total Assets	$ 104,978	$ 120,533
Liabilities and Stockholders' (Deficit) Equity		
Current Liabilities:		
Accounts payable	$ 2,649	$ 2,070
Accrued liabilities	4,905	4,540
Long-term debt, current portion	2,083	8,611
Deferred revenue, current portion	315	315
Operating lease liabilities, current portion	791	—
Liability related to the sale of future royalties, current portion	688	392
Total current liabilities	11,431	15,928
Long-term debt, net of current portion	21,924	3,380
Deferred revenue, net of current portion	2,912	3,148
Operating lease liabilities, net of current portion	4,043	—
Liability related to the sale of future royalties, net of current portion	92,375	93,287
Other long-term liabilities	567	537
Total liabilities	133,252	116,280
Commitments and Contingencies		
Stockholders' (Deficit) Equity:		
Common stock, $0.001 par value—200,000,000 shares authorized as of September 30, 2019 and 100,000,000 shares authorized as of December 31, 2018; 79,573,001 and 78,757,930 shares issued and outstanding as of September 30, 2019 and December 31, 2018, respectively	79	78
Additional paid-in capital	355,330	349,194
Accumulated deficit	(383,683)	(345,019)
Total stockholders' (deficit) equity	(28,274)	4,253
Total Liabilities and Stockholders' (Deficit) Equity	$ 104,978	$ 120,533

(1) The condensed consolidated balance sheet as of December 31, 2018 has been derived from the audited financial statements as of that date included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018.

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Statements of Comprehensive Loss
(Unaudited)
(In thousands, except share and per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Revenue:				
Net product sales	$ 116	$ —	$ 218	$ —
Collaboration agreement	492	177	1,596	802
Contract and other	—	200	—	736
Total revenue	608	377	1,814	1,538
Operating costs and expenses:				
Cost of goods sold	2,148	875	5,188	2,738
Research and development	1,058	3,642	3,598	10,433
Selling, general and administrative	10,936	5,188	32,241	13,117
Total operating costs and expenses	14,142	9,705	41,027	26,288
Loss from operations	(13,534)	(9,328)	(39,213)	(24,750)
Other income (expense):				
Interest expense	(828)	(529)	(1,704)	(1,758)
Interest income and other income (expense), net	645	312	1,728	643
Non-cash interest income (expense) on liability related to future sale of royalties	986	(2,913)	375	(8,724)
Total other income (expense)	803	(3,130)	399	(9,839)
Net loss before income taxes	(12,731)	(12,458)	(38,814)	(34,589)
Provision for income taxes	—	—	(3)	(2)
Net loss	$ (12,731)	$ (12,458)	$ (38,817)	$ (34,591)
Comprehensive loss	$ (12,731)	$ (12,458)	$ (38,817)	$ (34,591)
Net loss per share of common stock, basic and diluted	$ (0.16)	$ (0.21)	$ (0.49)	$ (0.64)
Shares used in computing net loss per share of common stock, basic and diluted	79,461,121	60,004,416	79,053,256	54,292,206

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Statements of Stockholders' Equity (Deficit)
(Unaudited)
(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, 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	—	—	1,107	—	—	1,107
Issuance of common stock upon exercise of stock options	13,583	—	31	—	—	31
Issuance of common stock upon ESPP purchase	85,135	1	238	—	—	239
Net loss	—	—	—	(13,674)	—	(13,674)
Balance as of March 31, 2019	78,856,648	$ 79	$ 350,570	$ (358,540)	$ —	$ (7,891)
Stock-based compensation	—	—	1,346	—	—	1,346
Issuance of common stock upon exercise of stock options	57,522	—	155	—	—	155
Issuance of warrants related to debt financing	—	—	383	—	—	383
Net loss	—	—	—	(12,412)	—	(12,412)
Balance as of June 30, 2019	78,914,170	$ 79	$ 352,454	$ (370,952)	$ —	$ (18,419)
Stock-based compensation	—	—	1,326	—	—	1,326
Issuance of common stock in connection with equity financings	500,000	—	1,233	—	—	1,233
Issuance of common stock upon exercise of stock options	40,497	—	83	—	—	83
Issuance of common stock upon ESPP purchase	118,334	—	234	—	—	234
Net loss	—	—	—	(12,731)	—	(12,731)
Balance as of September 30, 2019	79,573,001	$ 79	$ 355,330	$ (383,683)	$ —	$ (28,274)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Other Comprehensive Income (Loss)	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance as of December 31, 2017	50,899,154	$ 51	$ 261,310	$ (297,870)	$ —	$ (36,509)
Stock-based compensation	—	—	1,080	—	—	1,080
Issuance of common stock upon ESPP purchase	92,290	—	141	—	—	141
Net loss	—	—	—	(11,592)	—	(11,592)
Balance as of March 31, 2018	50,991,444	$ 51	$ 262,531	$ (309,462)	$ —	$ (46,880)
Stock-based compensation	—	—	1,048	—	—	1,048
Issuance of common stock in connection with equity financings	2,335,743	2	7,405	—	—	7,407
Net loss	—	—	—	(10,541)	—	(10,541)
Balance as of June 30, 2018	53,327,187	$ 53	$ 270,984	$ (320,003)	$ —	$ (48,966)
Stock-based compensation	—	—	1,808	—	—	1,808
Issuance of common stock upon exercise of stock options	9,453	—	29	—	—	29
Issuance of common stock upon ESPP purchase	90,070	—	134	—	—	134
Issuance of common stock in connection with equity financings	8,363,636	8	21,658	—	—	21,666
Net loss	—	—	—	(12,458)	—	(12,458)
Balance as of September 30, 2018	61,790,346	$ 61	$ 294,613	$ (332,461)	$ —	$ (37,787)

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Statements of Cash Flows
(Unaudited)
(In thousands)

	Nine Months Ended September 30,	
	2019	**2018**
Cash flows from operating activities:		
Net loss	$ (38,817)	$ (34,591)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash royalty revenue related to royalty monetization	(238)	(220)
Non-cash interest (income) expense on liability related to royalty monetization	(375)	8,724
Depreciation and amortization	1,153	435
Non-cash interest expense related to debt financing	471	489
Stock-based compensation	3,779	3,936
Inventory impairment charge	855	—
Other	(563)	(147)
Changes in operating assets and liabilities:		
Accounts receivable	(195)	1,346
Inventories	(2,981)	100
Prepaid expenses and other assets	(430)	(563)
Other assets	(279)	—
Accounts payable	843	403
Accrued liabilities	465	236
Operating lease liabilities	(477)	—
Deferred rent	—	39
Deferred revenue	(236)	(272)
Net cash used in operating activities	(37,025)	(20,085)
Cash flows from investing activities:		
Purchase of property and equipment	(3,228)	(573)
Purchase of investments	(81,924)	(12,844)
Proceeds from maturities of investments	41,700	14,500
Net cash (used in) provided by investing activities	(43,452)	1,083
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)	(5,711)
Extinguishment of debt	(8,864)	—
Net proceeds from issuance of common stock in connection with equity financings	1,233	29,073
Net proceeds from issuance of common stock through equity plans	742	304
Net cash provided by financing activities	14,451	23,666
Net (decrease) increase in cash and cash equivalents	(66,026)	4,664
Cash and cash equivalents—Beginning of period	87,975	52,902
Cash and cash equivalents—End of period	$ 21,949	$ 57,566

See notes to condensed consolidated financial statements.

1. Organization and Summary of Significant Accounting Policies

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 Company is currently evaluating the timing of the resubmission of the new drug application, or NDA, for Zalviso. 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. The Company is currently evaluating the timing of the NDA resubmission for Zalviso.

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 countries of the European Union, or EU, 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.

Principles of Consolidation

The condensed 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. All intercompany accounts and transactions have been eliminated in consolidation. Refer to Note 8 “Liability Related to Sale of Future Royalties” for additional information.

Reclassifications

Certain prior year amounts in the condensed consolidated financial statements have been reclassified to conform to the current year's presentation.

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States for interim financial information and the rules and regulations of the United States. Securities and Exchange Commission, or SEC. Accordingly, they do not include all of the information and footnotes required by accounting principles generally accepted in the United States for complete financial statements. In the opinion of management, all adjustments (consisting of normal recurring adjustments) considered necessary for a fair presentation have been included.

Operating results for the three and nine months ended September 30, 2019, are not necessarily indicative of the results that may be expected for the year ending December 31, 2019. The condensed consolidated balance sheet as of December 31, 2018, was derived from the Company’s audited financial statements as of December 31, 2018, included in the Company’s Annual Report on Form 10-K filed with the SEC. These financial statements should be read in conjunction with the Company’s Annual Report on Form 10-K for the year ended December 31, 2018, which includes a broader discussion of the Company’s business and the risks inherent therein.

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 condensed 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.

Inventories, net

Inventories are valued at the lower of cost and 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 market 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.

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*. The 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.

Net 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, such as hospitals, surgical centers, and emergency departments. 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. 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. 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 customers, 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 customers 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.

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 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 condensed consolidated balance sheets as Accrued liabilities. 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.

Collaboration agreement revenue

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.

Contract and other 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. The DoD Contract period of performance ended on February 28, 2019.

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, demo 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 condensed 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

Revenues from product sales are recognized when distributors obtain control of the Company's products, which occurs at a point in time, upon delivery to such distributors. 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 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 realizable on a lower of cost or market 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.

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 Collaboration and License Agreement, dated as of December 16, 2013, as amended, to PDL for gross proceeds of $65.0 million, referred to as the Royalty Monetization. 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 estimates are updated related to the Royalty Monetization, accordingly.

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), within its condensed 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.

Significant Accounting Policies

The Company's significant accounting policies are detailed in its Annual Report on Form 10-K for the year ended December 31, 2018. Aside from the adoption of ASU No. 2016-02, *Leases (Topic 842)* described below under "Recently Adopted Accounting Standards" and explained more fully above in "Leases," and in Note 7 "Leases" below, there have been no significant changes to the Company's significant accounting policies during the three and nine months ended September 30, 2019, from those previously disclosed in its 2018 Annual Report on Form 10-K.

Recently Adopted Accounting Standards

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 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' equity (deficit) in the notes or as a separate statement for each period for which a statement of comprehensive income (loss) is required to be filed. The new interim reconciliation of changes in stockholders' equity (deficit) is included herein as a separate statement.

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 condensed consolidated balance sheet 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 Standards

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 September 30, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 1,052	$ —	$ —	$ 1,052
Money market funds	1,072	—	—	1,072
Commercial paper	15,625	—	—	15,625
Corporate debt securities	4,200	—	—	4,200
Total cash and cash equivalents	21,949	—	—	21,949
Short-term investments:				
U.S. government agency securities	$ 14,274	$ —	$ —	$ 14,274
Commercial paper	29,001	—	—	29,001
Corporate debt securities	15,176	—	—	15,176
Total short-term investments	58,451	—	—	58,451
Total cash, cash equivalents and investments	$ 80,400	$ —	$ —	$ 80,400

	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 investments	$ 105,715	$ —	$ —	$ 105,715

As of September 30, 2019 and December 31, 2018, none of the available-for-sale securities held by the Company had material unrealized losses. There were no other-than-temporary impairments for these securities at September 30, 2019 or December 31, 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 three and nine months ended September 30, 2019 and September 30, 2018.

As of September 30, 2019 and December 31, 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 September 30, 2019, the Company held, in addition to Level II assets, a contingent put option liability associated with the Loan and Security Agreement, or the Loan Agreement, with Oxford Finance LLC, or 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 condensed consolidated balance sheets. Changes to the estimated fair value of these liabilities are recorded in interest income and other income, net in the condensed 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 September 30, 2019			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$ 1,072	$ 1,072	$ —	$ —
U.S. government agency securities	14,274	—	14,274	—
Corporate debt securities	44,626	—	44,626	—
Commercial paper	19,376	—	19,376	—
Total assets measured at fair value	$ 79,348	$ 1,072	$ 78,276	$ —
Liabilities				
Contingent put option liability	$ 514	$ —	$ —	$ 514
Total liabilities measured at fair value	$ 514	$ —	$ —	$ 514

	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 tables set forth a summary of the changes in the fair value of the Company's Level III financial liabilities for the three and nine months ended September 30, 2019 and September 30, 2018 (in thousands):

	Three Months Ended September 30, 2019	Nine Months Ended September 30, 2019
Fair value—beginning of period	$ 657	$ 121
Change in fair value of contingent put option associated with the Loan Agreement	(143)	514
Change in fair value of contingent put option associated with the Prior Agreement	—	(121)
Fair value—end of period	$ 514	$ 514

	Three Months Ended September 30, 2018	Nine Months Ended September 30, 2018
Fair value—beginning of period	$ 166	$ 207
Change in fair value of contingent put option associated with the Prior Agreement	(22)	(63)
Fair value—end of period	$ 144	$ 144

3. Inventories, net

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

	Balance as of	
	September 30, 2019	**December 31, 2018**
Raw materials	$ 1,192	$ 694
Work-in-process	1,044	160
Finished goods	744	—
Total	$ 2,980	$ 854

During the quarter ended September 30, 2019, the Company recorded a write-down of inventory of approximately $0.9 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. Inventory that was forecasted to become obsolete due to expiration is recorded in Cost of goods sold in the accompanying condensed consolidated statements of comprehensive loss.

4. Revenue

As described in Note 1 “Organization and Summary of Significant Accounting Policies,” the Company began its commercial launch of DSUVIA in the first quarter of 2019. The Company has entered into the Amended Agreements with Grünenthal related to Zalviso. At September 30, 2019, approximately $3.2 million of deferred revenue is attributable to the discount on future manufacturing services of Zalviso for Grünenthal, which the Company expects to be recognized through 2029. 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.”

The following table presents changes in the Company’s contract liability for the nine months ended September 30, 2019:

	Balance at Beginning of the Period	Additions	Deductions	Balance at the end of the Period
	(in thousands)			
Contract liability:				
Deferred revenue	$ 3,463	$ 131	$ (367)	$ 3,227

During the three and nine months ended September 30, 2019, the Company recognized the following revenue (in thousands):

	Three months ended September 30, 2019	**Nine months ended September 30, 2019**
Amounts included in contract liabilities at the beginning of the period:		
Performance obligations satisfied – Amended Agreements	$ 78	$ 236
New activities in the period from performance obligations satisfied:		
Performance obligations satisfied – Amended Agreements	366	1,043
Total revenue from performance obligations satisfied	444	1,279
Royalty revenue	48	317
Net product sales of DSUVIA	116	218
Total revenue	$ 608	$ 1,814

5. Collaboration Agreement

As described in Note 1 “Organization and Summary of Significant Accounting Policies,” the Company has entered into the Amended Agreements with Grünenthal related to Zalviso.

Amended License Agreement

Under the Amended License Agreement, 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, 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.

Unless earlier terminated, the Amended MSA continues in effect until the later of the expiration of the obligation of Grünenthal to make royalty and supply and trademark fee payments or the end of any transition period for manufacturing obligations due to the expiration or termination of the Amended License Agreement. The Amended MSA is subject to earlier termination in connection with certain termination events in the Amended License Agreement, in the event the parties mutually agree, by a party in the event of an uncured material breach by the other party or upon the bankruptcy or insolvency of either party.

For the three and nine months ended September 30, 2019, the Company recognized $0.5 million and $1.6 million in revenue under the Amended Agreements, respectively. For the three and nine months ended September 30, 2018, the Company recognized $0.2 million and $0.8 million in revenue under the Amended Agreements, respectively. As of September 30, 2019, the Company had current and noncurrent portions of the deferred revenue balance under the Amended Agreements of $0.3 million and $2.9 million, respectively. The deferred revenue balance consists primarily of the significant and incremental discount on manufacturing services, which is being recognized on a straight-line basis over the period such discount is made available to Grünenthal, which began in February 2016 and is estimated to continue through 2029.

6. Long-Term Debt

Prior Agreement with Hercules

The Prior Agreement with Hercules required 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. We 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.

Interest expense related to the Amended Loan Agreement with Hercules was $0.6 million, $0.2 million of which represented amortization of the debt discount, for the nine months ended September 30, 2019. Interest expense related to the Amended Loan Agreement with Hercules was $0.5 million, $0.2 million of which represented amortization of the debt discount, for the three months ended September 30, 2018, and $1.7 million, $0.5 million of which represented amortization of the debt discount, for the nine months ended September 30, 2018.

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, as described above. 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%. 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 financial statements. As of September 30, 2019, the estimated fair value of the contingent put option liability was $0.5 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. The resulting difference between the two estimated fair values is the estimated fair value of the default provisions, or the contingent put option. 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 contingent put option liability is revalued at the end of each reporting period and any change in the fair value is recognized in interest income and other income (expense), net in the condensed consolidated statements of comprehensive loss.

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 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".

Interest expense related to the Loan Agreement was $0.8 million, $0.2 million of which represented amortization of the debt discount, for the three months ended September 30, 2019, and $1.1 million, $0.3 million of which represented amortization of the debt discount, for the nine months ended September 30, 2019.

7. Leases

Office Lease

The Company leases office and laboratory space for its corporate headquarters, located at 301 – 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, and the first two months to be abated provided that the Company is not in default thereunder. 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. The New Lease provided for an initial tenant incentive allowance of approximately $0.4 million with an expiration of the unused portion in December 2019. 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 1st, 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):

	Three months ended September 30, 2019	Nine months ended September 30, 2019
Operating lease costs	$ 340	$ 1,020
Sublease income	(150)	(446)
Net lease costs	$ 190	$ 574

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

	Three months ended September 30, 2019	Nine months ended September 30, 2019
Cash paid for amounts included in the measurement of lease liabilities		
Operating cash flows used for operating leases	$ 308	$ 921
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:

	September 30, 2019
Weighted-average remaining term – operating lease	4.13
Weighted-average discount rate – operating lease	11.72%

Maturities of lease liabilities as of September 30, 2019 are presented in the following table (in thousands):

Year:		
2019 (remaining three months)	$	362
2020		1,468
2021		1,505
2022		1,345
2023		1,386
Thereafter		116
Total future minimum lease payments		6,182
Less imputed interest		(1,348)
Total	$	4,834
Reported as:		
Operating lease liabilities	$	791
Operating lease liabilities, net of current portion		4,043
Total lease liability	$	4,834

Future minimum sublease payments as of September 30, 2019 are presented in the following table (in thousands):

Year:		
2019 (remaining three months)	$	144
2020		593
2021		610
2022		629
2023		648
Thereafter		54
Total future minimum sublease payments	$	2,678

The rent receivable balance is reported in the condensed consolidated balance sheet as follows (in thousands):

Reported as:		
Prepaid expenses and other current assets	$	73
Other assets		374
Total rent receivable	$	447

8. Liability Related to Sale of Future Royalties

On September 18, 2015, the Company entered into the Royalty Monetization with PDL for which it received gross proceeds of $65.0 million. Under the Royalty Monetization, PDL will receive 75% of the European royalties under the Amended License Agreement with Grünenthal, as well as 80% of the first four commercial milestones worth $35.6 million (or 80% of $44.5 million), up to a capped amount of $195.0 million over the life of the arrangement.

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. From inception through December 31, 2018, the Company's effective annual interest expense rate was approximately 13.0%. 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 $36 million, therefore, a contingent gain of approximately $29 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. The change in estimate resulted in a decrease of $2.7 million to the net loss, or $0.03 per share of common stock, basic and diluted, for the three months ended September 30, 2019, and a decrease of $5.4 million to the net loss, or $0.07 per share of common stock, basic and diluted, for the nine months ended September 30, 2019. The effective interest income rate for the three months ended September 30, 2019 was approximately 4.2%. The effective interest income rate for the nine months ended September 30, 2019 was 0.5%. The effective interest expense rate was approximately 12.7% and 13.2% for the three and nine months ended September 30, 2018, respectively.

The following table shows the activity within the liability account for the nine months ended and the period from inception to September 30, 2019 (in thousands):

	Nine months ended September 30, 2019	Period from inception to September 30, 2019
Liability related to sale of future royalties — beginning balance	$ 93,679	$ —
Proceeds from sale of future royalties	—	61,184
Non-cash royalty revenue	(241)	(618)
Non-cash interest (income) expense recognized	(375)	32,497
Liability related to sale of future royalties as of September 30, 2019	93,063	93,063
Less: current portion	(688)	(688)
Liability related to sale of future royalties — net of current portion	$ 92,375	$ 92,375

As royalties and milestones are remitted to PDL from the Company's subsidiary, 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 records non-cash royalty revenues and non-cash interest income (expense) within its condensed 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 September 30, 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.

10. Stock-Based Compensation

The Company recorded total stock-based compensation expense for stock options, stock awards and the 2011 Employee Stock Purchase Plan, or ESPP, as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Cost of goods sold	$ 68	$ 119	$ 197	$ 280
Research and development	242	769	699	1,578
Selling, general and administrative	1,016	920	2,883	2,078
Total	$ 1,326	$ 1,808	$ 3,779	$ 3,936

As of September 30, 2019, there were 2,037,468 shares available for grant, 12,590,964 options outstanding and 959,704 restricted stock units outstanding under the Company's 2011 Equity Incentive Plan and 655,420 shares available for grant under the ESPP.

11. Stockholders' Equity

Common Stock

ATM Agreement

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 Controlled Equity Offering[SM] Sales Agreement, or the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent by $40.0 million. During the nine months ended September 30, 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. As of September 30, 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.

12. 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 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:

	September 30,	
	2019	**2018**
RSUs, ESPP and stock options to purchase common stock	13,712,081	12,003,600
Common stock warrants	176,679	176,730

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis should be read in conjunction with the unaudited financial statements and notes thereto included in Part I, Item 1 of this Quarterly Report on Form 10-Q and with the audited consolidated financial statements and related notes thereto included as part of our Annual Report on Form 10-K for the year ended December 31, 2018, or Annual Report.

About AcelRx Pharmaceuticals, Inc.

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 utilizes sufentanil, delivered via a non-invasive route of sublingual administration, exclusively for use in medically supervised settings.

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 Commission, or EC, 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.

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.

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.

Zalviso® (sufentanil sublingual tablet system, 15 mcg)

While still under development in the United States, 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.

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 countries of the EU, 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 “Collaboration Agreement” in the accompanying notes to the condensed consolidated financial statements.

Zalviso was approved for commercial sale by the EC in September 2015 and our collaboration partner, Grünenthal, began its commercial launch of Zalviso in the EU 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 BioPharma, Inc., or PDL, which we refer to in this Quarterly Report as the Royalty Monetization. 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 condensed consolidated financial statements. Royalty revenues and non-cash royalty revenues from the commercial sales of Zalviso in the EU are expected to be minimal for 2019.

We submitted a new drug application, or 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. We are currently evaluating the timing of the resubmission of the Zalviso NDA.

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.

We launched the commercialization of DSUVIA in the United States in the first quarter of 2019. As we continue developing as a commercial enterprise, we plan to continue to add personnel and incur additional costs related to the maturation of our business and the commercialization of DSUVIA and potential commercialization of Zalviso in the United States, subject to FDA approval. In addition, we will incur capital expenditures related to the installation of our high-volume automated packaging line for DSUVIA, which we expect to have qualified product being packaged using this new equipment beginning in 2020. We anticipate that the high-volume line for DSUVIA will contribute to a significant decrease in costs of goods sold in 2020 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 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 of its agreements or that we will be able to meet the milestones specified in the agreements. Under the terms of the DoD contract, the DoD has 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 loss for the three and nine months ended September 30, 2019 was $12.7 million and $38.8 million, respectively, compared to net losses of $12.5 million and $34.6 million for the three and nine months ended September 30, 2018, respectively. As of September 30, 2019, we had an accumulated deficit of $383.7 million. As of September 30, 2019, we had cash, cash equivalents and short-term investments totaling $80.4 million compared to $105.7 million as of December 31, 2018.

Critical Accounting Policies and Significant Judgments and Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our unaudited condensed 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 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. Our critical accounting policies and estimates are detailed in our Annual Report.

There have been no significant changes to our critical accounting policies or significant judgements and estimates for the three and nine months ended September 30, 2019, from those previously disclosed in our Annual Report aside from the adoption of ASU No. 2016-02, *Leases (Topic 842)* which is explained more fully in Note 1 “Organization and Summary of Significant Accounting Policies - Leases,” and in Note 7 “Leases” in the accompanying notes to the condensed consolidated financial statements, and updates to our “Non-Cash Interest Income (Expense) on Liability Related to Sale of Future Royalties” policy which is explained more fully in Note 1 “Organization and Summary of Significant Accounting Policies.”

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.

Three and Nine Months Ended September 30, 2019 and 2018

Revenue

Net Product Sales Revenue

We began commercial sales of DSUVIA 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, such as hospitals, surgical centers, and emergency departments. 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.

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 and GPO administrative fees 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.

For the three and nine months ended September 30, 2019, net product sales of DSUVIA were $0.1 million and $0.2 million, respectively.

Collaboration Agreement Revenue

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.

For the three months ended September 30, 2019, we recognized $0.5 million in revenue under the Amended Agreements, consisting primarily of product sales revenue. For the three months ended September 30, 2018, we recognized $0.2 million in revenue under the Amended Agreements, consisting primarily of product sales revenue. Revenue recognized under the Amended Agreements for the nine months ended September 30, 2019 was $1.6 million, $0.2 million of which was non-cash royalty revenue, with the remainder consisting primarily of product sales revenue, compared to $0.8 million for the nine months ended September 30, 2018, $0.2 million of which was non-cash royalty revenue, with the remainder consisting primarily of product sales revenue. The increase in collaboration agreement revenue for the three and nine months ended September 30, 2019, as compared to the prior year period, was primarily the result of increased orders from Grünenthal. In 2020, we expect our collaboration agreement revenue related to product sales will continue to be modest. 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, collaboration agreement 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. We anticipate that royalty revenues and non-cash royalty revenues from European sales of Zalviso in 2020 will be minimal.

As of September 30, 2019, we had current and non-current portions of the deferred revenue balance under the Amended Agreements of $0.3 million and $2.9 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 collaboration revenue under the Amended Agreements.

Contract and Other Revenue

For the three and nine months ended September 30, 2019, we did not recognize any revenue under the DoD Contract for DSUVIA, while we recognized $0.2 million and $0.7 million, respectively, in DoD Contract revenue for the three and nine months ended September 30, 2018. 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. The DoD Contract period of performance ended on February 28, 2019.

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. 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.

Total cost of goods sold for the three and nine months ended September 30, 2019 and 2018 was as follows (in thousands):

	Three Months Ended September 30,				Nine Months Ended September 30,			
	2019	2018	$ Change 2019 vs. 2018	% Change 2019 vs. 2018	2019	2018	$ Change 2019 vs. 2018	% Change 2019 vs. 2018
	(In thousands, except percentages)							
Cost of goods sold	$ 2,148	$ 875	$ 1,273	145%	$ 5,188	$ 2,738	$ 2,450	89%

Direct costs from contract manufacturers for DSUVIA and Zalviso in the three and nine months ended September 30, 2019 totaled $1.4 million and $2.0 million, respectively. During the quarter ended September 30, 2019, we recorded an inventory impairment reserve of approximately $0.9 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. In the three and nine months ended September 30, 2018, direct costs included in costs of goods sold for Zalviso totaled $0.1 million and $0.6 million, 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 in the three and nine months ended September 30, 2019 totaled $0.8 million and $3.2 million, respectively. Indirect costs included in costs of goods sold for Zalviso totaled $0.8 million and $2.1 million in the three and nine months ended September 30, 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 market approach as that used to value the inventory. For the foreseeable future, we anticipate negative gross margins on Zalviso product delivered to Grünenthal.

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.

We track external development expenses on a program-by-program basis. Our development resources are shared among all of 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 three and nine months ended September 30, 2019 and 2018 (in thousands, except percentages):

	Three Months Ended September 30,				Nine Months Ended September 30,			
Drug Indication/Description	**2019**	**2018**	**$ Change 2019 vs. 2018**	**% Change 2019 vs. 2018**	**2019**	**2018**	**$ Change 2019 vs. 2018**	**% Change 2019 vs. 2018**
	(In thousands, except percentages)							
DSUVIA	$ 118	$ 678	$ (560)	(83)%	$ 394	$ 2,163	$ (1,769)	(82)%
Zalviso	148	65	83	128%	487	567	(80)	(14)%
Overhead	792	2,899	(2,107)	(73)%	2,717	7,703	(4,986)	(65)%
Total research and development expenses	$ 1,058	$ 3,642	$ (2,584)	(71)%	$ 3,598	$ 10,433	$ (6,835)	(66)%

The $2.6 million decrease in research and development expenses for the three months ended September 30, 2019, as compared to the three months ended September 30, 2018, and the $6.8 million decrease for the nine months ended September 30, 2019, as compared to the nine months ended September 30, 2018, were 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 have substantially completed our DSUVIA and Zalviso development programs resulting in decreased DSUVIA- and Zalviso-related spending in the first nine months of 2019 as compared to the first nine months of 2018.

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. We expect selling, general and administrative expenses in the fiscal year 2019 to increase as compared to fiscal year 2018 expenses, as we focus our efforts on the commercialization of DSUVIA in the United States.

Total selling, general and administrative expenses for the three and nine months ended September 30, 2019 and 2018 were as follows:

	Three Months Ended September 30,				Nine Months Ended September 30,			
	2019	2018	$ Change 2019 vs. 2018	% Change 2019 vs. 2018	2019	2018	$ Change 2019 vs. 2018	% Change 2019 vs. 2018
	(In thousands, except percentages)							
Selling, general and administrative expenses	$ 10,936	$ 5,188	$ 5,748	111%	$ 32,241	$ 13,117	$ 19,124	146%

Selling, general and administrative expenses for the three months ended September 30, 2019 increased by $5.7 million, as compared to the three months ended September 30, 2018 and increased by $19.1 million during the nine months ended September 30, 2019, as compared to the nine months ended September 30, 2018. In both periods, the increases were 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 by 51 employees as compared to September 30, 2018.

Other Income (Expense)

Total other income (expense) for the three and nine months ended September 30, 2019 and 2018 was as follows (in thousands, except percentages):

	Three Months Ended September 30,				Nine Months Ended September 30,			
	2019	2018	$ Change 2019 vs. 2018	% Change 2019 vs. 2018	2019	2018	$ Change 2019 vs. 2018	% Change 2019 vs. 2018
	(In thousands, except percentages)							
Interest expense	$ (828)	$ (529)	$ (299)	57%	$ (1,704)	$ (1,758)	$ 54	(3)%
Interest income and other income (expense), net	645	312	333	107%	1,728	643	1,085	169%
Non-cash interest income (expense) on liability related to sale of future royalties	986	(2,913)	3,899	(134)%	375	(8,724)	9,099	(104)%
Total other income (expense)	$ 803	$ (3,130)	$ 3,933	(126)%	$ 399	$ (9,839)	$ 10,238	(104)%

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 three months ended September 30, 2019, as compared to the three months ended September 30, 2018, primarily as a result of a higher outstanding loan balance. As of September 30, 2019, the accrued balance due under the Loan Agreement with Oxford was $24.0 million. Refer to Note 6 “Long-Term Debt” in the accompanying notes to the condensed consolidated financial statements for additional information.

Interest income and other income (expense), net, for the three and nine months ended September 30, 2019 and 2018 primarily related to interest earned on our investments. The increase is primarily due to a larger average investment balance during the three and nine months ended September 30, 2019 as compared to the prior year periods.

The increase in non-cash interest income on the liability related to the sale of future royalties for the three and nine months ended September 30, 2019 as compared to the three and nine months ended September 30, 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. 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 $2.7 million and $5.4 million to the net loss for the three and nine months ended September 30, 2019, respectively. The effective interest income rate for the three and nine months ended September 30, 2019 was approximately 4.2%, and 0.5%, respectively. The effective interest expense rate for the three and nine months ended September 30, 2018 was approximately 12.7% and 13.2%, respectively. We anticipate that we will record approximately $1 million in non-cash interest income related to the Royalty Monetization for the year ended December 31, 2019.

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 September 30, 2019, we had cash, cash equivalents and investments totaling $80.4 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 middle of the fourth quarter of 2020. While we believe we have sufficient capital to meet our operational requirements through the middle of the fourth quarter of 2020, 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 likely 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 September 30, 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 $34.7 million, after deducting commissions, fees and expenses of $1.0 million. As of September 30, 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 September 30, 2019, the accrued balance under the Loan Agreement was $24.0 million. For more information, see Note 6 "Long-Term Debt" in the accompanying notes to the condensed 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 condensed 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

The following is a summary of our cash flows for the periods indicated and has been derived from our condensed consolidated financial statements which are included elsewhere in this Form 10-Q (in thousands):

	Nine Months Ended September 30,	
	2019	2018
Net cash used in operating activities	$ (37,025)	$ (20,085)
Net cash used in investing activities	(43,452)	1,083
Net cash provided by financing activities	14,451	23,666

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 $37.0 million during the nine months ended September 30, 2019, reflected a net loss of $38.8 million, partially offset by aggregate non-cash charges of $5.1 million. Non-cash charges included $3.8 million in stock-based compensation expense, $1.2 million in depreciation expense, a $0.9 million inventory impairment charge and $0.4 million in non-cash interest income on the liability related to the Royalty Monetization. The net change in our operating assets and liabilities of $3.3 million included a $3.0 million increase in inventories.

Cash used in operating activities of $20.1 million during the nine months ended September 30, 2018, reflected a net loss of $34.6 million, partially offset by aggregate non-cash charges of $13.2 million. Non-cash charges included $8.7 million in non-cash interest expense on the liability related to the royalty monetization and $3.9 million for stock-based compensation expense. The net change in our operating assets and liabilities included a decrease in accounts receivable of $1.3 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 nine months ended September 30, 2019, cash used in investing activities of $43.5 million was the net result of $81.9 million for purchases of investments and $3.2 million for purchases of property and equipment, offset by $41.7 million in proceeds from maturity of investments. During the nine months ended September 30, 2018, cash provided by investing activities of $1.1 million was the net result of $14.5 million in proceeds from maturity of investments, offset by $12.8 million for purchases of investments and purchases of property and equipment of $0.6 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 nine months ended September 30, 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 nine months ended September 30, 2018, cash provided by financing activities was primarily due to net proceeds of $29.1 million from the issuance of common stock, including $21.7 million in net proceeds from our underwritten public offering plus $7.4 million in net proceeds received under the Sales Agreement. In addition, we used $5.7 million during the nine months ended September 30, 2018 to repay our long-term debt with Hercules.

Operating Capital and Capital Expenditure Requirements

Our current operating plan includes anticipated activities required to resubmit the Zalviso NDA, to support the FDA review of the resubmitted Zalviso NDA, and expenditures related to the launch of DSUVIA in the United States. 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;
- 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 likely will not be sufficient to fund our operations until such time as we may be able to generate sufficient revenues to sustain our operations. To the extent that our capital resources are insufficient to meet our future capital requirements, 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 continue our development programs.

Please see “Part II. Other Information - Item 1A. Risk Factors—Risks Related to Our Financial Condition and Need for Additional Capital.”

Off-Balance Sheet Arrangements

Through September 30, 2019, we have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

During the nine months ended September 30, 2019, there were no material changes to our market risk disclosures as set forth in Part II, Item 7A, “Quantitative and Qualitative Disclosures About Market Risk” in our Annual Report.

Item 4. Controls and Procedures

We maintain disclosure controls and procedures (as defined in Exchange Act Rule 13a–15(e) and 15d-15(e)) that are designed to ensure that information required to be disclosed in our reports under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the rules and regulations thereunder, is recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Evaluation of disclosure controls and procedures. As required by Rule 13a-15(b) under the Exchange Act, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in internal control over financial reporting. There have been no changes in our internal control over financial reporting during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. 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 proceedings are subject to uncertainty and, if they happen, could have a material adverse effect on our business, results of operations, financial position or cash flows.

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. If any of the following risks actually materialize, our business, financial condition, results of operations, liquidity, and future prospects could be materially harmed and the price of our common stock could decline.

The following description of the risk factors associated with our business includes any material changes to and supersedes the description of the risk factors associated with our business previously disclosed in Part I, Item 1A of the Annual Report.

We have marked with an asterisk (*) those risks described below that reflect substantive changes from, or additions to, the risks described in the Annual Report for the year ended December 31, 2018.

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 payors;
- 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, if approved, Zalviso, in the United States; however, if these third parties do not perform as expected or there are delays in establishing such relationships for, if approved, Zalviso, 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.

We have recently increased, and will continue to increase, the size of our organization. We may encounter difficulties with managing our growth, which could adversely affect our results of operations.*

As of September 30, 2019, we had approximately 96 full-time employees. Although we have substantially increased the size of our organization, we may need to add additional qualified personnel and resources to address our commercialization efforts for DSUVIA and potential commercialization of Zalviso in the United States, subject to FDA approval. Our current infrastructure may be inadequate to support our development and commercialization efforts and expected growth. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees, and may take time away from running other aspects of our business, including development and commercialization of DSUVIA and our product candidates.

Our future financial performance and our ability to successfully commercialize DSUVIA and our other product candidates that may receive regulatory approval will depend, in part, on our ability to manage any future growth effectively. In particular, as we continue to commercialize DSUVIA, we will need to support the training and ongoing activities of our sales force and will likely need to continue to expand the size of our employee base for managerial, operational, financial and other resources. To that end, we must be able to successfully:

- manage our development efforts effectively;
- integrate additional management, administrative and manufacturing personnel;
- further develop our marketing and sales organization; and
- maintain sufficient administrative, accounting and management information systems and controls.

We may not be able to accomplish these tasks or successfully manage our operations and, accordingly, may not achieve our research, development, and commercialization goals. Our failure to accomplish any of these goals could materially and adversely affect our business and operations.

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 Department of Health and Human Services, or 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, and, if successful claims are brought against us, 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 payor reimbursement regimes, governmental payors, 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 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 its territory which includes the 28 EU member states as well as Norway, Iceland and Liechtenstein. 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.

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 2019 contains additional drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid and to eliminate cost sharing for generic drugs for low-income patients. 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, 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.

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 will 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 labelling 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 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. The potential impact of this new FDA guidance on the Zalviso resubmission is unclear; however, the Zalviso clinical program does include a comparative safety and efficacy study versus IV PCA morphine.

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.

Some of the provisions of the Affordable Care Act have yet to be implemented, and there have been 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, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision 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, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain fees mandated by the Affordable Care Act, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. In July 2018, CMS published a final rule permitting further collections and payments to and from certain PPACA qualified health plans and health insurance issuers under the PPACA 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. While the Texas U.S. District Court Judge, as well as the Trump Administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the Affordable Care Act will impact the PPACA. 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 Tax Payer 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.

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 labelling 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. The potential impact of this on the Zalviso resubmission is unclear; however, the Zalviso clinical program does include a comparative safety and efficacy study versus IV PCA morphine.

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 resubmit our NDA seeking 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, in part, relies 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 a 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. We intend to submit the IAP312 study results as part of our resubmission of the NDA for Zalviso. We are currently evaluating the timing of the resubmission of our NDA for Zalviso.

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. 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. There is no guarantee such funding would be available to us on favorable terms, if at all. We intend to resubmit the Zalviso NDA seeking a label indication 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.

We have not yet resubmitted the Zalviso NDA. Activities that we have undertaken to address issues raised in the Zalviso CRL may be deemed insufficient by the FDA.

We completed bench testing and additional Human Factors studies that we believed addressed certain items contained in the Zalviso CRL. However, before the results from these studies were submitted as a part of the proposed NDA resubmission, the FDA, in March 2015, notified us of the need for a clinical trial prior to the resubmission of the Zalviso NDA. In early September 2015, we had a Type C meeting with the FDA to discuss the FDA's request for an additional clinical trial and our planned response to the Zalviso CRL. In response to discussions with the FDA, we agreed to complete an additional open-label study with Zalviso in post-operative patients, known as IAP312. We completed the protocol review for IAP312 and announced positive results from this study in August 2017, which we intend to use to support our NDA resubmission. We are currently evaluating the timing of the resubmission of our NDA for Zalviso.

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. While we designed the protocols for bench testing and the Human Factors studies to address the issues raised in the Zalviso CRL and designed the protocol for the additional Zalviso clinical trial to further address these issues, there is no guarantee the FDA will deem such protocols and results sufficient to address those issues when they are formally reviewed as a part of an NDA resubmission. Any delay in obtaining, or inability to obtain, regulatory approval would prevent us from commercializing Zalviso in the United States, generating revenues and achieving profitability. If any of these events occur, we may be forced to delay or abandon our development and commercialization efforts for Zalviso in the United States, which would have a material adverse effect on our business.

Lastly, while we believe the results from our bench testing, Human Factors studies and the IAP312 clinical trial are positive, the FDA may hold a different opinion and deem the results insufficient. The FDA may provide review commentary at any time during the resubmission and review process that could adversely affect or even prevent the approval of Zalviso, which would adversely affect our business. 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.

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. For example, although we had achieved the primary endpoints in each of our three Phase 3 clinical trials for Zalviso which were included in our NDA filed in 2013, 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 would be needed to assess the risk of inadvertent dispensing and overall risk of dispensing failures. While we believe Zalviso met safety, satisfaction and device usability expectations in this trial, known as IAP312, there is no guarantee the FDA will agree with our interpretation of these 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 decreased, 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 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.

We cannot predict when we will obtain regulatory approval to commercialize Zalviso, if at all, and we cannot, therefore, predict the timing of any future associated revenue.

In the United States, we received the Zalviso CRL on July 25, 2014, which contains requests for additional information on the Zalviso System. In addition, 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 is needed to assess the risk of inadvertent dispensing and overall risk of dispensing failures. Based on our Type C meeting with the FDA in early September 2015 to discuss the FDA's request for an additional clinical trial and our planned response to the Zalviso CRL, we submitted a protocol to the FDA for a clinical 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. We completed the protocol review and announced positive results from this study in August 2017, which we intend to use to support our NDA resubmission. We are currently evaluating the timing of the resubmission of our NDA for Zalviso.

Although the FDA reviewed the protocol for IAP312, the FDA required us to complete additional clinical work prior to resubmitting the NDA for Zalviso. Additional delays may result if Zalviso is taken before an FDA advisory committee which may recommend restrictions on approval or recommend non-approval.

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 these products 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. 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 2019 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 September 30, 2019, we had an accumulated deficit of $383.7 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, sale of royalty 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. Even if Grünenthal is successful in commercialization of Zalviso, as a result of our sale to PDL of certain expected royalties from the sales of Zalviso by Grünenthal and a majority of our first four commercial sales milestones, we will receive only 25% of the sales royalties and 20% of the first four commercial milestones under these arrangements. In addition, we do not anticipate generating significant revenues from DSUVIA or Zalviso, if approved in the United States, in the near term. 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 a collaboration, a hospital-directed 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 incurring 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 28 EU member states, Switzerland, Liechtenstein, Iceland, Norway and Australia, or 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.

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 the commercialization of 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.

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 at least the end of the second quarter of 2020, 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.*

In order to raise additional funds to support our operations, we may sell additional equity securities, including under the Controlled Equity Offering^{SM} 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 stockholders. 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. 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 September 30, 2019, we have approximately $24.0 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.

The costs incurred under the DoD Contract are subject to audit by the Department of Defense and any identified deficiencies could jeopardize past funding.

On May 11, 2015, we entered into an award contract supported by the Clinical and Rehabilitative Medicine Research Program, or CRMRP, of the United States Army Medical Research and Materiel Command, or USAMRMC, within the DoD in which the DoD agreed to provide up to $17.0 million to support the development of DSUVIA, referred to as the DoD Contract. Under the terms of the DoD Contract, the DoD has reimbursed us for costs incurred for development, manufacturing, regulatory and clinical costs outlined in the DoD Contract, including reimbursement for certain personnel and overhead expenses. The period of performance under the DoD Contract began on May 11, 2015 and extended through February 28, 2019. Funding under the DoD Contract will be subject to audit by the DoD to ensure adherence to specific guidance, policies and procedures. The DoD may find deficiencies during the course of an audit which could jeopardize, or even eliminate, continued funding from the DoD, as well as require repayment of any funds they had provided us since inception of the DoD Contract. In addition, if the DoD determines that we have failed to comply with specific contractual or legal requirements, or fail to satisfy an audit, a variety of penalties can be imposed in addition to monetary damages, including criminal and civil penalties. The DoD could suspend or debar us from all government contract work. The occurrence of any of these actions could harm our reputation and could have a material adverse impact on our results of 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 agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing 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 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 is changing its process for manufacturing our drug, which could impact our commercial supply of API. This change in process requires a regulatory submission to the FDA and the European Health Authority which must be approved before the new process API can be used commercially in each corresponding territory. There is no guarantee that the FDA or European Health Authority will approve such a submission. Both the U.S. and EU regulatory submissions have been submitted to support the use of the API made with the new manufacturing process, but there is no guarantee that the FDA or European Health Authority will approve the submissions. 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 alternative vendor would need to be qualified through an NDA supplement and/or an MAA variation which could result in further delay. 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 and have not identified a back-up commercial facility to date. 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 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 have a secondary contract packaging facility identified. We also intend to 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. We expect to complete the acquisition and installation of this line in 2019. There is no assurance that we will be able to successfully purchase, install or validate the automated filling and packaging line for DSUVIA. 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 UK, or BSI-UK. Recently, 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 the Brexit situation. The ISO certification issued through BSI-UK was recently upgraded to the latest version of the standard, ISO 13485:2016 through BSI-UK and remains in effect, regardless of the Brexit situation. 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 28 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.

The UK's planned withdrawal from the EU, commonly referred to as Brexit, may have a negative effect on global economic conditions, financial markets and our business.

Brexit has created significant uncertainty concerning the future relationship between the UK and the EU, particularly if the UK withdraws from the EU without a ratified withdrawal agreement in place. From a regulatory perspective, there is uncertainty about which laws and regulations will apply. A significant portion of the regulatory framework in the UK is derived from EU laws. However, it is unclear which EU laws the UK will decide to replace or replicate in connection with its withdrawal from the EU and the regulatory regime applicable to our operations may change.

A basic requirement related to the grant of a marketing authorization for a medicinal product in the EU is the requirement that the applicant be established in the EU. Following withdrawal of the UK from the EU, marketing authorizations previously granted to applicants established in the UK through the centralized, mutual recognition or decentralized procedures may no longer be valid. Moreover, depending upon the exact terms of the UK's withdrawal, there is a risk that the scope of a marketing authorization for a medicinal product granted by the EC pursuant to the centralized procedure, or by the competent authorities of other EU member states through the decentralized or mutual recognition procedures, would not encompass the UK. In that circumstance, a separate authorization granted by the UK competent authorities would be required to place medicinal products on the UK market.

Brexit has also given rise to calls for the governments of other EU member states to consider withdrawal from the EU. These developments, or the perception that they could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, including by significantly reducing global market liquidity or restricting the ability of key market participants to operate in certain financial markets.

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, natural disasters, or man-made incidents. 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 face potential product liability claims, and, if such claims are successful, we may incur substantial liability.

Commercial sales of DSUVIA and Zalviso exposes 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 payor, or those claims arising from a multi-plaintiff action. 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 September 30, 2019, we are the owner of record of 74 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 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 of 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, our stock price dropped by 60% on October 12, 2017, the day we announced the receipt of the DSUVIA CRL from the FDA. 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 and/or to successfully develop and commercialize Zalviso in the United States;
- inability to obtain additional funding;
- the perception of limited market sizes or pricing for our products;

- any delay 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 existing 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. 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.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our Sales Agreement with Cantor and our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing additional equity securities, including pursuant to the Sales Agreement with Cantor, our stockholders may experience substantial dilution. 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. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to the 2011 Equity Incentive Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under our 2011 Equity Incentive Plan will automatically increase each year by 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our Board of Directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under our 2011 Equity Incentive Plan each year. If our Board of Directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

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.

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 year ended December 31, 2015, we used net operating losses to reduce our income tax liability. 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.

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 2. Unregistered Sales of Equity Securities and Use of Proceeds

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-35068	3.1	02/18/2011
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-35068	3.1	06/25/2019
3.3	Amended and Restated Bylaws of the Registrant.	S-1	333-170594	3.4	01/07/2011
10.1	Agreement between the Registrant and SpecGX, LLC, dated June 16, 2017.#				
10.2	Amendment to Agreement between the Registrant and SpecGX, LLC, dated September 23, 2019.				
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 and Accounting 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

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Material in the exhibit marked with a "[*]" 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 Quarterly Report on Form 10-Q 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.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: November 6, 2019

AcelRx Pharmaceuticals, Inc.
(Registrant)

/s/ Raffi M. Asadorian

Raffi M. Asadorian
Chief Financial Officer
(Duly Authorized and Principal Financial and Accounting Officer)

Exhibit 10.1

[*] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED

June 16, 2017

Mr. Anil Dasu
Chief Engineering Officer
AcelRx Pharmaceuticals Inc.
351 Galveston Drive
Redwood City, CA 94063

Dear Mr. Dasu,

Mallinckrodt LLC ("Mallinckrodt") is pleased to offer the following agreement ("Agreement") to AcelRx Pharmaceuticals, Inc. ("AcelRx") for Sufentanil Citrate (codes 0672 and 0678) (hereinafter referred to as "Product") delivered during the period beginning on the 1st day of January 2017 (the "Effective Date") and ending on December 31, 2019 (the "Initial Term"). This Agreement may be extended only by written agreement of both Mallinckrodt and AcelRx (any extension, together with the Initial Term, shall be referred to as the "Term").

For purposes hereof, the first Contract Year will commence on the Effective Date and end on December 31st of the same year. Thereafter, each subsequent Contract year will commence on January 1st of such year and end on December 31st of such year.

Mallinckrodt agrees to supply and AcelRx agrees to purchase Product initially at the prices listed below:

Product	Codes	Contract Year Volume	Price per Gram
Sufentanil Citrate	0672 & 0678	**[*]**	**[*]**
		[*]	**[*]**
		[*]	**[*]**

The prices above shall be firm through December 31, 2017. Effective January 1, 2018 for the balance of the new Contract Year, and every subsequent January 1 for the balance of the Contract Year then commenced, the price for Product shall be adjusted to reflect any increases or decreases in the cost to Mallinckrodt of all raw materials, labor, utilities and regulatory compliance costs associated directly with the manufacture and supply of such Product hereunder incurred during the immediately prior Contract Year, provided that the price of Product shall not increase or decrease by more than **[*]** percent (**[*]**%) from the price in effect for such Product during the immediately previous Contract Year. By December 1, 2017, and on every subsequent December 1 during the Term of this Agreement, Mallinckrodt will notify AcelRx in writing of the adjusted prices to be charged for Product for the following Contract Year.

Absent written agreement of the parties, invoices during each Contract Year shall be based upon the volumes projected in the initial 12-month forecast for each Contract Year. Within thirty days after the end of each Contract Year, Mallinckrodt shall provide to AcelRx a reconciliation of the actual pricing applicable to that Contract Year (the "Annual Pricing Reconciliation"). Mallinckrodt shall invoice AcelRx for any amount due from AcelRx in accordance with the Annual Pricing Reconciliation which undisputed payment shall be due within thirty (30) days from the date thereof. In the event the Annual Pricing Reconciliation results in a credit due to AcelRx, Mallinckrodt shall issue a credit to AcelRx to be applied to any open invoices or amounts due from AcelRx to Mallinckrodt. If AcelRx does not have any open invoices or amounts due to Mallinckrodt, Mallinckrodt shall refund any credits to AcelRx within thirty (30) days.

Except as otherwise expressly stated in this Agreement, AcelRx agrees that it will purchase during every Contract Year during the term of this Agreement at least **[*]** percent (**[*]**%) of its annual requirements for Product for delivery during such Contract Year, subject to Mallinckrodt's ability to supply. Mallinckrodt agrees that, except as specified in the paragraph below, it will supply all quantities of Product that are ordered by AcelRx by the delivery date specified in the applicable purchase order. If Mallinckrodt is unable to supply all quantities of Product meeting the specifications in Exhibit A and the other requirements of this Agreement by the delivery date specified in orders placed by AcelRx hereunder, then Mallinckrodt shall provide AcelRx with prompt written notice of such inability. If Mallinckrodt is unable to supply at least **[*]** percent (**[*]**%) of the quantities of Product meeting the specifications in Exhibit A and the other requirements of this Agreement within **[*]** (**[*]**) days of the delivery date specified in orders placed by AcelRx hereunder on **[*]** (**[*]**) or more occasions during any Contract Year, AcelRx shall thereafter be relieved of its obligation under this Agreement to purchase at least **[*]** percent (**[*]**%) of its annual requirements for Product from Mallinckrodt and may purchase unlimited quantities of Product from other suppliers. For clarity, purchases of Product will be deemed to occur during the Contract Year in which such Product is to be delivered for purposes hereof, and thus any purchase orders for Product submitted by AcelRx at the price in effect for the first Contract Year and otherwise in accordance with the requirements hereof, prior to the beginning of the first Contract Year shall be deemed to be purchased by AcelRx during the first Contract Year hereof.

AcelRx agrees to supply Mallinckrodt, on a quarterly basis, a rolling forecast of its requirements for Product during the next twelve (12) months. The forecast for the first **[*]** (**[*]**) months is considered to be firm and binding, such that AcelRx is obligated to order, and Mallinckrodt is obligated to supply, the quantities of Product contained in the first **[*]** (**[*]**) month of each forecast. The forecast for the last **[*]** (**[*]**) months of that period is a non-binding, good-faith estimate of AcelRx' requirements for that period and will be used by Mallinckrodt for production planning. If Mallinckrodt is unable to timely deliver a quantity of any Product ordered by AcelRx, then AcelRx will be permitted to purchase the same quantity of that Product of like grade and quality from another supplier and such amount shall be used in determining whether AcelRx has met its purchase obligations for that Product for any given Contract Year (i.e., the quantity purchased by AcelRx from another supplier shall be counted as part of AcelRx's annual requirements of Product for such year).

Notwithstanding any other provision hereof, Mallinckrodt's obligation to supply Product to AcelRx hereunder and AcelRx's obligation to purchase such Product from Mallinckrodt hereunder is subject, at any given time, to the availability of sufficient quota granted by the United States Drug Enforcement Administration ("DEA"). Mallinckrodt and AcelRx both agree that they shall at all times cooperate in good faith in the exercise and use of their commercially reasonable efforts to ensure that there is sufficient quota available to allow both parties fully to perform their obligations hereunder. If Mallinckrodt has insufficient quota to satisfy AcelRx's requirements for any Product as well as its other customers, Mallinckrodt shall immediately notify AcelRx of same in writing and shall consult with AcelRx regarding AcelRx's anticipated orders. Mallinckrodt shall allocate available Product among all of its customers, including AcelRx, in as fair and equitable a manner as possible, giving due consideration to historical purchasing patterns, forecasts, and all other relevant commercial factors.

Mallinckrodt shall provide written notice to AcelRx if it intends to terminate its manufacture of the Product, which notice shall be provided at least **[*]** (**[*]**) months prior to the date on which Mallinckrodt will cease manufacturing Product.

All sales of Product between AcelRx and Mallinckrodt will be in accordance with the following terms and conditions:

- payment for Products shall be made in US Dollars ("USD") and, if undisputed, is due thirty (30) days from the date of invoice. Mallinckrodt shall not issue an invoice for Products prior to the date on which it has shipped such Products to AcelRx or AcelRx's designee,

- delivery is Ex Works (Incoterms 2016); and

- all Products will be ordered in writing with at least ninety (90) days advance notice.

Mallinckrodt represents and warrants, with respect to all Product supplied to AcelRx hereunder, that:

- Products will be manufactured by Mallinckrodt in accordance with the terms of the quality agreement to be entered into by the parties promptly after the execution of this Agreement (the "Quality Agreement"), all applicable laws and regulations and current Good Manufacturing Practices as determined by the United States Food and Drug Administration ("FDA") using the manufacturing process described in Mallinckrodt's Drug Master File ("DMF");

- Products will meet the specifications attached as Exhibit A, as well as any other specifications mutually agreed to in writing by Mallinckrodt and AcelRx; and

- In the event of any conflict or inconsistency between the terms of this Agreement and the Quality Agreement, this Agreement shall prevail in every case.

AcelRx shall have the right, in accordance with the procedures specified in this paragraph, to reject any volume of any Product supplied to it hereunder if any such Product fails to meet the specifications attached hereto as Exhibit A. AcelRx or its designee may inspect Product received by it from Mallinckrodt and if, within sixty (60) days of the date of receipt of such Product, AcelRx has not given written notice to Mallinckrodt rejecting any such Product (which notice will provide a detailed description of the reason for such rejection), such Product will be deemed to have been accepted for all purposes hereof. Notwithstanding the foregoing, if at any time after initial acceptance as provided in the above paragraph, AcelRx discovers that Products supplied by Mallinckrodt do not meet the applicable specifications and all other applicable requirements of this Agreement, and the nature of such defect could not have been reasonably have been discovered or suspected by AcelRx from a review of the documents regarding such Products provided to it by Mallinckrodt with the shipment of the applicable Products or from a visual inspection of the Products performed within sixty (60) days after delivery to the delivery destination, AcelRx may revoke its acceptance of such Products by providing written notice to Mallinckrodt of such revocation. Such notice will identify in reasonable detail the nature of the defect and will be provided within thirty (30) days of the date on which AcelRx determines the existence of the defect. In the event AcelRx provides a timely rejection notice or revocation of acceptance to Mallinckrodt with respect to any given volume of any Product and Mallinckrodt does not give written notice to AcelRx within twenty (20) days after its receipt of any such rejection or revocation notice that it disagrees with AcelRx's rejection or revocation of acceptance of such Product, any Product that is the subject of such rejection or revocation notice shall be deemed to have been rejected for all purposes hereof. If, however, within twenty (20) days of its receipt of any rejection or revocation notice from AcelRx, Mallinckrodt, reasonably and in good faith, disagrees that any particular volume of any Product was properly rejected or that acceptance of such Product was properly revoked by AcelRx, Mallinckrodt shall provide notice of such disagreement to AcelRx setting forth the reasons for its disagreement. If, within a reasonable period of time after the date of any notice of disagreement given by Mallinckrodt (not, in any event, to exceed thirty (30) days) the parties are unable to resolve any dispute relative to the rejection of any particular volume of any Product, the matter will be referred to an independent third party expert acceptable to both parties whose decision as to whether or not any such Product was properly rejected or acceptance of such Product was properly revoked shall be final and binding on the parties. If the independent third party expert determines that the Product in question was not properly rejected or acceptance of such Product was not properly revoked, then such Product shall be deemed to have been accepted by AcelRx for all purposes hereof and the fees and expenses of such independent third party expert shall be paid by AcelRx. If the independent third party expert determines that the Product in question was properly rejected or revoked or if the parties have previously agreed that such Product was properly rejected or revoked, then Mallinckrodt shall, at the option of AcelRx and as AcelRx's sole remedies in the event of properly rejected or revoked Product, either refund or credit AcelRx for any amounts payable hereunder for such Product or promptly replace the rejected Product or revoked Product with Product that meets applicable specifications and all other applicable requirements hereof. Any properly rejected or properly revoked Product shall, at the option of Mallinckrodt, either be returned to Mallinckrodt or destroyed by AcelRx in an environmentally responsible manner, in either event at the sole cost and expense of Mallinckrodt.

If Mallinckrodt intends to make any material changes in its production, testing or packaging procedures in the DMF documented process for Product as required by FDA's "Guidance for Industry to an approved NDA or ANDA" and Note for Guidance on the European Drug Master File procedure, CPMP/QWP/227/02, Mallinckrodt will notify AcelRx in writing and will provide to AcelRx (in accordance with the pricing and other terms and conditions hereof) sufficient quantities of validation material of Product made using such changes in production, testing or packaging procedures (the "Modified Product") at least twelve (12) months (unless a lesser time to implement any change is dictated by law) before filling orders for Product placed by AcelRx with Modified Product. The parties acknowledge that the purpose of the immediately preceding sentence is to allow AcelRx a reasonable amount of time to receive appropriate regulatory approval prior to Mallinckrodt implementing a significant change to its DMF.

All information that is provided by or on behalf of AcelRx to Mallinckrodt in connection with this Agreement including, without limitations, all quantities of Product forecasted or ordered by AcelRx and all delivery dates and delivery destinations for such Product shall be AcelRx's confidential information under the Non-Disclosure Agreement entered into by Mallinckrodt and AcelRx effective January 6, 2017 (the "Confidentiality Agreement"). Similarly, all information that is disclosed to AcelRx by Mallinckrodt in connection this Agreement (except to the extent that it obtains AcelRx's confidential information) and all information observed by AcelRx during any inspection of Mallinckrodt's manufacturing operations conducted in accordance with this Agreement will be deemed to be Mallinckrodt's confidential information under the Confidentiality Agreement. Each party acknowledges and agrees that their obligations of confidentiality and restrictions on use with respect to the other party's confidential information shall be governed by the terms of the Confidentiality Agreement. The terms and obligations of the Confidentiality Agreement are hereby incorporated into this Agreement and shall bind the Parties as if fully set forth herein.

Except as expressly authorized herein, neither party hereto shall (i) use the name, insignia, symbol, trademark, trade name, logotype or products (or any abbreviation or adaptation thereof) of the other party or any affiliate or employee thereof in any advertising, press release, publicity or promotional materials, or on any website, without such party's prior written consent, or (ii) disclose the terms of this Agreement to any third party. For clarity, the existence of this Agreement is not confidential but the terms and conditions contained therein are confidential. All press releases and other public announcements relating to this Agreement or the transactions contemplated hereby will be prepared and issued only with the prior written consent of both Parties.

AcelRx will have the right during normal business hours and upon advance arrangement with Mallinckrodt to inspect Mallinckrodt's manufacturing operations to determine whether or not Mallinckrodt is complying in all respects with its obligations hereunder. AcelRx warrants that all such inspections and audits shall be carried out in a manner calculated not to unreasonably interfere with Mallinckrodt's conduct of business and to insure the continued confidentiality of Mallinckrodt's business and technical information. Further, AcelRx agrees to comply with all of Mallinckrodt's safety and security requirements during any visits to the Mallinckrodt facilities.

Mallinckrodt shall indemnify, defend and hold AcelRx, its affiliates and its and their respective directors, officers, employees, agents, successors and assigns harmless from and against any damages, liabilities, costs and expenses (including, without limitation, reasonable attorneys' fees) incurred in connection with any claims, suits or actions brought by a third party (collectively, "Losses") to the extent resulting from or alleged to result from (i) any breach of this Agreement by Mallinckrodt, or (ii) any negligence or willful misconduct of Mallinckrodt. **Notwithstanding the preceding sentence, in no event shall Mallinckrodt be liable to AcelRx for incidental, consequential, exemplary, special, punitive or any other similar type of damages whether or not Mallinckrodt has been advised of the possibility of such damages and whether or not, in any particular set of circumstances, such damages are reasonably foreseeable.**

Mallinckrodt hereby disclaims the implied warranties of merchantability and fitness for a particular purpose and it is understood that the express warranties (if any) of Mallinckrodt set forth herein are in lieu of all other warranties, express or implied.

AcelRx shall indemnify, defend and hold Mallinckrodt, its affiliates and its and their respective directors, officers, employees, agents, successors and assigns (the "Mallinckrodt Indemnitees") harmless from and against any Losses resulting from or alleged to result from: (i) the handling, storage, transportation, use, sale or marketing of any product containing any of the Products supplied hereunder to AcelRx, (ii) any breach of this Agreement by AcelRx, or (iii) any negligence or willful misconduct of AcelRx, except to the extent any such Losses are attributable to Mallinckrodt's breach of its obligations, representations or warranties under this Agreement or to any negligence or willful misconduct of Mallinckrodt. **Notwithstanding the preceding sentence, in no event shall AcelRx be liable to Mallinckrodt for incidental, consequential, exemplary, special, punitive or any other similar type of damages whether or not AcelRx has been advised of the possibility of such damages and whether or not, in any particular set of circumstances, such damages are reasonably foreseeable.**

Each party's agreement to indemnify, defend, and hold harmless the other party and its respective indemnitees is conditioned upon: (a) the indemnified party providing written notice to the indemnifying party of any claim, demand, or action arising out of the indemnified activities within thirty (30) days after the indemnified party has knowledge of such claim, demand or action, provided that any failure on the part of an indemnified party to notify the indemnifying party of receipt of notice of a claim will relieve the notified party of its obligation to indemnify the notifying party for such claim under this Agreement only to the extent that the notified party has been prejudiced by the lack of timely and adequate notice, (b) the indemnified party permitting the indemnifying party to assume full responsibility and authority to investigate, prepare for, settle and defend against any such claim, demand or action provided that, the indemnified party shall be allowed to participate and intervene in any action at its own expense, (c) the indemnified party assisting the indemnifying party, at the indemnifying party's reasonable expense, in the investigation of, preparation for and defense of any such claim, demand or action, (d) the indemnified party not compromising or settling such claim, demand or action without the indemnifying party's written consent, and (e) the indemnifying party not compromising or settling such claim, demand or action (except for any such settlement or compromises that involves only the payment of money by the indemnifying party) without the indemnified party's written consent.

No provision of any purchase order submitted by AcelRx or of any acknowledgment submitted by Mallinckrodt or of any other document submitted by either party shall be controlling to the extent it sets forth any terms or conditions that are additional to, or in conflict or inconsistent with, the terms or conditions of this Agreement. This Agreement represents the entire understanding of the parties with respect to its subject matter and supersedes any prior agreements, other than the Confidentiality Agreement, which shall remain in effect and apply to disclosures of confidential information made between the parties under this Agreement. This Agreement shall be governed by the laws of the State of Delaware, without reference to its conflict of law principles that might apply the law of another jurisdiction. Those provisions that by their nature are intended to survive termination or expiration of this Agreement including, without limitation, confidentiality and indemnity obligations, shall survive the termination or expiration of this Agreement for any reason,

Mallinckrodt hereby represents and warrants that it is not using and it will not use the services of any person or entity if such a person or entity is, debarred by the FDA under the Generic Drug Enforcement Act of 1992. If, during the term of this Agreement, Mallinckrodt or any person or entity whose services are being used by Mallinckrodt is debarred by the FDA, Mallinckrodt will immediately notify AcelRx of same.

Neither Party shall be entitled to assign this Agreement or its rights under this Agreement, including by merger or operation of law, without the express written consent of the other Party hereto, except that Mallinckrodt may assign this Agreement, in whole or in part: (i) to an Affiliate upon written notice to the AcelRx; or (ii) to a purchaser who acquires the business or the assets of Mallinckrodt to which this Agreement relates. Any attempted assignment not in accordance with the preceding sentence shall be null and void.

If a court or other body of competent jurisdiction finds any provision of this Agreement, or portion thereof, to be invalid or unenforceable, such provision will be enforced to the maximum extent permissible so as to effect the intent of the Parties, and the remainder of this Agreement will continue in full force and effect.

Either party may terminate this Agreement upon written notice if the other party materially breaches this Agreement and fails to cure the breach within thirty (30) days after receipt of written notice from the non-breaching party specifying the nature of such breach.

All notices permitted or required under this Agreement shall be in writing and shall be deemed given (a) when received, if hand-delivered or sent by a reputable express delivery service, or (b) when received, as documented with confirmation of successful receipt if sent via email. Notices shall be sent to the addresses identified below:

To AcelRx:

AcelRx Pharmaceuticals, Inc.
Attn:
351 Galveston Drive
Redwood City, California 94063
Mandatory copy to: AcelRx Legal Department

To Mallinckrodt:

Mallinckrodt LLC
Attn: Jaime Macke CC, Legal Department
675 McDonnel Blvd.
Hazelwood, Missouri 63042

Mallinckrodt appreciates the opportunity to work with AcelRx in supplying the highest quality bulk narcotics products for AcelRx dosage product production. Please call your Mallinckrodt Sales Representative, Nick Litzsinger, with any additional requests.

Mallinckrodt LLC

By: /s/ Karen Lasker (signature)
Karen Lasker
V.P. Commercial Operations

Understood and Agreed by
AcelRx Pharmaceuticals, Inc.

By: /s/ Anil Dasu (signature)
Anil Dasu
Chief Engineering Officer

Exhibit A

Mallinckrodt Specification for Sufentanil Citrate Code 0672

TEST AND SPECIFICATION LIMITS

Appearance	White to almost white powder
Identification A (IR) (USP<197K>) (EP <2.2.24>)	Matches standard
Identification B (UV) (USP <197U>)	Matches standard
Identification C (Citrate) (USP<191>)	Light red color
Identification D (Major Peak) (USP)	Retention matches
Loss On Drying (USP<731>) (EP<2.2.32>)	0.50% max
Heavy Metals (As Pb) (USP<231>Method II)	0.002% max
Assay (HPLC) (Dried Basis) (USP):	
Sufentanil Citrate	98.0 – 102.0% w/w
Related Substances (HPLC) (VR#480):	
Step IV Intermediate	0.10% max
Step V Intermediate (EP Impurity C)	0.15% max
Step VI Intermediate (EP Impurity E)	0.15% max
Unknown Related Substances (Each)	0.10% max
Total Related Substances	1.0% max
Assay (Titration) (Dried Basis) (EP)	99.0 – 101.0% w/w
Appearance of Solution (EP<2.2.1 & 2.2.2>Method II):	
Degree of Clarity	Clear
Degree of Coloration	Colorless
Related Substances (HPLC) (EP<2.2.29>):	
EP Impurity D	0.5% Area Max.
EP Impurity F	0.5% Area Max.
EP Impurity H	0.5% Area Max.
Other Impurities (Each)	0.10% Area Max.
Total Related Substances	1% Area Max

Mallinckrodt Specification for Sufentanil Citrate Code 0678

[*]

Exhibit 10.2

AMENDMENT TO AGREEMENT

This AMENDMENT TO AGREEMENT ("Amendment") is made as of the 23rd day of September 2019, by and between **SpecGx LLC** (as successor to Mallinckrodt LLC) ("Mallinckrodt") and **AcelRx Pharmaceuticals, Inc.** ("AcelRx").

Recitals

WHEREAS, AcelRx and Mallinckrodt are parties to a supply agreement dated June 16, 2017 (the "Agreement");

WHEREAS, the Initial Term (as defined in the Agreement) expires on December 31, 2019; and

WHEREAS, the parties desire to extend the term of the Agreement and make certain other changes as set forth herein.

NOW, THEREFORE, in consideration of the mutual covenants herein contained and other good and sufficient consideration, receipt of which is hereby acknowledged, the parties agree as follows:

1. The Term (as defined in the Agreement) is extended through December 31, 2022.

2. The term of the Confidentiality Agreement (as defined in the Agreement) is extended through December 31, 2022.

3. All other provisions of the Agreement not specifically and expressly amended by this Amendment shall remain in full force and effect.

IN WITNESS WHEREOF, this Amendment has been executed and delivered by the parties hereto by their respective duly authorized representatives as of the date first above written.

AcelRx Pharmaceuticals, Inc.

By: /s/ Anil Dasu

Name: Anil Dasu

Title: Chief Engineering Officer

SpecGx LLC

By: /s/ Karen Lasker

Name: Karen Lasker

Title: VP Commercial Operations

Exhibit 31.1

CERTIFICATION

I, Vincent J. Angotti, certify that:

1. I have reviewed this quarterly report on Form 10-Q 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: November 6, 2019

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

Exhibit 31.2

CERTIFICATION

I, Raffi M. Asadorian, certify that:

1. I have reviewed this quarterly report on Form 10-Q 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: November 6, 2019

/s/ Raffi M. Asadorian
Raffi M. Asadorian
Chief Financial Officer
(Principal Financial and Accounting 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 M. Asadorian, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended September 30, 2019, to which this Certification is attached as Exhibit 32.1 (the "Periodic 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 Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned has set his hands hereto as of the 6th day of November 2019.

/s/ Vincent J. Angotti
Vincent J. Angotti
Chief Executive Officer

/s/ Raffi M. Asadorian
Raffi M. Asadorian
Chief Financial Officer

This certification accompanies the Form 10-Q 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-Q), irrespective of any general incorporation language contained in such filing.