ACELRX PHARMACEUTICALS INC
Form 10-Q
August 02, 2018

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 June 30, 2018

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)

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark 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	(Do not check if a smaller reporting company)	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 July 26, 2018, the number of outstanding shares of the registrant's common stock was 60,599,914.

ACELRX PHARMACEUTICALS, INC.

QUARTERLY REPORT ON FORM 10-Q FOR THE QUARTER ENDED JUNE 30, 2018

Table of Contents

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Balance Sheets

(In thousands, except share data)

	June 30, 2018 (Unaudited)	**December 31, 2017[(1)]**
Assets		
Current Assets:		
Cash and cash equivalents	$ 33,273	$ 52,902
Short-term investments	16,849	7,567
Accounts receivable, net	773	1,533
Tax receivable	352	—
Inventories	663	956
Prepaid expenses and other current assets	1,051	455
Total current assets	52,961	63,413
Property and equipment, net	10,923	11,051
Restricted cash	178	178
Long-term tax receivable	351	703
Other assets	207	207
Total Assets	$ 64,620	$ 75,552
Liabilities and Stockholders' Deficit		
Current Liabilities:		
Accounts payable	$ 1,804	$ 1,424
Accrued liabilities	2,548	3,543
Long-term debt, current portion	8,139	7,727
Deferred revenue, current portion	338	362
Liability related to the sale of future royalties, current portion	384	604
Total current liabilities	13,213	13,660
Deferred rent, net of current portion	468	378

Long-term debt, net of current portion	7,539	11,369
Deferred revenue, net of current portion	3,305	3,463
Liability related to the sale of future royalties, net of current portion	88,895	82,984
Contingent put option liability	166	207
Total liabilities	113,586	112,061
Commitments and Contingencies		
Stockholders' Deficit:		
Common stock, $0.001 par value—100,000,000 shares authorized as of June 30, 2018 and December 31, 2017; 53,327,187 and 50,899,154 shares issued and outstanding as of June 30, 2018 and December 31, 2017	53	51
Additional paid-in capital	270,984	261,310
Accumulated deficit	(320,003)	(297,870)
Total stockholders' deficit	(48,966)	(36,509)
Total Liabilities and Stockholders' Deficit	$ 64,620	$ 75,552

(1) The condensed consolidated balance sheet as of December 31, 2017 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, 2017.

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 June 30,		Six Months Ended June 30,	
	2018	**2017**	**2018**	**2017**
Revenue:				
Collaboration agreement	$351	$2,192	$625	$5,219
Contract and other	467	467	536	549
Total revenue	818	2,659	1,161	5,768
Operating costs and expenses:				
Cost of goods sold	749	3,543	1,863	7,668
Research and development	3,278	4,901	6,791	11,820
General and administrative	3,944	4,156	7,929	8,294
Total operating costs and expenses	7,971	12,600	16,583	27,782
Loss from operations	(7,153)	(9,941)	(15,422)	(22,014)
Other (expense) income:				
Interest expense	(586)	(903)	(1,229)	(1,677)
Interest income and other income (expense), net	195	396	331	250
Non-cash interest expense on liability related to future sale of royalties	(2,995)	(2,609)	(5,811)	(5,167)
Total other expense	(3,386)	(3,116)	(6,709)	(6,594)
Net loss before income taxes	(10,539)	(13,057)	(22,131)	(28,608)
Provision for income taxes	(2)	(2)	(2)	(2)
Net loss	(10,541)	(13,059)	(22,133)	(28,610)
Other comprehensive loss:				
Unrealized gains (losses) on available-for-sale securities	—	2	—	(3)
Comprehensive loss	$(10,541)	$(13,057)	$(22,133)	$(28,613)
Net loss per share of common stock, basic and diluted	$(0.20)	$(0.29)	$(0.43)	$(0.63)
Shares used in computing net loss per share of common stock, basic and diluted	51,841,550	45,379,471	51,388,762	45,363,949

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Statements of Cash Flows

(Unaudited)

(In thousands)

	Six Months Ended June 30,	
	2018	**2017**
Cash flows from operating activities:		
Net loss	$(22,133)	$(28,610)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash royalty revenue related to royalty monetization	(155)	(46)
Non-cash interest expense on liability related to royalty monetization	5,811	5,167
Depreciation and amortization	293	948
Non-cash interest expense related to debt financing	344	471
Stock-based compensation	2,128	2,222
Revaluation of put option and PIPE warrant liabilities	(41)	(124)
Inventory impairment charge	—	369
Other	(38)	(3)
Changes in operating assets and liabilities:		
Accounts receivable	760	3,763
Inventories	293	574
Prepaid expenses and other assets	(561)	(276)
Accounts payable	469	2
Accrued liabilities	(837)	(538)
Deferred revenue	(182)	(181)
Deferred rent	65	(43)
Net cash used in operating activities	(13,784)	(16,305)
Cash flows from investing activities:		
Purchase of property and equipment	(387)	(1,961)
Purchase of investments	(12,844)	—
Proceeds from maturities of investments	3,600	—
Net cash used in investing activities	(9,631)	(1,961)
Cash flows from financing activities:		
Principal payments on long-term debt	(3,762)	—
Net proceeds from issuance of common stock in connection with equity financings	7,407	—
Net proceeds from issuance of common stock through equity plans	141	104
Net cash provided by financing activities	3,786	104
Net decrease in cash, cash equivalents and restricted cash	(19,629)	(18,162)
Cash, cash equivalents and restricted cash—Beginning of period	53,080	80,488

Cash, cash equivalents and restricted cash—End of period	$33,451	$62,326

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the condensed consolidated balance sheets that sum to the total of the same such amounts shown in the condensed consolidated statement of cash flows (in thousands):

	June 30, 2018	**June 30, 2017**
Cash and cash equivalents	33,273	62,148
Restricted cash	178	178
Cash, cash equivalents and restricted cash shown in the statement of cash flows	33,451	62,326

Amounts included in restricted cash represent letters of credit required to be maintained under the Company's facility lease and corporate credit card agreements as security for performance under these agreements. The letters of credit are secured by certificates of deposit in amounts equal to the letters of credit.

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Notes to Condensed Consolidated Financial Statements

(Unaudited)

(In thousands, except where otherwise noted)

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 the treatment of acute pain. AcelRx's lead product candidate, DSUVIA™ (known as DZUVEO™ outside of the United States), and its follow-on product candidate, Zalviso®, each utilize sublingual sufentanil, delivered via a non-invasive route of sublingual administration. DSUVIA, is a 30 mcg sufentanil sublingual tablet in a single-dose applicator intended for the treatment of moderate-to-severe acute pain administered by a healthcare professional. Zalviso delivers 15 mcg sufentanil sublingually through a non-invasive delivery route via a pre-programmed, patient-controlled analgesia, or PCA, system. Subject to obtaining regulatory approvals, AcelRx anticipates developing a distribution capability and commercial organization in the United States to market and sell DSUVIA in the United States by itself. In geographies where AcelRx decides not to commercialize products by itself, the Company may seek to out-license commercialization rights. The Company currently intends to commercialize and promote DZUVEO in Europe with a potential strategic partner. 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, is a 30 mcg sufentanil sublingual tablet in a single-dose applicator intended for the treatment of moderate-to-severe acute pain administered by a healthcare professional. DSUVIA is known as DZUVEO outside the

United States. DSUVIA was initially developed at the request of the U.S. Department of Defense as a replacement for injections of morphine on the battlefield. In addition to the military application, AcelRx is developing DSUVIA for the treatment of patients suffering from moderate-to-severe acute pain in multiple settings, such as 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. The Company completed the Phase 3 clinical program for DSUVIA and in February 2017 a New Drug Application, or NDA, was accepted for filing by the U.S. Food and Drug Administration, or FDA, for DSUVIA for the treatment of moderate-to-severe acute pain to be administered by a healthcare professional in medically supervised settings. In October 2017, the Company received a Complete Response Letter, or CRL, from the FDA regarding its NDA for DSUVIA which states the FDA determined it could not approve the NDA and provided recommendations for resubmission. The CRL contained two primary recommendations. First, while the safety database was suitable in number of patients, the collection of additional data was requested on at least 50 patients to assess the safety of DSUVIA dosed at the maximum amount described in the proposed labelling. Second, to ensure proper administration of the tablet with the single-dose applicator, the FDA recommended certain changes to the Directions for Use, or DFU, to address use-related errors, including dropped tablets, which changes would need to be validated through a Human Factors, or HF, study. The Company had a Type A post-action meeting with the FDA in January 2018 to discuss the topics covered in the CRL and to clarify the path to move towards resubmission of the DSUVIA NDA. In the Type A meeting, a proposal was discussed to address the safety of DSUVIA dosed at the maximum amount by reducing the maximum dose in the proposed label. In April 2018, the Company successfully completed the HF study to validate the revised DFU with no dropped tablets during the study. In May 2018, the Company announced the resubmission of the NDA for DSUVIA to the FDA. The FDA has assigned a Prescription Drug User Fee Act, or PDUFA, goal date of November 3, 2018.

The Company filed a Marketing Authorisation Application, or MAA, for DZUVEO (sufentanil sublingual tablet, 30 mcg) for the treatment of patients with moderate-to-severe acute pain in a medically supervised setting with the European Medicines Agency, or EMA. In June 2018, the Company announced that the European Commission, or EC, had granted marketing approval of DZUVEO for the treatment of patients with moderate-to-severe acute pain in medically monitored settings.

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 U.S. The Company had initially submitted to the FDA an NDA seeking approval for Zalviso in September 2013 but received a 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 plans to resubmit the NDA for Zalviso in the second half of 2018.

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 Zalviso PCA system, or the Product, in the countries of the 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, or the Field. In September 2015, the EC approved the 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 related 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 has been 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. As a result, the Company expects to continue to incur operating losses and negative cash flows.

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. “DSUVIA” and “DZUVEO” are trademarks, and “ACELRX” and “Zalviso” are registered trademarks, all owned by AcelRx Pharmaceuticals, Inc. This report also contains trademarks and trade names that are the property of their respective owners.

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 monetization transaction with PDL of the expected royalty stream and milestone payments due from the sales of Zalviso in Europe by the Company’s commercial partner, Grünenthal, pursuant to the Amended License Agreement, or 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.

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 U.S. 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 six months ended June 30, 2018, are not necessarily indicative of the results that may be expected for the year ending December 31, 2018. The condensed consolidated balance sheet as of December 31, 2017, was derived from the Company's audited financial statements as of December 31, 2017, 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, 2017, 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.

Revenue Recognition

Beginning January 1, 2018, the Company has followed the provisions of ASC Topic 606, *Revenue from Contracts with Customers*. The guidance provides a unified model to determine how revenue is recognized.

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.

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

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.

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

Timing of Recognition

Significant management judgment is required to determine the level of effort required under an arrangement 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.

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, 2017. Aside from the adoption of ASC Topic 606 described below under "Recently Adopted Accounting Standards" and explained more fully above in "Revenue Recognition," and in Note 4 "Adoption of ASC Topic 606, *Revenue from Contracts with Customers*" below, there have been no significant changes to the Company's significant accounting policies during the three and six months ended June 30, 2018, from those previously disclosed in its 2017 Annual Report on Form 10-K.

Recently Adopted Accounting Standards

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)*, to provide guidance on revenue recognition. In August 2015 and March, April, May and December 2016, the FASB issued additional amendments to the new revenue guidance relating to reporting revenue on a gross versus net basis, identifying performance obligations, licensing arrangements, collectability, noncash consideration, presentation of sales tax, transition, and clarifying examples. Collectively these are referred to as ASC Topic 606, which replaces all legacy GAAP guidance on revenue recognition and eliminates all industry-specific guidance. The new revenue recognition guidance provides a unified model to determine how revenue is recognized. The core principal of the guidance is that an entity should recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. In applying ASC Topic 606, companies need to use more judgment and make more estimates than under

legacy guidance. This includes identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each distinct performance obligation. ASC Topic 606 is effective for interim and annual reporting periods beginning after December 15, 2017, with early adoption permitted one year earlier.

The Company adopted the new standard effective January 1, 2018 under the modified retrospective transition method, applying the new guidance to the most current period presented. Upon adoption, there was no change to the units of accounting previously identified under legacy GAAP, which are now considered performance obligations under the new guidance, and there was no change to the revenue recognition pattern for each performance obligation. Therefore, the adoption of the new standard resulted in no cumulative effect to the opening accumulated deficit balance.

In May 2017, the FASB issued ASU 2017-09, *Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting*, to clarify which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting under ASC 718. Under the new guidance, an entity will not apply modification accounting to a share-based payment award if all of the following remain unchanged immediately before and after the change of terms and conditions:

- The award’s fair value (or calculated value or intrinsic value, if those measurement methods are used),
- The award’s vesting conditions, and
- The award’s classification as an equity or liability instrument.

ASU 2017-09 is effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2017 for all entities. Early adoption is permitted, including adoption in any interim period for which financial statements have not yet been issued or made available for issuance. The ASU will be applied prospectively to awards modified on or after the adoption date. The adoption of ASU 2017-09 effective January 1, 2018 did not have a material effect on the Company’s results of operations, financial condition or cash flows.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash*. ASU No. 2016-18 is intended to reduce diversity in practice in the classification and presentation of changes in restricted cash on the condensed consolidated statement of cash flows. The ASU requires that the condensed consolidated statement of cash flows explain the change in total cash and equivalents and amounts generally described as restricted cash or restricted cash equivalents when reconciling the beginning-of-period and end-of-period total amounts. The ASU also requires a reconciliation between the total of cash and equivalents and restricted cash presented on the condensed consolidated statement of cash flows and the cash and equivalents balance presented on the condensed consolidated balance sheet. The Company adopted ASU No. 2016-18, and the guidance has been retrospectively applied to all periods presented. The adoption of the guidance did not have an impact on the Company's condensed consolidated balance sheets or statements of comprehensive loss.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments,* addressing eight specific cash flow issues in an effort to reduce diversity in practice. The amended guidance is effective for fiscal years beginning after December 15, 2017, and for interim periods within those years. The adoption of ASU 2016-15 effective January 1, 2018, did not have a material impact on the Company's condensed consolidated statements of cash flows.

Recently Issued Accounting Standards

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which establishes a new lease accounting model for lessees. Unlike current GAAP which requires only capital leases to be recognized on the balance sheet, the new ASU will require both types of leases (i.e. operating and capital leases) to be recognized on the balance sheet. The FASB lessee accounting model will continue to account for both types of leases. The capital lease will be accounted for in substantially the same manner as capital leases are accounted for under existing GAAP. The operating lease will be accounted for in a manner similar to operating leases under existing GAAP, except that lessees will recognize a lease liability and a lease asset for all of those leases. The amended guidance is effective for fiscal years, and interim periods within those years, beginning after December 15, 2018, with early adoption permitted. The Company expects to adopt this standard beginning in 2019. The Company does not expect that this standard will have a material impact on its condensed consolidated statements of comprehensive loss; however, the Company does expect that upon adoption, this standard will impact the carrying value of its assets and liabilities on its condensed consolidated balance sheets as a result of the requirement to record right-of-use assets and corresponding lease obligations for current operating leases. The Company is still evaluating whether there are other existing contracts that may become leases under the new lease standard, and the impact of the adoption of this standard on its condensed consolidated financial statements and disclosures. The Company will continue to monitor additional modifications, clarifications or interpretations undertaken by the FASB that may impact its current conclusions, and will expand its analysis to include any new lease arrangements initiated prior to adoption.

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 June 30, 2018			
	Amortized Cost	**Gross Unrealized Gains**	**Gross Unrealized Losses**	**Fair Value**
Cash and cash equivalents:				
Cash and money market funds	$19,267	$ —	$ —	$19,267
U.S. government agency securities	14,006	—	—	14,006
Total cash and cash equivalents	$33,273	$ —	$ —	$33,273
Marketable securities:				
U.S. government agency securities	$16,849	$ —	$ —	$16,849
Total marketable securities	$16,849	$ —	$ —	$16,849
Total cash, cash equivalents and investments	$50,122	$ —	$ —	$50,122

	As of December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$29,765	$ —	$ —	$29,765
U.S. government agency securities	23,137	—	—	23,137
Total cash and cash equivalents	$52,902	$ —	$ —	$52,902
Marketable securities:				
U.S. government agency securities	$7,567	$ —	$ —	$7,567
Total marketable securities	$7,567	$ —	$ —	$7,567
Total cash, cash equivalents and investments	$60,469	$ —	$ —	$60,469

As of June 30, 2018 and December 31, 2017, 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 June 30, 2018 or December 31, 2017. 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 six months ended June 30, 2018 and June 30, 2017.

As of June 30, 2018 and December 31, 2017, the contractual maturity of all investments held was less than one year.

Fair Value Measurement

The Company's financial instruments consist of Level II assets and Level III liabilities. 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 and U.S. government agency obligations. On March 2, 2017, the Company entered into an amended and restated loan agreement, or the Amended Loan Agreement with Hercules Capital Funding Trust 2014-1 and Hercules Technology II, L.P., together, Hercules, which contains a contingent put option liability. The Company's estimate of fair value of the contingent put option liability 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. Changes to the estimated fair value of these liabilities are recorded in interest income and other income (expense), 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 June 30, 2018			
	Fair Value	Level I	Level II	Level III
Assets				
U.S. government agency obligations	$30,855	$ —	$30,855	$—
Total assets measured at fair value	$30,855	$ —	$30,855	$—
Liabilities				
Contingent put option liability	$166	$ —	$—	$166
Total liabilities measured at fair value	$166	$ —	$—	$166

	As of December 31, 2017			
	Fair Value	Level I	Level II	Level III
Assets				
U.S. government agency obligations	$30,704	$ —	$30,704	$—
Total assets measured at fair value	$30,704	$ —	$30,704	$—
Liabilities				
Contingent put option liability	$207	$ —	—	$207
Total liabilities measured at fair value	$207	$ —	$—	$207

As of June 30, 2017, the Company also held a Level III liability associated with warrants, or PIPE warrants, issued in connection with the Company's private placement equity offering, completed in June 2012. The PIPE warrants were considered a liability and were valued using the Black-Scholes option-pricing model, the inputs for which included exercise price of the PIPE warrants, market price of the underlying common shares, expected term, volatility based on a group of the Company's peers and the risk-free rate corresponding to the expected term of the PIPE warrants. Changes to any of these inputs could have a significant impact to the estimated fair value of the PIPE warrants. The PIPE warrants expired in November 2017.

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 six months ended June 30, 2018 and June 30, 2017 (in thousands):

	Three Months Ended June 30, 2018	Six Months Ended June 30, 2018
Fair value—beginning of period	$ 186	$ 207
Change in fair value of contingent put option associated with Amended Loan Agreement	(20)	(41)
Fair value—end of period	$ 166	$ 166

	Three Months Ended June 30, 2017	Six Months Ended June 30, 2017
Fair value—beginning of period	$ 609	$ 412
Change in fair value of PIPE warrants	(267)	(260)
Change in fair value of contingent put option associated with Amended Loan Agreement	(54)	136
Fair value—end of period	$ 288	$ 288

3. Inventories

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

	Balance as of June 30, 2018	December 31, 2017
Raw materials	$663	$ 702
Work-in-process	—	254
Total	$663	$ 956

4. **Adoption of ASC Topic 606, *Revenue from Contracts with Customers***

On January 1, 2018, the Company adopted Topic 606 using the modified retrospective method applied to those contracts which were not completed as of January 1, 2018. Results for reporting periods beginning after January 1, 2018, are presented under Topic 606, while prior period amounts are not adjusted and continue to be reported in accordance with the Company's historical accounting under Topic 605. The adoption of the new revenue recognition guidance resulted in no changes to deferred revenue or the accumulated deficit as of January 1, 2018.

Revenue Recognition

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. At June 30, 2018, approximately $3.6 million of the transaction price under the Amended Agreements is allocated to the discount on future manufacturing services, 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 Recognition."

The following table presents changes in the Company's contract liabilities for the six months ended June 30, 2018:

	Balance at Beginning of the Period	Additions	Deductions	Balance at the end of the Period
	(in thousands)			
Contract liability:				
Deferred revenue	$3,825	$ -	$ (182)	$3,643

During the three and six months ended June 30, 2018, the Company recognized the following revenue (in thousands):

	Three months ended June 30, 2018	**Six months ended June 30, 2018**
Amounts included in contract liabilities at the beginning of the period:		
Performance obligations satisfied – Amended Agreements	$ 91	$ 182
New activities in the period from performance obligations satisfied:		
Performance obligations satisfied – Amended Agreements	239	392
Total revenue from performance obligations satisfied	$ 330	$ 574
Royalty revenue	21	51
Contract and other	467	536
Total revenue	$ 818	$ 1,161

5. U.S. Department of Defense

On May 11, 2015, the Company entered into an award contract (referred to as the DoD Contract) supported by the Clinical and Rehabilitative Medicine Research Program, or CRMRP, of the United States Army Medical Research and Materiel Command, or the USAMRMC, within the DoD, in which the DoD agreed to provide up to $17.0 million to the Company in order to support the development of DSUVIA (sufentanil sublingual tablet, 30 mcg), a proprietary, non-invasive, single-use tablet in a disposable, pre-filled single-dose applicator, or SDA, for the treatment of moderate-to-severe acute pain. Under the terms of the DoD Contract, the DoD has and continues to reimburse the Company 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. The DoD Contract gives the DoD the option to extend the term of the DoD Contract and provide additional funding for the research. On March 2, 2016, the DoD Contract was amended to approve enrollment of additional patients in the SAP302 study, approve the addition of the SAP303 study, and extend the DoD Contract period of performance by four months from November 10, 2016 to March 9, 2017, to accommodate the increased SAP302 patient enrollment and the SAP303 study. The costs for these changes were absorbed within the current DoD Contract value. On March 9, 2017, the DoD Contract was amended to incorporate additional activities including the development and testing of packaging changes; additional stability testing; and preparation for any FDA advisory committee meeting for DSUVIA. The amendment also extends the DoD Contract period of performance by 11 months through February 28, 2018 to accommodate these additional activities. At December 31, 2017, the additional activities as outlined under the DoD Contract through February 28, 2018 were substantially complete. On February 28, 2018, the DoD contract was amended to incorporate additional services in the amount of $0.5 million and to extend the contract period by twelve months through February 28, 2019. If DSUVIA is approved by the FDA, the DoD has the option to purchase a certain number of units of commercial product pursuant to the terms of the DoD Contract.

Revenue is recognized based on expenses incurred by the Company in conducting research and development activities, including overhead, as set forth in the agreement. Revenue attributable to the research and development performed under the DoD Contract, recorded as contract and other revenue in the condensed consolidated statements of comprehensive loss, was $0.4 million and $0.5 million for the three and six months ended June 30, 2018, respectively, and $0.5 million and $0.6 million for the three and six months ended June 30, 2017, respectively.

6. 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.

During the three and six months ended June 30, 2018, the Company recognized $0.3 million and $0.6 million in revenue under the Amended Agreements, respectively, $0.1 million and $0.2 million of which was non-cash royalty revenue, with the remainder consisting primarily of product sales revenue, respectively. During the three and six months ended June 30, 2017, the Company recognized $2.2 million and $5.2 million in revenue under the Amended Agreements, respectively, primarily product sales revenue. As of June 30, 2018, the Company had current and noncurrent portions of the deferred revenue balance under the Amended Agreements of $0.3 million and $3.3 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.

14

7. Long-Term Debt

Amended Loan Agreement

The Company has long-term debt with Hercules under the Amended Loan Agreement that requires equal monthly payments of principal and interest through the scheduled maturity date of March 1, 2020. A final payment equal to 6.5% of the aggregate principal amount of $20.5 million in loans funded under the Amended Loan Agreement, or the End of Term Fee, will be due on the earliest of (i) the maturity date, (ii) prepayment in full of the loans (other than by a refinancing with Hercules) or (iii) the date on which the loans under the Amended Loan Agreement become due and payable.

The accrued balance due under the Amended Loan Agreement was $15.7 million at June 30, 2018 and $19.1 million at December 31, 2017. Interest expense related to the Amended Loan Agreement was $0.6 million, $0.1 million of which represented amortization of the debt discount, for the three months ended June 30, 2018, and $1.2 million, $0.3 million of which represented amortization of the debt discount, for the six months ended June 30, 2018. Interest expense related to the Amended Loan Agreement was $0.9 million, $0.4 million of which represented amortization of the debt discount, for the three months ended June 30, 2017, and $1.7 million, $0.7 million of which represented amortization of the debt discount, for the six months ended June 30, 2017.

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 following table shows the activity within the liability account during the six months ended June 30, 2018 (in thousands):

	Six months ended June 30, 2018	Period from inception to June 30, 2018
Liability related to sale of future royalties — beginning balance	$83,588	$ —
Proceeds from sale of future royalties	—	61,184
Non-cash royalty revenue	(120)	(247)
Non-cash interest expense recognized	5,811	28,342
Liability related to sale of future royalties as of June 30, 2018	89,279	89,279
Less: current portion	(384)	(384)
Liability related to sale of future royalties — net of current portion	$88,895	$ 88,895

As royalties 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 will record non-cash royalty revenues and non-cash interest expense within its condensed consolidated statements of comprehensive loss over the term of the Royalty Monetization.

9. Warrants

Amended Loan Agreement Warrants

In connection with the Company's Amended Loan Agreement, warrants to purchase 176,730 shares of common stock at $3.07 per share were issued to Hercules. As of June 30, 2018, these warrants had not been exercised and were still outstanding. These warrants expire in December 2018.

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 June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Cost of goods sold	$74	$79	$161	$163
Research and development	377	448	809	985
General and administrative	597	551	1,158	1,074
Total	$1,048	$1,078	$2,128	$2,222

As of June 30, 2018, there were 1,277,823 shares available for grant, 11,582,233 options outstanding and no restricted stock units outstanding under the Company's 2011 Equity Incentive Plan and 948,959 shares available for grant under the ESPP.

11. Stockholders' Equity

Common Stock

2016 ATM Agreement

During the three and six months ended June 30, 2018, the Company issued and sold 2.3 million shares of common stock pursuant to the 2016 ATM Agreement, for which the Company received net proceeds of approximately $7.4 million, after deducting commissions, fees and expenses of $0.2 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:

	June 30,	
	2018	**2017**
ESPP and stock options to purchase common stock	11,779,042	8,700,169
Common stock warrants	176,730	689,186

13. Subsequent Event

On July 16, 2018, the Company completed an underwritten public offering of 7,272,727 shares of common stock, at a price of $2.75 per share to the public. The total gross proceeds of this offering were approximately $20.0 million with estimated net proceeds to the Company of $18.7 million after deducting underwriting discounts and commissions and other estimated expenses payable by the Company. The Company has granted the underwriters an option for a period of 30 days to purchase up to an additional 1,090,909 shares of our common stock at the public offering price of $2.75 per share, less underwriting discounts and commissions.

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

This Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by those sections. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to them. In some cases you can identify forward-looking statements by words such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. Examples of these statements include, but are not limited to, statements related to the process and timing of anticipated future development of our product candidates, DSUVIA™ (sufentanil sublingual tablet, 30 mcg), known as DZUVEO™ outside the United States, and Zalviso® (sufentanil sublingual tablet system), including the timing and review of the NDA resubmission for DSUVIA; the anticipated timing of any FDA advisory committee meeting or PDUFA date regarding DSUVIA; the timing of the planned NDA resubmission for Zalviso; the accuracy of our estimates regarding expenses, capital requirements and the need for financing; the status of the Amended Agreements with Grünenthal, including potential milestones and royalty payments under the Amended Agreements, or any other future potential collaborations; and the therapeutic and commercial potential of our product candidates, including potential market opportunities for DSUVIA, DZUVEO and Zalviso.

Forward-looking statements are based on AcelRx's current expectations and inherently involve significant risks and uncertainties. Actual results and timing of events could differ materially from those anticipated in such forward-looking statements as a result of various factors. For a more detailed discussion of the potential risks and uncertainties that may impact the accuracy of these forward-looking statements, see the "Risk Factors" section in Part II, Item 1A of this Quarterly Report on Form 10-Q. You should not place undue reliance on these forward-looking statements, which reflect AcelRx's view only as of the date of this Quarterly Report on Form 10-Q. You should read this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from those we expect. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this Quarterly Report on Form 10-Q. And while we believe that information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

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, 2017.

About AcelRx Pharmaceuticals

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings. Our product candidates, focused on the treatment of acute pain are, DSUVIA™ (known as DZUVEO™ outside of the United States), and Zalviso®, each utilize sublingual sufentanil, delivered via a non-invasive route of sublingual administration, exclusively for use in medically supervised settings. In May 2018, we announced the resubmission of the NDA for DSUVIA to the FDA. The FDA has assigned a Prescription Drug User Fee Act, or PDUFA, goal date of November 3, 2018. In June 2018, we announced that the European Commission, or EC, had granted marketing approval of DZUVEO for the treatment of patients with moderate-to-severe acute pain in medically monitored settings. We anticipate developing a distribution capability and commercial organization to market and sell DSUVIA, if approved, in the United States by ourselves. In geographies where we decide not to commercialize ourselves, including the potential commercialization of DZUVEO in Europe, we may seek to out-license commercialization rights. We currently intend to commercialize and promote DZUVEO in Europe with a potential strategic partner, although we have not yet entered into such an arrangement. We plan to resubmit our NDA for Zalviso in the second half of 2018. If we are successful in obtaining approval of Zalviso in the United States, we plan to potentially promote Zalviso either by ourselves or with strategic partners. Zalviso is approved in Europe and is currently being commercialized by Grünenthal GmbH, or Grünenthal.

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

We have created a proprietary sublingual (under the tongue) formulation of sufentanil intended for the treatment of moderate-to-severe acute pain. The sublingual formulation retains the therapeutic value of sufentanil and novel delivery devices provide a non-invasive route of administration. Sufentanil is highly lipophilic which provides for rapid absorption in the mucosal tissue, or fatty cells, found under the tongue, and for rapid transit across the blood-brain barrier to reach the mu-opioid receptors in the brain. The sublingual route of delivery used by DSUVIA and Zalviso provides a predictable onset of analgesia. The sublingual delivery system also eliminates the risk of intravenous, or IV, complications, such as catheter-related infections. In addition, because patients do not require direct connection to an IV infusion pump, or IV line, DSUVIA and Zalviso may allow for ease of patient mobility.

DSUVIA (sufentanil sublingual tablet, 30 mcg), known as DZUVEO outside the United States

DSUVIA is a non-invasive investigational product candidate consisting of 30 mcg sufentanil tablets delivered sublingually by a healthcare professional using a disposable, pre-filled, single-dose applicator, or SDA. We are developing DSUVIA for the treatment of moderate-to-severe acute pain to be administered by a healthcare professional to a patient in medically supervised settings. If approved, 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. In addition, based on our recent interactions with healthcare providers, and also as reported in recent media coverage, the need for new acute pain treatment options is further highlighted by the current shortage of IV opioids in hospitals throughout the United States. We believe this situation creates an environment to demonstrate how DSUVIA, if approved, could help U.S. hospitals manage through the intravenous opioid shortage they are experiencing in their facilities today.

With the completion of the clinical program for DSUVIA, and the positive data obtained from all the clinical studies, we submitted an NDA under section 505(b)(2) with the FDA for DSUVIA for the treatment of adult patients experiencing moderate-to-severe acute pain in a medically supervised setting. The NDA contained the results of the entire DSUVIA clinical program, including data from four (three Phase 3 and one Phase 2) clinical trials in which DSUVIA was assessed as a treatment for moderate-to-severe acute pain in post-operative and emergency department patients. In each of these clinical studies, patients treated with DSUVIA demonstrated mean improvements in pain intensity as early as 15-to-30 minutes after the start of dosing. Adverse events reported in the studies were typical of opioid therapy, with the most common being nausea, headache, vomiting and dizziness.

In October 2017, we received a CRL from the FDA regarding the DSUVIA NDA which stated that the FDA determined it could not approve the NDA in its present form and provided recommendations for resubmission. The CRL contained two primary recommendations. First, while the safety database was suitable in number of patients, the collection of additional data was requested on at least 50 patients to assess the safety of DSUVIA dosed at the maximum amount described in the proposed label. Second, to ensure proper administration of the tablet with the SDA, the FDA recommended certain changes to the Directions for Use, or DFU, to address use-related errors, which changes should be validated through a Human Factors, or HF, study. We had a Type A post-action meeting with the FDA in January 2018 to discuss the topics covered in the CRL and to clarify the path to move towards resubmission of the DSUVIA NDA. In the Type A meeting, we discussed a proposal to address the safety of DSUVIA dosed at the maximum amount by reducing the maximum dose in the proposed label. In April 2018, we successfully completed the HF study to validate the revised DFU with no dropped tablets during the study, and as mentioned above, in May 2018, we announced the resubmission of the DSUVIA NDA to the FDA and the PDUFA goal date of November 3, 2018.

On May 11, 2015, we entered into an award contract (referred to as the DoD Contract) supported by the Clinical and Rehabilitative Medicine Research Program, or CRMRP, of the United States Army Medical Research and Materiel Command, or USAMRMC, within the U.S. Department of Defense, or the DoD, in which the DoD agreed to provide up to $17.0 million to support the development of DSUVIA. Under the terms of the DoD Contract, the DoD 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. The DoD Contract gives the DoD the option to extend the term and provide additional funding. On March 2, 2016, the DoD Contract was amended to approve enrollment of additional patients in the SAP302 study, approve the addition of the SAP303 study, and extend the DoD Contract period of performance by four months from November 10, 2016 to March 9, 2017, to accommodate the increased SAP302 patient enrollment and the SAP303 study. The costs for these changes were included within the current DoD Contract value. On March 9, 2017, the DoD Contract was amended to incorporate additional activities including the development and testing of packaging changes; and additional stability testing. The amendment also extended the DoD Contract period of performance by 11 months through February 28, 2018 to accommodate these additional activities. At December 31, 2017, the additional activities as outlined under the DoD Contract through February 28, 2018 were substantially complete. On February 28, 2018, the DoD contract was amended to incorporate additional services in the amount of $0.5 million and to extend the contract period by twelve months through February 28, 2019. If DSUVIA is approved by the FDA, the DoD has the option to purchase 112,000 units of commercial product pursuant to the terms of the DoD Contract.

As mentioned above, 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 anticipate we may need comparator studies in the EU to ensure premium reimbursement in certain countries. As mentioned above, we intend to commercialize and promote DZUVEO in Europe with a potential strategic partner, but we have not yet entered into such an arrangement.

Zalviso (sufentanil sublingual tablet system)

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 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. While still under development in the U.S., as discussed further below, Zalviso is approved and marketed in Europe.

On December 16, 2013, AcelRx and Grünenthal entered into a Collaboration and License Agreement, or the License Agreement, and related Manufacture and Supply Agreement, or the MSA, and together with the License Agreement, the Agreements. The License Agreement grants Grünenthal rights to commercialize Zalviso, our novel sublingual PCA system, or the Product, 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, or the Field. We retain rights with respect to the Product in countries outside the Territory, including the United States, Asia and Latin America. Under the MSA, we will exclusively manufacture and supply the Product to Grünenthal for the Field in the Territory. We entered into amendments to the License Agreement, effective July 17, 2015 and September 20, 2016, or the License Amendments, and together with the License Agreement, the Amended License Agreement, and entered into an amendment to the MSA, or the MSA Amendment, and together with the MSA, the Amended MSA, effective as of July 17, 2015, and together, the Amended Agreements. For additional information on the Amended Agreements, see Note 6 “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 Grünenthal began its European launch of Zalviso with its first commercial sale occurring in April 2016. On September 18, 2015, we sold a majority of the expected royalty stream and commercial milestones from the European sales of Zalviso by Grünenthal to PDL, or 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.

We submitted an NDA for Zalviso in September 2013, or the Zalviso NDA, and on July 25, 2014, the Division of Anesthesia, Analgesia, and Addiction Products, or the Division, of the FDA issued a CRL for the Zalviso NDA. The

CRL contained requests for additional information on the Zalviso System to ensure proper use of the device. The requests include submission of data demonstrating a reduction in the incidence of device errors, changes to address inadvertent dosing, among other items, and submission of additional data to support the shelf life of the product. In March 2015, we received correspondence from the FDA stating that, in addition to the work we had performed to address the items in the CRL, a clinical study would be required to test the modifications to the Zalviso device and mitigations put in place to reduce the risk of inadvertent dosing/misplaced tablets.

Our IAP312 study was designed to evaluate the effectiveness of changes made to the functionality and usability of the Zalviso device and to take into account comments from the FDA on the study protocol. In the IAP312 study, 320 hospitalized, post-operative patients used Zalviso to self-administer 15 mcg sublingual sufentanil tablets as often as once every 20 minutes for 24-to-72 hours to manage their moderate-to-severe acute pain. A total of 7,293 sufentanil tablets were dispensed by the 320 patients, of which 2.2% of these patients experienced a Zalviso device error over the course of the study. This error rate was statistically less than the 5% limit specified in the study objectives and none of these device errors resulted in an over-dosing event. Separate from device errors, 6 patients called the nurse when they failed to properly self-administer a single tablet to allow the nurse to properly retrieve and dispose of the tablet. Also, during inspection by the nurse, which occurred every two hours per protocol, a total of 7 misplaced tablets (<0.1% of total dispensed tablets) were discovered with 6 additional patients. Overall, efficacy and safety results of this study supported earlier clinical findings, with favorable tolerability and a significant majority of “good” or “excellent” ratings provided by both patients and healthcare providers when assessing the method of pain control. We intend to submit the results from the IAP312 study, together with our earlier Phase 3 studies (IAP309, IAP310 and IAP311), all of which met safety and efficacy endpoints, as part of our resubmission of the NDA for Zalviso in the second half of 2018.

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 our research and development and pre-commercialization activities and support Grünenthal's European sales of Zalviso, especially in light of continued delays in obtaining regulatory approvals from the FDA. As a result, we expect to continue to incur operating losses and negative cash flows.

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

As we continue to pursue development of our product candidates, including regulatory review and potential commercial development, subject to FDA approval, we expect the business aspects of our company to become more complex. We plan to add personnel and incur additional costs related to the maturation of our business and the potential commercialization of DSUVIA and Zalviso in the United States. In addition, we believe that continued investment in research and development is critical to attaining our strategic objectives. In order to develop our product candidates as commercially viable therapeutics, we expect to expend significant resources for expertise in manufacturing, regulatory affairs, clinical research and other aspects of pharmaceutical development.

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 sales of Zalviso by Grünenthal, and funding from the Department of Defense, or DoD.

Our revenues since inception have consisted primarily of revenues from our Amended License Agreement with Grünenthal and our research contracts with the DoD. There can be no assurance that our relationship with Grünenthal will continue beyond the initial term or that we will be able to meet the milestones specified in the Amended License Agreement As mentioned above, in May 2015, the DoD agreed to provide us up to $17.0 million to support the development of DSUVIA. 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 received approval of DZUVEO in Europe in June 2018, but we have not yet entered into a collaboration agreement with a potential 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 and we cannot provide assurance that we will obtain marketing approval for any of our product candidates, outside of Zalviso and DZUVEO in Europe, and subsequently generate revenue from those product

candidates in excess of our operating expenses.

Our net loss for the three months and six months ended June 30, 2018 was $10.5 million and $22.1 million, respectively, compared to net losses of $13.1 million and $28.6 million for the three and six months ended June 30, 2017, respectively. As of June 30, 2018, we had an accumulated deficit of $320.0 million. As of June 30, 2018, we had cash, cash equivalents and short-term investments totaling $50.1 million compared to $60.5 million as of December 31, 2017.

Critical Accounting Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our 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 on Form 10-K for the year ended December 31, 2017. Aside from the adoption of *Revenue from Contracts with Customers (Topic 606*) explained more fully in Note 1 “Organization and Summary of Significant Accounting Policies - Revenue Recognition,” and in Note 4 “Adoption of ASC Topic 606, *Revenue from Contracts with Customers*,” in the accompanying notes to the condensed consolidated financial statements, there have been no significant changes to our critical accounting policies and estimates during the three and six months ended June 30, 2018, from those previously disclosed in our 2017 Annual Report on Form 10-K.

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 research and development efforts and variations in the level of expenses related to developmental 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. We are subject to risks common to companies in our industry and at our stage of development, including risks inherent in our research and development efforts, reliance upon our collaborator, enforcement of our patent and proprietary rights, need for future capital, potential competition and uncertainty of clinical trial results or regulatory approvals or clearances. In order for a product candidate to be commercialized based on our research, we and our collaborators must conduct preclinical tests and clinical trials, demonstrate the efficacy and safety of our product candidates, obtain regulatory approvals or clearances and enter into manufacturing, distribution and marketing arrangements, as well as obtain market acceptance.

Three and Six Months Ended June 30, 2018 and 2017

Revenue

Collaboration Agreement Revenue

In September 2015, the EC granted marketing approval for Zalviso to our commercial partner, Grünenthal, and Grünenthal commercially launched Zalviso in Europe, with the first commercial sale occurring in April 2016. 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 June 30, 2018, we recognized $0.3 million in revenue under the Amended Agreements, $0.1 million of which was non-cash royalty revenue, with the remainder consisting primarily of product sales revenue. For the three months ended June 30, 2017, we recognized $2.2 million in revenue under the Amended Agreements, primarily product sales revenue. Revenue recognized under the Amended Agreements for the six months ended June 30, 2018 was $0.6 million, $0.2 million of which was non-cash royalty revenue, with the remainder consisting primarily of product sales revenue, compared to $5.2 million for the six months ended June 30, 2017, consisting primarily of product sales revenue. The decrease in collaboration agreement revenue for the three and six months ended June 30, 2018, as compared to the prior year periods, was primarily the result of Grünenthal working down its

existing inventories. While Grünenthal anticipates positive sales growth for Zalviso in fiscal year 2018, this trend will not always closely align with the timing of our product sales revenue as Grünenthal continues to work down its existing inventories. Therefore, despite Grünenthal's continued growth expectations for Zalviso, we expect our collaboration agreement revenue related to product sales to continue to decline in fiscal year 2018 before increasing modestly in 2019. 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 European Zalviso royalties and milestones were already monetized with PDL in 2015. We anticipate that royalty revenues and non-cash royalty revenues from the commercial sale of Zalviso in 2018 will continue to be minimal.

As of June 30, 2018, we had current and non-current portions of the deferred revenue balance under the Amended Agreements of $0.3 million and $3.3 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 value assigned to this portion of the total allocated consideration was $4.4 million. We anticipate that the long-term 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

During the three and six months ended June 30, 2018, we recognized revenue of $0.4 million and $0.5 million, respectively for services performed under the DoD Contract for DSUVIA, as compared to $0.5 million and $0.6 million, during the three and six months ended June 30, 2017, respectively. Under the terms of the DoD Contract, the DoD reimburses 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.

Cost of goods sold

Total cost of goods sold for the three and six months ended June 30, 2018 and 2017 was as follows (in thousands):

	Three Months Ended June 30,				Six Months Ended June 30,			
	2018	2017	$ Change 2018 vs. 2017	% Change 2018 vs. 2017	2018	2017	$ Change 2018 vs. 2017	% Change 2018 vs. 2017
	(In thousands, except percentages)							
Cost of goods sold	$749	$3,543	$(2,794)	(79)%	$1,863	$7,668	$(5,805)	(76)%

In October 2015, we initiated commercial production of Zalviso for Grünenthal. Under the Amended Agreements, we will sell Zalviso at a predetermined transfer price. We will not recover internal indirect costs as part of the transfer price. At current low volume levels, our direct costs are in excess of the transfer prices we are receiving from Grünenthal. In addition, 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 yet resubmitted the NDA for Zalviso and sales by Grünenthal in Europe have not been substantial. If we do not timely resubmit the NDA for Zalviso 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.

Cost of goods sold for Zalviso delivered to Grünenthal 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 and impairment charges. These direct costs included in costs of goods sold totaled $0.1 million and $0.5 million in the three and six months ended June 30, 2018, respectively, and $2.3 million and $5.1 million in the three and six months ended June 30, 2017, respectively. The indirect costs to manufacture include internal personnel and related costs for purchasing, supply chain, quality assurance, depreciation and related expenses. Indirect costs included in costs of goods sold totaled $0.7 million and $1.4 million in the three and six months ended June 30, 2018, respectively, and $1.3 million and $2.6 million in the three and six months ended June 30, 2017, respectively. We periodically evaluate the carrying value of inventory on hand for potential excess amounts over demand using the same lower of cost or net realizable value approach as that used to value the inventory. 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.

While we completed the Phase 3 clinical development programs for DSUVIA and Zalviso in fiscal year 2017, we expect to incur future research and development expenditures to support the FDA regulatory review of the resubmitted DSUVIA NDA as well as the Zalviso NDA, once it is resubmitted.

We track external development expenses on a program-by-program basis. Our internal 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 six months ended June 30, 2018 and 2017 (in thousands, except percentages):

	Three Months Ended June 30,				Six Months Ended June 30,			
Drug Indication/Description	2018	2017	$ Change 2018 vs. 2017	% Change 2018 vs. 2017	2018	2017	$ Change 2018 vs. 2017	% Change 2018 vs. 2017
	(In thousands, except percentages)							
DSUVIA	$869	$1,178	$(309)	(26)%	$1,485	$2,223	$(738)	(33)%
ZALVISO	105	1,554	(1,449)	(93)%	502	5,292	(4,790)	(91)%
Overhead	2,304	2,169	135	6%	4,804	4,305	499	12%
Total research and development expenses	$3,278	$4,901	$(1,623)	(33)%	$6,791	$11,820	$(5,029)	(43)%

Due to the inherently unpredictable nature of product development, development timelines and the probability of success, development costs can differ materially from expectations. In addition, we cannot predict which product candidates may be subject to future collaborations, when these arrangements will be secured, if at all, and to what degree these arrangements would affect our development plans and capital requirements.

The $1.6 million decrease in research and development expenses for the three months ended June 30, 2018, as compared to the three months ended June 30, 2017, was primarily due to a $1.4 million decrease in Zalviso-related expenses and a $0.3 million decrease in DSUVIA-related development spending. The $5.0 million decrease in research and development expenses for the six months ended June 30, 2018, as compared to the six months ended June 30, 2017, was mainly due to a $4.8 million decrease in Zalviso-related expenses and a $0.7 million decrease in DSUVIA-related development spending, offset by a $0.5 million net increase in other research and development expenses. The decrease in Zalviso-related spending in 2018 as compared to the prior year periods is primarily due to the IAP312 clinical study which was completed in the third quarter of 2017.

General and Administrative Expenses

General and administrative expenses consisted primarily of salaries, benefits and stock-based compensation for personnel engaged in administration, finance, pre-commercialization and business development activities. Other

significant expenses included allocated facility costs and professional fees for general legal, audit and consulting services. We expect general and administrative expenses in the fiscal year 2018 to increase as compared to fiscal year 2017 expenses, as we focus our efforts on preparing for the potential commercialization of DSUVIA in the United States.

Total general and administrative expenses for the three and six months ended June 30, 2018 and 2017 were as follows:

	Three Months Ended June 30,				Six Months Ended June 30,			
	2018	2017	$ Change 2018 vs. 2017	% Change 2018 vs. 2017	2018	2017	$ Change 2018 vs. 2017	% Change 2018 vs. 2017
	(In thousands, except percentages)							
General and administrative expenses	$3,944	$4,156	$ (212)	(5)%	$7,929	$8,294	$ (365)	(4)%

General and administrative expenses during the three months ended June 30, 2018 decreased by $0.2 million, as compared to the three months ended June 30, 2017 and decreased by $0.4 million during the six months ended June 30, 2018, as compared to the six months ended June 30, 2017. In both periods, the decreases were primarily due to decreased expenses in support of DSUVIA-related pre-commercialization activities.

Other (Expense) Income

Total other (expense) income for the three and six months ended June 30, 2018 and 2017 was as follows (in thousands, except percentages):

	Three Months Ended June 30,				Six Months Ended June 30,			
	2018	2017	$ Change 2018 vs. 2017	% Change 2018 vs. 2017	2018	2017	$ Change 2018 vs. 2017	% Change 2018 vs. 2017
	(In thousands, except percentages)							
Interest expense	$(586)	$(903)	$ 317	35 %	$(1,229)	$(1,677)	$ 448	(27) %
Interest income and other income (expense), net	195	396	(201)	(51)%	331	250	81	32 %
Non-cash interest expense on liability related to sale of future royalties	(2,995)	(2,609)	(386)	15 %	(5,811)	(5,167)	(644)	12 %
Total other (expense) income	$(3,386)	$(3,116)	$ (270)	9 %	$(6,709)	$(6,594)	$ (115)	2 %

Interest expense consisted primarily of interest accrued or paid on our debt obligation agreements and amortization of debt discounts. Interest expense pertains to interest on the Amended Loan Agreement with Hercules Capital Funding Trust 2014-1 and Hercules Technology II, L.P., together, Hercules. Refer to Note 7 “Long-Term Debt” in the accompanying notes to the condensed consolidated financial statements for additional information. Primarily as a result of the lower principal balance in the three and six months ended June 30, 2018 as compared to the three and six months ended June 30, 2017, the amount of interest expense incurred decreased. As of June 30, 2018, the accrued balance due to Hercules was $15.7 million.

Interest income and other income (expense), net, for the three and six months ended June 30, 2018 primarily related to interest earned on our investments, while for the three and six months ended June 30, 2017 it consisted primarily of the change in the fair value of our warrants, or PIPE warrants, which were issued in connection with the June 2012 private placement of our common stock and expired in November 2017, and the change in the fair value of the contingent put option related to the Amended Loan Agreement with Hercules.

The increase in non-cash interest expense on the liability related to the sale of future royalties for the three and six months ended June 30, 2018 as compared to the three and six months ended June 30, 2017, is attributable to the Royalty Monetization that we completed in September 2015. As described above, the Royalty Monetization has been

recorded as debt under the applicable accounting guidance. We impute interest on the liability and record interest expense based on the amount and timing of royalty and milestone payments expected to be received by PDL over the life of the arrangement. There are a number of factors that could materially affect the estimated interest rate and we will assess this estimate on a periodic basis. As a result, future interest rates could differ significantly and any such change in interest rate will be adjusted prospectively. We anticipate that we will incur approximately $12 million in non-cash interest expense related to the Royalty Monetization during the year ended December 31, 2018.

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 2018 and may incur significant losses and negative cash flows from operations for the foreseeable 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, and our contracts with the DoD.

As of June 30, 2018, we had cash, cash equivalents and investments totaling $50.1 million compared to $60.5 million as of December 31, 2017. The decrease was primarily due to cash required to fund our continuing operations, as we continue our research and development and pre-commercialization activities and support Grünenthal's European sales of Zalviso. We anticipate that our existing capital resources will permit us to meet our capital and operational requirements through at least the end of the third quarter of 2019. However, our expectations may change depending on a number of factors including any changes or delays in the NDA resubmission of Zalviso and the FDA approval process for DSUVIA and 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. Additional capital may not be available on terms acceptable to us, or at all. If adequate funds are not available, or if the terms underlying potential funding sources are unfavorable, our business and our ability to develop our product candidates would be harmed.

On July 16, 2018, we completed an underwritten public offering of 7,272,727 shares of common stock, at a price of $2.75 per share to the public. The total gross proceeds of this offering were approximately $20.0 million with estimated net proceeds to us of $18.7 million after deducting underwriting discounts and commissions and other estimated expenses payable by us. We have granted the underwriters an option for a period of 30 days to purchase up to an additional 1,090,909 shares of our common stock at the public offering price of $2.75 per share, less underwriting discounts and commissions.

On June 21, 2016, we entered into a Controlled Equity Offering℠ Sales Agreement, or the Sales Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent, pursuant to which AcelRx may offer and sell, from time to time through Cantor, shares of the Company's common stock, or the Common Stock, having an aggregate offering price of up to $40.0 million. During the six months ended June 30, 2018, we issued and sold an aggregate of 2.3 million shares of common stock pursuant to the Sales Agreement, for which we received net proceeds of approximately $7.4 million, after deducting commissions, fees and expenses of $0.2 million. As of June 30, 2018, we had issued and sold an aggregate of 7.7 million shares of common stock pursuant to the Sales Agreement, for which we had received net proceeds of approximately $23.1 million, after deducting commissions, fees and expenses of $0.7 million.

On September 18, 2015, we sold a portion of the expected royalty stream and commercial milestone payments from the European sales of Zalviso by Grünenthal to PDL. The total liability related to sale of future royalties to PDL as of June 30, 2018 was $89.3 million.

Under the terms of the Amended Agreements with Grünenthal, we received an upfront cash payment of $30.0 million, a milestone payment of $5.0 million related to the MAA submission in the third quarter of 2014 and an additional $15.0 million milestone payment related to the EC approval of the MAA for Zalviso in September 2015. In addition, under the terms of the Amended Agreements, we are eligible to receive approximately $194.5 million in additional milestone payments, based upon successful regulatory and product development efforts ($28.5 million) and net sales target achievements ($166.0 million). Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, depending on the level of sales achieved, on net sales of Zalviso in the Territory. 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, as discussed above.

On March 2, 2017, we amended and restated the Original Loan Agreement with Hercules, which is referred to as the Amended Loan Agreement. Pursuant to the Amended Loan Agreement, we borrowed approximately $20.5 million upon closing of the transaction on March 2, 2017, which is represented by secured term promissory notes, or the Notes. Our obligations under the Amended Loan Agreement are secured by a security interest in substantially all of our assets, other than our intellectual property. Loans under the Amended Loan Agreement now mature in March 2020. For more information, see Note 7 "Long-Term Debt" in the accompanying notes to the condensed consolidated financial statements.

As of June 30, 2018, the accrued balance due under the Amended Loan Agreement was $15.7 million, which includes the accrued portion of the End of Term Fee.

Our cash and investment balances are held in a variety of interest bearing instruments, including obligations of U.S. government agencies, money market funds and time deposits. 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):

	Six Months Ended June 30,	
	2018	**2017**
Net cash used in operating activities	$(13,784)	$(16,305)
Net cash used in investing activities	(9,631)	(1,961)
Net cash provided by financing activities	3,786	104

Cash Flows from Operating Activities

The primary use of cash for our operating activities during these periods was to fund the development of our product candidates, including commercial readiness activities for our product candidates, DSUVIA and Zalviso, in addition to the support of Grünenthal's European sales of Zalviso. Our cash used for 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 expense related to the sale of future royalties, interest expense related to our debt financings and the contingent put option liability.

Cash used in operating activities of $13.8 million during the six months ended June 30, 2018, reflected a net loss of $22.1 million, partially offset by aggregate non-cash charges of $8.3 million. Non-cash charges included $5.8 million in non-cash interest expense on the liability related to the royalty monetization and $2.1 million for stock-based compensation expense. The net change in our operating assets and liabilities included a decrease in accounts receivable of $0.8 million and a decrease in accrued liabilities of $0.8 million.

Cash used in operating activities of $16.3 million during the six months ended June 30, 2017, reflected a net loss of $28.6 million, partially offset by aggregate non-cash charges of $9.0 million, and a net change of $3.3 million in our net operating assets and liabilities. Non-cash charges included $5.2 million in non-cash interest expense on the liability related to the royalty monetization, $2.2 million for stock-based compensation, $0.9 million in depreciation expense, $0.5 million in non-cash interest expense related to the Amended Loan Agreement, $0.4 million in inventory impairment due to excess ZALVISO inventory. The net change in our operating assets and liabilities included a decrease in accounts receivable of $3.8 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 six months ended June 30, 2018, cash used in investing activities of $9.6 million was the result of $12.8 million for purchases of investments and purchases of property and equipment of $0.4 million offset by $3.6 million in proceeds from maturity of investments. During the six months ended June 30, 2017, cash used in investing activities of $2.0 million was due to purchases of property and equipment.

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 six months ended June 30, 2018, cash provided by financing activities was primarily due to net proceeds of $7.6 million from the issuance of common stock, including $7.4 million in net proceeds received under the Sales Agreement, offset by $3.8 million in payments of long-term debt. During the six months ended June 30, 2017, cash provided by financing activities of $0.1 million was due to proceeds from the issuance of common stock upon the exercise of common stock options under our EIP and stock purchases made under our ESPP.

Operating Capital and Capital Expenditure Requirements

Our rate of cash usage may increase in the future, in particular to support our product development activities, including activities undertaken to support the FDA review of the resubmitted DSUVIA NDA, resubmission of the Zalviso NDA to the FDA, and prepare for the potential commercialization of our product candidates, if approved. In the short-term, we anticipate that our existing capital resources will permit us to meet our capital and operational requirements through at least the end of the third quarter of 2019. Our current operating plan includes anticipated activities required to support the FDA review of the resubmitted DSUVIA NDA, to resubmit the NDA for Zalviso in the second half of 2018, and expenditures related to our preparation for the commercialization 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 gain approval of DSUVIA and 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. Additional capital may not be available on terms acceptable to us, or at all. If adequate funds are not available, or if the terms underlying potential funding sources are unfavorable, our business and our ability to develop our product candidates would be harmed.

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

- the outcome, timing and cost of the regulatory resubmission of Zalviso and any approvals for DSUVIA and Zalviso;
- the initiation, progress, timing and completion of any post-approval clinical trials for our product candidates, if approved;
- expenditures related to our preparation for the potential commercialization of DSUVIA and Zalviso;

26

- future manufacturing, selling and marketing costs related to DSUVIA and Zalviso, including our contractual obligations to Grünenthal for Zalviso;
- 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 number of product candidates that we pursue;
- 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 our product candidates;
- the extent to which we acquire or invest in businesses, products or technologies; and
- the expenses associated with any possible litigation.

We will need substantial funds to:

- commercialize any products we market, including DSUVIA and Zalviso, if approved in the United States;
- manufacture and market our product candidates;
- conduct preclinical and clinical testing of our product candidates, and;

- conduct research and development programs.

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. We may be unable to raise such additional capital on favorable terms, or at all. If we raise additional capital by selling our equity or convertible debt securities, the issuance of such securities could result in dilution of our shareholders' equity positions. If adequate funds are not available we may have to:

- significantly curtail or put on hold commercialization or development efforts of our product candidates or other operations;

- obtain funds through entering into collaboration agreements on unattractive terms, and/or;

- delay, postpone or terminate planned clinical trials.

Off-Balance Sheet Arrangements

Through June 30, 2018, 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

Our cash, cash equivalents and short-term investments as of June 30, 2018, consisted primarily of money market funds and U.S. government agency securities. We do not have any auction rate securities on our condensed consolidated balance sheet, as they are not permitted by our investment policy. Our cash is invested in accordance with an investment policy approved by our Board of Directors which specifies the categories, allocations, and ratings of securities we may consider for investment. We do not believe our cash, cash equivalents and short-term investments have significant risk of default or illiquidity.

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because the majority of our investments are in short-term marketable debt securities. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. In an attempt to limit interest rate risk, we follow guidelines to limit the average and longest single maturity dates, place our investments with high quality

issuers and follow internally developed guidelines to limit the amount of credit exposure to any one issuer. Some of the securities that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the value of the investment to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of our investment may decline. If a 10 percent change in interest rates were to have occurred on June 30, 2018, this change would not have had a material effect on the fair value of our investment portfolio as of that date. In general, money market funds are not subject to market risk because the interest paid on such funds fluctuates with the prevailing interest rate.

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

Item 4. Controls and Procedures

We maintain disclosure controls and procedures 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 U.S. Securities and Exchange Commission'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 matters are subject to uncertainty and there can be no assurance that such legal proceedings will not have a material adverse effect on our business, results of operations, financial position or cash flows.

Item 1A. Risk Factors

This Quarterly Report on Form 10-Q contains forward-looking information based on our current expectations. Because our actual results may differ materially from any forward-looking statements made by or on behalf of us, this section includes a discussion of important factors that could affect our actual future results, including, but not limited to, our revenues, expenses, net loss and loss per share. You should carefully consider these risk factors, together with all of the other information included in this Quarterly Report on Form 10-Q as well as our other publicly available filings with the U.S. Securities and Exchange Commission, or SEC.

We have marked with an asterisk (*) those risks described below that reflect substantive changes from, or additions to, the risks described in our Annual Report on Form 10-K for the year ended December 31, 2017.

Risks Related to Clinical Development and Regulatory Approval

We depend substantially on the success of DSUVIA™ (known as DZUVEO™ outside of the United States), which may not receive regulatory approval in the United States.*

We believe the importance of DSUVIA (sufentanil sublingual tablet, 30 mcg) is critical to our future success. In December 2016, we submitted the New Drug Application, or NDA, for DSUVIA for the treatment of patients experiencing moderate-to-severe acute pain in a medically supervised setting to the United States Food and Drug Administration, or FDA. The NDA was accepted for filing by the FDA. In October 2017, we received a CRL from the FDA regarding the NDA for DSUVIA which states the FDA determined it cannot approve the NDA in its present form and provides recommendations for resubmission. The CRL contained two primary recommendations. First, the collection of additional data was requested on at least 50 patients to assess the safety of DSUVIA dosed at the maximum amount described in the proposed label. Second, to ensure proper administration of the tablet with the single-dose applicator, the FDA recommended certain changes to the Directions for Use, or DFU, to address use-related errors, which changes should be validated through a Human Factors, or HF, study. We held a Type A post-action meeting with the FDA in January 2018 to discuss the topics covered in the CRL and to clarify the path to move towards resubmission of the DSUVIA NDA. In the Type A meeting, we discussed a proposal to address the safety of DSUVIA dosed at the maximum amount by reducing the maximum dose in the proposed label. In April 2018, we successfully completed the HF study to validate the revised DFU with no dropped tablets during the study, and in May 2018, we announced the resubmission of the DSUVIA NDA. The FDA has assigned a Prescription Drug User Fee Act, or PDUFA, goal date of November 3, 2018. While we have resubmitted the NDA for DSUVIA, there is no guarantee that the information provided to the FDA will be adequate to address the recommendations made in the

DSUVIA CRL or that we will be successful in obtaining FDA approval of DSUVIA. Although we have resubmitted the DSUVIA NDA, the FDA could require us to complete further clinical, Human Factors or other studies, which could further delay or preclude any approval of the NDA and require us to obtain significant additional funding. In addition, given that both DSUVIA and Zalviso utilize a sublingual tablet formulation of sufentanil, it is possible that an adverse regulatory outcome for one product candidate may affect regulatory outcome for the other product candidate.

We anticipate that the FDA will hold an advisory committee meeting to obtain committee input on the safety and efficacy of DSUVIA. 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 DSUVIA. Additionally, we may choose to engage in the dispute resolution process with the FDA.

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 potential strategic partner for the commercialization of DZUVEO in Europe and there can be no assurance that we will successfully enter into such an agreement. In addition, we anticipate we may need comparator studies in Europe to ensure premium reimbursement in certain countries. If DSUVIA is not approved for sale in the United States, or we are unable to enter into a collaboration agreement for DZUVEO, or DZUVEO does not receive premium reimbursement in certain European countries, it could have a significant impact on our ability to generate cash flows from product sales of DSUVIA or DZUVEO. If we are unable to receive approval to commercialize DSUVIA in the United States, we would be required to find alternative sources of capital to continue operations. If DSUVIA is not approved for sale in the United States, and we are unsuccessful in finding alternative sources of capital, it will be difficult for us to continue as a going concern under our current operating plan.

Our proposed trade name of DSUVIA has 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 DSUVIA prior to commercialization may be worthless.

Our development efforts for DSUVIA in the United States were delayed as a result of the DSUVIA CRL from the FDA. As a result, our ability to commercialize and generate revenues from DSUVIA in the United States has been delayed. Any further delay in approval by the FDA of the resubmitted DSUVIA NDA, including the receipt of a second CRL for DSUVIA, may also negatively impact our stock price and harm our business operations. Any additional delays in obtaining, or inability to obtain, regulatory approval would further delay or prevent us from commercializing DSUVIA 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 DSUVIA in the United States, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We depend on the clinical and regulatory success of Zalviso®, which may not receive 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 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 the Type C meeting with the FDA, which took place in September 2015, we submitted a protocol to the FDA for a clinical study. 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 have been 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 Risk Evaluation and Mitigation Strategies, or REMS, for Zalviso to address dropped tablets. We intend to submit the IAP312 study results as part of our resubmission of the NDA for Zalviso in the second half of 2018.

There is no guarantee that the additional work we performed related to Zalviso, including the IAP312 trial, will be supportive of, or guarantee, an NDA resubmission, or 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. In addition, given that both DSUVIA and Zalviso utilize a sublingual tablet formulation of sufentanil, it is possible that an adverse regulatory outcome for one product candidate may affect the regulatory outcome for the other product candidate. 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.

If the Zalviso NDA is resubmitted, 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, if, and when, 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 and could potentially cause us to cease operations.

Positive clinical results obtained to date for our product candidates 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 our three Phase 3 clinical trials for DSUVIA, or SAP301, SAP302, and SAP303, as well as each of our four Zalviso Phase 3 clinical trials completed to date, in addition to all of our Phase 2 clinical trials for DSUVIA and 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 patients treated with DSUVIA demonstrated improvements in pain intensity as early as 15-to-30 minutes after the start of dosing in our each of our clinical trials included in the NDA for DSUVIA, we received the DSUVIA CRL from the FDA in October 2017 which states the FDA determined it cannot approve the NDA in its present form and provides recommendations for resubmission. We held a Type A post-action meeting with the FDA In January 2018 to discuss the topics covered in the CRL and to clarify the path to move towards resubmission of the DSUVIA NDA. In the Type A meeting, we discussed a proposal to address the safety of DSUVIA dosed at the maximum amount by reducing the maximum dose in the proposed label. In April 2018, we completed the HF study to validate the revised DFU and in May 2018, we announced the resubmission of the DSUVIA NDA to the FDA and the PDUFA goal date of November 3, 2018. As a result of the DSUVIA CRL, the timing of our commercialization plan for DSUVIA in the United States has been delayed. Similarly, 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, or accept our planned NDA resubmission without requiring additional clinical trials of Zalviso. 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, or further development of our other product candidates, 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 three Phase 3 clinical trials for DSUVIA, four Phase 3 clinical trials for Zalviso, one Phase 2 clinical trial for DSUVIA 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, in October 2017, we received the DSUVIA CRL from the FDA for the NDA for DSUVIA which states the FDA determined it cannot approve the NDA in its present form and provides recommendations for resubmission. We held a Type A post-action meeting with the FDA in January 2018 to discuss the topics covered in the CRL and to clarify the path to move towards resubmission of the DSUVIA NDA. In the Type A meeting, we discussed a proposal to address the safety of DSUVIA dosed at the maximum amount by reducing the maximum dose in the proposed label. In April 2018, we completed the HF study to validate the revised DFU and in May 2018, we announced the resubmission of the DSUVIA NDA and the PDUFA goal date of November 3, 2018. As a result, the completion of the Phase 3 clinical program for DSUVIA has been delayed and our research and development expenses for DSUVIA will increase. Finally, 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 clinical trials for any of our product candidates 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, IRBs 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 Institutional Review Board approval at each site;
- delays in recruiting suitable patients to participate in a trial;

- delays in the testing, validation, manufacturing and delivery of the tablets and device components of our product candidates;
- 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 clinical trials are delayed for any of the above reasons, our development costs may increase, our approval process could be delayed and our ability to commercialize and commence sales of our product candidates could be materially harmed, which could have a material adverse effect on our business.

We have recently resubmitted the DSUVIA NDA. Activities that we have undertaken to address recommendations made in the DSUVIA CRL may be deemed insufficient by the FDA.*

In October 2017, we received a CRL from the FDA regarding the NDA for DSUVIA which states the FDA determined it cannot approve the NDA in its present form and provides recommendations for resubmission. The CRL contained two primary recommendations. First, the collection of additional data was requested on at least 50 patients to assess the safety of DSUVIA dosed at the maximum amount described in the proposed label. Second, to ensure proper administration of the tablet with the single-dose applicator, the FDA recommended certain changes to the DFU to address use-related errors, which changes should be validated through an HF study. We had a Type A post-action meeting with the FDA in January 2018 to discuss the topics covered in the CRL and to clarify the path to move towards resubmission of the DSUVIA NDA. In the Type A meeting, we discussed a proposal to address the safety of DSUVIA dosed at the maximum amount by reducing the maximum dose in the proposed label. In April 2018, we completed the HF study to validate the revised DFU and in May 2018, we announced the resubmission of the DSUVIA NDA to the FDA and the PDUFA goal date of November 3, 2018.

Although we have resubmitted the DSUVIA NDA, there is no guarantee that we have successfully addressed the recommendations made by the FDA in the DSUVIA CRL. Inability to obtain FDA regulatory approval would prevent us from commercializing DSUVIA 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 and commercialization efforts for DSUVIA in the United States, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Although we believe that we have successfully addressed the recommendations made in the DSUVIA CRL, the FDA may 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 DSUVIA, 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.

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 plan to resubmit our NDA for Zalviso in the second half of 2018.

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. 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 and could potentially cause us to cease operations.

If we are able to resubmit an NDA for Zalviso with this new clinical data, there is no guarantee that such data will be deemed sufficient 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.

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.

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

Adverse events, or AEs, caused by our product candidates could cause us, other reviewing entities, clinical trial sites or regulatory authorities to interrupt, delay or halt 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), 7% of Zalviso-treated patients dropped out of the trial prematurely due to an AE (10% in placebo group), and we observed three serious adverse events, or SAEs, that were assessed as possibly or probably related to study drug (one in the Zalviso group and two in the IV patient-controlled morphine group). In our Phase 3, double-blind, placebo-controlled, abdominal surgery trial (IAP310), 5% of Zalviso-treated patients dropped out of the trial prematurely due to an AE (7% 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). Two patients (one each in the Zalviso group and placebo group) experienced an SAE considered possibly or probably related to the trial drug by the investigator. In our Phase 3 multicenter, open-label study of Zalviso (IAP312), 2% of patients dropped out prematurely due to an AE. Five patients experienced SAEs in the IAP312 study (four in the sufentanil sublingual tablet group and one in the placebo group) considered possibly or probably related to the study drug by the investigator.

32

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), no DSUVIA-treated patients 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. 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 or probably 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 any of our future products, including DSUVIA or 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 modified Risk Evaluation and Mitigation Strategies, or REMS;
- 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 the affected product candidate and could substantially increase the costs of commercializing our product candidates.

Additional time may be required to obtain U.S. regulatory approval for DSUVIA and Zalviso because they are drug/device combination products.*

DSUVIA and Zalviso are combination product candidates 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 have in the past, and may in the future, experience delays in the development and commercialization of both DSUVIA and 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. For example, the DSUVIA CRL received from the FDA in October 2017 contains requests for additional information and testing of DSUVIA to assess the safety of DSUVIA dosed at the maximum amount described in the proposed label in at least 50 patients. AcelRx had a Type A post-action meeting with the FDA in January 2018 to discuss the topics covered in the CRL and to clarify the path to move towards resubmission of the DSUVIA NDA. In the Type A meeting, we discussed a proposal to address the safety of DSUVIA dosed at the maximum amount by reducing the maximum dose in the proposed label. In April 2018, we completed the HF study to validate the revised DFU and in May 2018, we announced the resubmission of the DSUVIA NDA and the PDUFA goal date of November 3, 2018.

Except for Zalviso and DZUVEO approval in Europe, we cannot predict when we will obtain regulatory approval to commercialize any of our product candidates, if at all, and we cannot, therefore, predict the timing of any future revenue.*

We cannot commercialize any of our product candidates, including DSUVIA or Zalviso, until the appropriate regulatory authorities, such as the FDA or the EMA, have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may be unable to obtain regulatory approval for our product candidates. As part of our development program, we met with the FDA in December 2015 to review plans for an NDA for DSUVIA. Based on feedback from the FDA, we expanded the clinical program for DSUVIA by 176 additional patients to include individuals from specific populations and settings, in order to increase the DSUVIA safety database. As a result, the completion of the Phase 3 clinical program for DSUVIA was extended and our clinical trial expenses increased.

In October 2017, we received a CRL from the FDA regarding the NDA for DSUVIA which states the FDA determined it cannot approve the NDA in its present form and provides recommendations for resubmission. The CRL contained two primary recommendations. AcelRx had a Type A post-action meeting with the FDA in January 2018 to discuss the topics covered in the CRL and to clarify the path to move towards resubmission of the DSUVIA NDA. In the Type A meeting, we discussed a proposal to address the safety of DSUVIA dosed at the maximum amount by reducing the maximum dose in the proposed label. In April 2018, we completed the HF study to validate the revised DFU and in May 2018, we announced the resubmission of the DSUVIA NDA and the PDUFA goal date of November 3, 2018. However, the DSUVIA CRL resulted in delays in our ability to obtain commercial approval of DSUVIA and increased our associated costs.

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 potential strategic partner for the commercialization of DZUVEO in Europe and there can be no assurance that we will successfully enter into such an agreement. In addition, we anticipate we may need comparator studies in Europe to ensure premium reimbursement in certain countries. Our inability to enter into a collaboration agreement for DZUVEO or to successfully complete these additional comparator studies may prevent or delay commercialization and any associated future revenues from DZUVEO in Europe.

In September 2015, the EC approved Grünenthal’s MAA for Zalviso for post-operative pain; however, we cannot predict the commercial success of Zalviso. 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 anticipate resubmitting the NDA for Zalviso in the second half of 2018.

Although the FDA provided feedback on the DSUVIA clinical program and reviewed the protocol for IAP312, the FDA has required us to complete additional clinical work prior to resubmitting the NDAs for both DSUVIA and Zalviso. Additional delays may result if any of our product candidates is taken before an FDA advisory committee which may recommend restrictions on approval or recommend non-approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. 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 May 2017, the current FDA Commissioner established an Opioid Policy Steering Committee 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. Neither DSUVIA nor Zalviso have been designed with an abuse-deterrent formulation and neither product candidate is tamper-resistant. As a result, neither DSUVIA nor Zalviso have undergone testing for tamper-resistance or abuse deterrence.

The FDA and other foreign regulatory agencies, such as the EMA, 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 candidates 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. In addition, in January 2015, EMA conducted a pre-approval inspection of our Zalviso contract manufacturer's manufacturing and packaging site and provided its observations on a Form 483. Although we believe we have adequately addressed these observations 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 EMA inspections could impact our ability to maintain EC approval of Zalviso, and Grünenthal's ability to expand and sustain European commercial sales of Zalviso.

Any delay in, or failure to receive or maintain, approval for any of our product candidates could prevent us from generating meaningful revenues or achieving profitability. Our product candidates may not be approved even if they achieve their endpoints in clinical trials. Regulatory agencies, including the FDA or EMA, 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. To date, our product candidates are being regulated as drug products under the NDA process administered by the FDA. The FDA could in the future require additional regulation of our product candidates 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. 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, as mentioned above, we anticipate we may need comparator studies of DZUVEO in Europe to ensure premium reimbursement in certain countries. In addition, 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 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 a product candidate 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.

Even if we obtain regulatory approval for DSUVIA, Zalviso and our other product candidates in the United States, we and our collaborators face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if we obtain regulatory approval in the United States, the FDA may impose significant restrictions on the indicated uses or marketing of our product candidates or impose ongoing requirements for potentially costly post-approval trials or post-market surveillance. Additionally, the labeling ultimately approved for DSUVIA, Zalviso and our other product candidates, if approved, will likely include restrictions on use due to the opioid nature of sufentanil.

DSUVIA, Zalviso and our other product candidates, if approved in the United States in the future, will also be 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.

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 product candidates, 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 any future approved products and generate revenues.

Except for Zalviso and DZUVEO approval in Europe, we may never obtain approval for, any other 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 potential strategic partner for the commercialization of DZUVEO in Europe and there can be no assurance that we will successfully enter into such an agreement.

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, 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, Zalviso and our other product candidates will require Risk Evaluation and Mitigation Strategies, or REMS.

Our product candidates, if approved in the United States, will require REMS. The REMS may include requirements for special labeling or medication guides for patients, special communication plans to health care professionals and restrictions on distribution and use, any of which may be subject to increased scrutiny or restriction in connection with the FDA's comprehensive opioids action plan. While we have received pre-clearance from the FDA regarding certain aspects of the proposed required REMS for Zalviso, we cannot predict the final REMS 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. DSUVIA, if approved, will also require a REMS program that may significantly increase our costs to commercialize this product candidate. Furthermore, risks of sufentanil that are not adequately addressed through proposed REMS programs for our future product candidates may also prevent or delay their approval for commercialization.

36

Existing and future legislation may increase the difficulty and cost for us to commercialize DSUVIA, Zalviso and any of our product candidates that may obtain commercial approval in the future 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, or our other product candidates, including DSUVIA, 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 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.

Legislative changes to the Affordable Care Act remain possible and appear likely in the 115th U.S. Congress and under the Trump Administration. 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 repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. Additionally, 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. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole”. Congress may still consider other legislation to repeal and replace elements of the Affordable Care Act. We expect that the Affordable Care Act, as currently enacted or as it may be amended or repealed in the future, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to successfully commercialize our product candidates, if approved. 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 product candidates may lose any regulatory approval that may have been obtained 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 new legislation, manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product.

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 product candidates, 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 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.

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 2018 and may continue to incur losses for the foreseeable future.*

We have incurred significant net losses in each year since our inception in July 2005, and as of June 30, 2018, we had an accumulated deficit of $320.0 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 conduct research and development activities for our product candidates, including support for the FDA regulatory review of the resubmitted DSUVIA NDA, continue our pre-commercialization activities for DSUVIA and Zalviso, and support the manufacturing and supply of Zalviso in Europe for Grünenthal. While Grünenthal has begun European commercial sales of Zalviso, if DSUVIA, Zalviso, or our other product candidates are 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 obtaining regulatory approval to market our product candidates outside of the United States through current and future collaborations which may not materialize or prove to be successful.

We have never 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 product candidates. We may never generate revenues from sales of DSUVIA, Zalviso or our other product candidates in the United States. Although DZUVEO was approved by the EC in June 2018, we have not yet entered into a collaboration agreement with a potential 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 recognize 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 the Amended License Agreement. In addition, we do not anticipate generating revenues from our other product candidates for the foreseeable future, if ever. Our ability to generate future revenues from product sales depends heavily on our success in:

- obtaining and maintaining regulatory approval for DSUVIA and/or Zalviso in the United States and/or in Europe; and
- launching and commercializing DSUVIA and/or Zalviso, including building internally or through entering a collaboration, a hospital-directed sales force in the United States and with third parties internationally, including Grünenthal, which may require additional funding.

Because of the numerous risks and uncertainties associated with 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, or in launching DSUVIA and/or 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.

Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Even if we are able to generate revenues from the sale of any future approved products, 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 amended agreements with Grünenthal, we have 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, and 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.

During the pilot and launch phases in the various European countries, Grünenthal has 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 was 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.

There is no guarantee that Grünenthal will achieve commercial success in its Zalviso launch in the European Union or anywhere in the Territory. 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 development of DSUVIA or 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 potential 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 potential 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 will sell Zalviso at a predetermined transfer price that approximates the direct cost of manufacture at our contract manufacturers. We will not recover internal indirect costs as part of the transfer price. In addition, 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. 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 not likely to achieve the manufacturing cost reductions required in order to accommodate these declining transfer prices which would affect our ability to achieve net gross profit on Zalviso product sales.

We have a limited operating history that 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 our product candidates, understanding the market potential for our product candidates and preparing for the potential commercialization of DSUVIA and Zalviso in the United States. We have not yet obtained regulatory approval of any of our product candidates in the United States and have never ourselves directly commercialized a product. Consequently, any predictions that are made about our future success, 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 product development programs and could cause us to cease operations.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect to incur significant expenditures in connection with our ongoing activities in support of our product candidates, including support for FDA regulatory review of the resubmitted DSUVIA NDA and the Zalviso NDA resubmissions, once resubmitted and preparation for potential commercialization of DSUVIA in the United States. Further development activities can be time consuming and costly. While we believe we have sufficient capital resources to continue planned operations through at least the end of the third quarter of 2019, we will need additional capital to pursue commercialization of any of our product candidates, including DSUVIA and Zalviso, if approved.

Future events and circumstances, including those beyond our control, may cause us to consume capital more rapidly than we currently anticipate. For example, in March 2015, we received correspondence from the FDA stating that we needed to complete an additional clinical trial of Zalviso. 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 announced positive results from this study, IAP312, in August 2017, which we intend to use to support our NDA resubmission. We plan to resubmit our NDA for Zalviso in the second half of 2018. The IAP312 clinical trial, and the corresponding extension of the Zalviso development program, unexpectedly increased our capital requirements.

Clinical trials, regulatory reviews, and a potential launch of a commercial product are expensive activities. In addition, commercialization costs for DSUVIA and Zalviso in the United States may be significantly higher than estimated. We may experience technical difficulties in our commercialization efforts or otherwise, which could substantially increase the costs of commercialization. Revenues may be lower than expected and accordingly 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 or debt securities, including under the Sales Agreement with Cantor, monetize or securitize certain assets including future royalty streams and milestones, obtain a credit facility, or enter into product development, license or distribution agreements with third parties, or divest one or more of our product candidates. Such arrangements may not be available on favorable terms, if at all.

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, delay, reduce the scope of, or eliminate, one or more of our research and development programs 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 develop and commercialize our product candidates. 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 delay, scale back or discontinue the development or commercialization of our product candidates;
- seek additional corporate partners for Zalviso on terms that might be less favorable than might otherwise be available; or
- relinquish, or license on unfavorable terms, our rights to technologies or product candidates 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 or debt securities, including under the Sales Agreement with Cantor, which would result in dilution to our stockholders or impose restrictive covenants that may adversely impact our business. The sale of additional equity or convertible debt securities would result in the issuance of additional shares of our capital stock and dilution to all of our stockholders. For example, as of June 30, 2018, we had issued and sold an aggregate of 7.7 million shares of common stock pursuant to the Sales Agreement with Cantor, for which we had received net proceeds of approximately $23.1 million. In addition, on July 16, 2018, we completed an underwritten public offering of 7,272,727 shares of common stock, at a price of $2.75 per share to the public. The incurrence of additional indebtedness would result in increased fixed payment obligations and could also result in certain 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.

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

As of June 30, 2018, we have approximately $15.7 million of debt, which includes the accrual portion of the End of Term Fee, under our Amended Loan Agreement with Hercules. The Amended Loan Agreement has a scheduled maturity date of March 2020 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, Hercules could elect to declare all amounts outstanding, together with accrued and unpaid interest and penalty, to be immediately due and payable. Additional capital may not be available on terms acceptable to us, or at all. In addition, the Royal Monetization has the effect of decreasing future cash flows otherwise potentially available to us under the Amended Agreements to repay this debt. 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, Hercules will have a first claim on our assets pledged under the Amended Loan Agreement. If Hercules 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 Amended 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 or future 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 U.S. Department of Defense, or 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. The DoD Contract gives the DoD the option to extend the term of the DoD Contract and provide additional funding for the research. On March 2, 2016, the DoD Contract was amended to approve enrollment of additional patients in the SAP302 study, approve the addition of the SAP303 study, and extend the DoD Contract period of performance by four months from November 10, 2016 to March 9, 2017, to accommodate the increased SAP302 patient enrollment and the SAP303 study. On March 9, 2017, the DoD Contract was amended to incorporate additional activities including the development and testing of packaging changes; and additional stability testing. The amendment also extended the DoD Contract period of performance by 11 months through February 28, 2018 to accommodate these additional activities. At December 31, 2017, the additional activities as outlined under the DoD Contract through February 28, 2018 were substantially complete. On February 28, 2018, the DoD contract was amended to incorporate additional services in the amount of $0.5 million and to extend the contract period by twelve months 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 our preclinical and clinical drug supplies and intend to rely on third parties to produce commercial supplies of any approved 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 product candidates 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;
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- 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.

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 drug component of our product candidates and any disruption in the chain of supply may cause delay in developing and commercializing our product candidates.

We have used two established suppliers of sufentanil citrate for our tablets. However, currently we only have one supplier qualified for our manufacture of DSUVIA, known as DZUVEO outside the United States, and Zalviso. For each product candidate, only one of the two suppliers will be qualified as a vendor with the FDA and EMA. 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. There is no guarantee that this change will not impact our commercial supply of API. This change in process will require a regulatory submission to the FDA and European Health Authority which must be approved before the new process API can be used commercially in each corresponding territory. 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 compound. 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 delay or impair our ability to complete our clinical trials or commercialize our product candidates and increase our cost.

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

As we scale up manufacturing of our product candidates and conduct required stability testing, product, packaging, equipment and process-related issues may require refinement or resolution in order to obtain regulatory approval for commercial marketing. In the past we have identified impurities in our product candidates. In the future, we may identify significant impurities which could result in increased scrutiny by the regulatory agencies, delays in clinical program and regulatory approval, increases in our operating expenses, or failure to obtain or maintain approval for our products.

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 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 potential sales in United States, 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 DSUVIA, and other foreign regulatory agency approval of DZUVEO and Zalviso outside Europe. These challenges may have a material adverse impact on our business, results of operations, financial condition and prospects.

Related to the Zalviso device, we have conducted multiple Design Validation, Software Verification and Validation, Reprocessing and Human Factors studies, and have manufactured for and completed Phase 3 clinical trials using the intended commercial device. We have made modifications to the design of the Zalviso device subsequent to the original submission of the Zalviso NDA, which we plan to include as a part of the resubmitted Zalviso NDA. 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 in response to the Zalviso CRL. We completed the protocol review with the FDA for the study, known as IAP312, and announced positive results from this study in August 2017, which we intend to use to support the planned NDA resubmission. We plan to resubmit our NDA for Zalviso in the second half of 2018. However, if any additional changes to the device are substantial, the FDA may require us to perform further clinical trials or studies in order to approve the device for commercial use.

We have manufactured and shipped commercial supplies of Zalviso for delivery to Grünenthal; however, our experience is limited. We will continue to rely on contract manufacturers, component fabricators and third-party service providers to produce the necessary Zalviso devices for the commercial marketplace. We currently outsource manufacturing and packaging of the controller, dispenser and cartridge components of the Zalviso device to third parties and intend to continue to do so. Some of these purchases and components 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 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, if approved in the U.S., Zalviso and DZUVEO in Europe, and Zalviso, if approved in the U.S. and any other foreign territories.

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 candidate 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 the first half of 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.

Reliance on third party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including the possible breach of the manufacturing agreements by the third parties because of factors beyond our control; and the possibility of termination or nonrenewal of the agreements by the third parties because of our breach of the manufacturing agreement or based on their own business priorities.

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 clinical programs for DSUVIA or DZUVEO, Zalviso, and any other product candidates, 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 of our 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 DSUVIA and Zalviso, or any other product candidates. As a result, our financial results and the commercial prospects for DSUVIA, Zalviso or any future product candidates for which we may obtain approval would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

Risks Related to Commercialization of Our Product Candidates

The commercial success of DSUVIA, if approved, 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 in the U.S., or DZUVEO and Zalviso in Europe, will depend on a number of factors, including:

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and health care payers;
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- 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 AEs or SAEs;
- overcoming any perceptions of sufentanil as a potentially unsafe drug due to its high potency;
- limitations or warnings contained in the FDA- or EMA-approved label for DSUVIA, DZUVEO, or Zalviso;
- restrictions or limitations placed on DSUVIA or Zalviso due to the REMS;
- 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 P&T Committees, we may not generate sufficient revenue and we may not become or remain profitable.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any product revenue.*

In order to commercialize any products that may be approved in the United States, including DSUVIA and Zalviso, we must build our internal sales, marketing, distribution, managerial and other capabilities or make arrangements with third parties to perform these services. In addition, we plan to enter into agreements with third parties for the

distribution of approved product candidates; however, if there are delays in establishing such relationships or those third parties do not perform as expected, 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 product candidates outside of the United States. DZUVEO was approved by the EC in June 2018, but we have not yet entered into a collaboration agreement with a potential 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 our product candidates 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 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 product candidates, if approved, 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 product candidates, if approved, our ability to generate revenues from product sales will be adversely affected.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing 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.

A key part of our business strategy is to establish collaborative relationships to commercialize and fund development and approval of our product candidates, 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 product candidates. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, including:

- 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 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 drug candidates, obtain regulatory approvals and our ability to successfully manufacture and achieve market acceptance of products developed from our product candidates;

- 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 product candidates; 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 delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital.

Approval of Zalviso and DZUVEO in Europe has resulted, and any future approvals of our product candidates outside of the United States will result, 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:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- 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.

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

The U.S. market for DSUVIA and Zalviso is characterized by intense competition and cost pressure. If our product candidates obtain FDA approval, they will compete with a number of existing and future pharmaceuticals and drug delivery devices developed, manufactured and marketed by others. We or our current and potential partners will compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies.

There are a wide variety of approved injectable and oral opioid products to treat moderate-to-severe acute pain, including IV opioids such as morphine, fentanyl, hydromorphone and meperidine or oral opioids such as oxycodone and hydrocodone. DSUVIA does not require placement of an IV line and therefore direct competitors in the emergency department are other non-invasive, rapid-acting analgesics. In this environment, DSUVIA may compete with Egalet Corporation's SPRIX (intranasal ketorolac) or products that are in development, such as INSYS' sublingual buprenorphine spray. Transmucosal fentanyl products, such as ACTIQ or FENTORA (Cephalon, Inc., a subsidiary of Teva Pharmaceutical Products Ltd.), are approved for opioid-tolerant patients suffering from cancer pain and therefore are not a competitor for DSUVIA. Orally administered tablets or liquids containing oxycodone or hydrocodone often have slower absorption and slower analgesic onset than transmucosal opioids. Examples of oral opioids include Acura Pharmaceuticals, Inc.'s OXAYDO (marketed by Egalet Corporation), Collegium Pharmaceuticals, Inc.'s NUCYNTA, and Purdue Pharma, L.P.'s OXYFAST, or generic oral opioids which have moderate-to-severe acute pain labeling.

Often used in combination with opioids are generic injectable local anesthetics, such as bupivacaine, or branded formulations thereof, including Pacira Pharmaceuticals, Inc.'s EXPAREL. In addition, Heron Therapeutics, Inc. is in Phase 3 development of HTX-011, a long-acting formulation of the local anesthetic bupivacaine in a fixed-dose combination with the anti-inflammatory meloxicam for the prevention of post-operative pain. These products may reduce the amount of opioids required to achieve adequate pain control but usually do not obviate the need for opioids completely. Similarly, there are many IV formulations of non-steroidal anti-inflammatory drugs, or NSAIDS, for treatment of acute pain, such as generic IV ketorolac, Pfizer's DYLOJECT, Cumberland Pharmaceuticals Inc.'s CALDOLOR and recently Recro Pharma, Inc. submitted an NDA for IV meloxicam for the treatment of moderate-to-severe acute pain. These products are all invasively administered via an IV and, as a result, we do not believe they are direct competitors to the non-invasive DSUVIA.

We believe that Zalviso would compete with a number of opioid-based treatment options that are currently available, as well as some products that are in development. The hospital market for opioids for moderate-to-severe acute pain is large and competitive. The primary competition for Zalviso is the IV PCA pump, which is widely used in the moderate-to-severe acute pain in the hospital setting. Leading manufacturers of IV PCA pumps include Hospira, Inc. (sold by Pfizer, Inc. to ICU Medical), CareFusion Corporation (purchased by Becton, Dickinson and Company), Baxter International, Inc., Curlin Medical, Inc. and Smiths Medical. The most common opioids used to treat moderate-to-severe acute pain are morphine, hydromorphone and fentanyl, all of which are available as generics both from generic product manufacturers as well as from compounding pharmacies. In addition, branded manufacturers (e.g., Hospira, Inc.) sell pre-filled glass syringes of morphine to fit their IV PCA pump systems. These systems, however, are invasive and require programming, which can lead to dosing errors, and therefore, while they are commonly used, we do not believe they are direct competitors for Zalviso.