ACELRX PHARMACEUTICALS INC
Form 10-Q
July 29, 2016

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, 2016

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, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer," and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer Accelerated filer

Non-accelerated filer (Do not check if a smaller reporting company) Smaller reporting company

Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2) Yes No

As of July 21, 2016, the number of outstanding shares of the registrant's common stock was 45,312,242.

ACELRX PHARMACEUTICALS, INC.

QUARTERLY REPORT ON FORM 10-Q FOR THE QUARTER ENDED JUNE 30, 2016

Table of Contents

		Page
Part I. Financial Information		3
Item 1.	Financial Statements	3
	Condensed Consolidated Balance Sheets as of June 30, 2016 (unaudited) and December 31, 2015	3
	Condensed Consolidated Statements of Comprehensive Loss for the three and six months ended June 30, 2016 and 2015 (unaudited)	4
	Condensed Consolidated Statements of Cash Flows for the six months ended June 30, 2016 and 2015 (unaudited)	5
	Notes to Condensed Consolidated Financial Statements (unaudited)	6
Item 2.	Management's Discussion and Analysis of Financial Condition and Results of Operations	21
Item 3.	Quantitative and Qualitative Disclosures About Market Risk	33
Item 4.	Controls and Procedures	34
Part II. OTHER Information		34
Item 1.	Legal Proceedings	34
Item 1A.	Risk Factors	34
Item 2.	Unregistered Sales of Equity Securities and Use of Proceeds	63
Item 3.	Defaults Upon Senior Securities	63
Item 4.	Mine Safety Disclosures	63
Item 5.	Other Information	63

Item 6. Exhibits 64

Unless the context indicates otherwise, the terms “AcelRx,” “AcelRx Pharmaceuticals,” “we,” “us” and “our” refer to AcelRx Pharmaceuticals, Inc. “ACELRX,” “ZALVISO,” and “ACCELERATE, INNOVATE, ALLEVIATE” are U.S registered trademarks owned by AcelRx Pharmaceuticals, Inc. This report also contains other trademarks and trade names that are the property of their respective owners.

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Balance Sheets

(In thousands, except share data)

	June 30, 2016 (Unaudited)	**December 31, 2015[(1)]**
Assets		
Current Assets:		
Cash and cash equivalents	$ 97,800	$ 107,922
Short-term investments	1,000	5,542
Accounts receivable, net	4,185	3,286
Inventories	1,328	466
Prepaid expenses and other current assets	1,237	1,731
Total current assets	105,550	118,947
Property and equipment, net	7,794	8,610
Restricted cash	178	178
Other assets	50	50
Total Assets	$ 113,572	$ 127,785
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$ 2,857	$ 1,561
Accrued liabilities	2,914	3,956
Long-term debt, current portion	13,942	4,541
Deferred revenue, current portion	957	2,604
Liability related to the sale of future royalties, current portion	357	118
Total current liabilities	21,027	12,780
Deferred rent, net of current portion	148	245
Long-term debt, net of current portion	7,406	16,381

Deferred revenue, net of current portion	3,113	593
Liability related to the sale of future royalties, net of current portion	67,775	63,494
Contingent put option liability	165	266
Warrant liability	440	913
Total liabilities	100,074	94,672
Commitments and Contingencies		
Stockholders' Equity:		
Common stock, $0.001 par value—100,000,000 shares authorized as of June 30, 2016 and December 31, 2015; 45,312,242 and 45,273,772 shares issued and outstanding as of June 30, 2016 and December 31, 2015	45	45
Additional paid-in capital	238,725	236,274
Accumulated deficit	(225,278)	(203,205)
Accumulated other comprehensive income (loss)	6	(1)
Total stockholders' equity	13,498	33,113
Total Liabilities and Stockholders' Equity	$ 113,572	$ 127,785

(1) The condensed consolidated balance sheet as of December 31, 2015 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, 2015.

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,	
	2016	**2015**	**2016**	**2015**
Revenue:				
Collaboration agreement	$1,314	$486	$3,107	$667
Contract and other	3,217	1,438	4,449	1,438
Total revenue	4,531	1,924	7,556	2,105
Operating costs and expenses:				
Cost of goods sold	2,976	—	6,575	—
Research and development	6,280	7,310	10,451	13,616
General and administrative	3,597	2,735	7,374	7,256
Restructuring costs	—	2	—	756
Total operating costs and expenses	12,853	10,047	24,400	21,628
Loss from operations	(8,322)	(8,123)	(16,844)	(19,523)
Other (expense) income:				
Interest expense	(687)	(777)	(1,367)	(1,583)
Interest income and other income, net	241	4	660	2,184
Non-cash interest expense on liability related to future sale of royalties	(2,324)	—	(4,520)	—
Total other (expense) income	(2,770)	(773)	(5,227)	601
Net loss before income taxes	(11,092)	(8,896)	(22,071)	(18,922)
Provision for income taxes	—	—	(2)	—
Net loss	(11,092)	(8,896)	(22,073)	(18,922)
Other comprehensive loss:				
Unrealized gains on available-for-sale securities	2	1	7	5
Comprehensive loss	$(11,090)	$(8,895)	$(22,066)	$(18,917)
Net loss per share of common stock, basic	$(0.24)	$(0.20)	$(0.49)	$(0.43)

Net loss per share of common stock, diluted	$(0.24)	$(0.20)	$(0.49)	$(0.47)
Shares used in computing net loss per share of common stock, basic	45,312,242	44,343,270	45,299,560	44,109,488
Shares used in computing net loss per share of common stock, diluted – see Note 11	45,312,242	44,343,270	45,299,560	44,397,471

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Statements of Cash Flows

(Unaudited)

(In thousands)

	Six Months Ended June 30,	
	2016	**2015**
Cash flows from operating activities:		
Net loss	$(22,073)	$(18,922)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash interest expense on liability related to royalty monetization	4,520	—
Depreciation and amortization	1,029	997
Amortization of premium/discount on investments, net	17	47
Interest expense related to debt financing	426	472
Restructuring costs	—	(756)
Stock-based compensation	2,330	2,649
Revaluation of put option and PIPE warrant liabilities	(574)	(2,148)
Changes in operating assets and liabilities:		
Accounts receivable	(899)	—
Inventories	(862)	—
Prepaid expenses and other assets	494	(1,376)
Accounts payable	1,391	(834)
Accrued liabilities	(1,042)	(850)
Deferred revenue	873	(667)
Deferred rent	(97)	(50)
Net cash used in operating activities	(14,467)	(21,438)
Cash flows from investing activities:		
Purchase of property and equipment	(308)	(894)
Purchase of investments	(993)	(5,543)
Proceeds from maturities of investments	5,525	5,460
Net cash provided by (used in) investing activities	4,224	(977)
Cash flows from financing activities:		
Payment of long-term debt	—	(2,240)
Net proceeds from issuance of common stock through equity plans and exercise of warrants	121	459
Net cash provided by (used in) financing activities	121	(1,781)

Net decrease in cash and cash equivalents	(10,122)	(24,196)
Cash and cash equivalents—Beginning of period	107,922	60,038
Cash and cash equivalents—End of period	$97,800	$35,842

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Notes to Condensed Consolidated Financial Statements

(Unaudited)

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 intends to commercialize its product candidates in the United States and license the development and commercialization rights to its product candidates for sale outside of the United States through strategic partnerships and collaborations. AcelRx may also consider the option to enter into strategic partnerships for its product candidates in the United States.

The Company has two late-stage development candidates based on sublingual sufentanil. The first, ARX-04, 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. ARX-04 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 ARX-04 as an investigational product 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 patient-controlled analgesia; post-operative patients who are transitioning from the operating room to the recovery floor; and patients being transported by paramedics. AcelRx has completed two placebo-controlled clinical studies (one Phase 2 and one Phase 3) demonstrating safety and efficacy of ARX-04. In October 2015, the Company initiated SAP302, an open-label Phase 3 study of ARX-04 for the treatment of adult patients who present in the emergency room with moderate-to-severe acute pain associated with trauma or injury, which treated 40 patients in the initial phase. In March 2016, the Company initiated the extension phase of the SAP302 study of ARX-04, which treated an additional 36 patients. Also in March 2016, the Company initiated SAP303, an open-label, single-arm study of ARX-04 in post-operative patients which treated 140 patients 40 years of age and older who had moderate-to-severe acute pain following a surgical procedure. The SAP303 study allowed for administration of ARX-04 for up to 12 hours. Both the SAP302 and SAP303 trials have had their last patient visits and data are currently being analyzed. The Company anticipates the top-line results for both studies will be available in the third quarter of 2016. Pending successful results of these two Phase 3 open-label studies, the Company intends to submit to the U.S. Food and Drug Administration, or FDA, a New Drug Application, or NDA, for ARX-04 for the treatment of moderate-to-severe acute pain to be administered by a

healthcare professional in medically-supervised settings by the end of 2016.

The Company's other late-stage investigational product candidate, Zalviso®, delivers 15 mcg sufentanil sublingually through a non-invasive delivery route via a pre-programmed, patient-controlled analgesia device. Zalviso is approved in the EU as well as Norway, Iceland and Liechtenstein and is in late-stage development in the U.S. In response to the NDA the Company submitted to the FDA seeking approval for Zalviso, the Company received a Complete Response Letter, or CRL, on July 25, 2014. Subsequently, the FDA requested an additional clinical study, IAP312, and the Company estimates that it may be able to begin IAP312 in September 2016. The Company does not intend to initiate the study until final supplies have been received and tested and clinical sites are ready. These activities may or may not occur in time to initiate the trial in September 2016. Timing of the completion of the IAP312 study will be dependent on the actual initiation date and other timing including, but not limited to, study enrollment.

On December 16, 2013, AcelRx and Grünenthal GmbH, or Grünenthal, entered into a Collaboration and License Agreement, or the License Agreement, which was amended effective July 17, 2015, or the Amended License Agreement, which grants Grünenthal rights to commercialize Zalviso, the Company's novel sublingual patient-controlled analgesia, or PCA, system, or the Product, in the countries of the European Union, 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. In September 2015, the European Commission approved the Marketing Authorization Application, or MAA, previously submitted to the European Medicines Agency, or EMA, for Zalviso for the management of acute moderate-to-severe post-operative pain in adult patients. The approval allows Grünenthal to market Zalviso in the 28 European Union member states as well as for the European Economic Area countries, Norway, Iceland and Liechtenstein, or EEA. Also 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 entered into an amendment to the MSA, or the MSA Amendment, and together with the MSA, the Amended MSA, between the Company and Grünenthal, each effective as of July 17, 2015, and together, with the Amended License Agreement, the Amended Agreements.

In April 2016, Grünenthal completed the first commercial sale of Zalviso. Grünenthal continues to sell Zalviso initially in a limited number of hospitals in Germany under a pilot program, whereby the hospital will use Zalviso in a small number of post-operative patients. The pilot program, which is expected to last approximately two months at each institution, is being made available to additional hospitals in Germany over the next several months. Pending success with the pilot program, Grünenthal expects to make the product widely available in Germany. With similar methodology, Grünenthal has also initiated the sale of Zalviso in France, the United Kingdom, Italy and Belgium, and intends to launch Zalviso in the Netherlands, Ireland and Portugal by the end of 2016.

The Company has incurred recurring operating losses and negative cash flows from operating activities since inception and expects to continue to incur negative cash flows. Although Zalviso has been approved for sale in the European Union, 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. As a result, the Company expects to continue to incur negative cash flows.

When we refer to "we," "our," "us," the "Company" or "AcelRx" in this document, we mean the current Delaware corporation, or AcelRx Pharmaceuticals, Inc., and its predecessor, as well as its consolidated subsidiary.

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 the European Union by its 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 7 “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, 2016, are not necessarily indicative of the results that may be expected for the year ending December 31, 2016. The condensed consolidated balance sheet as of December 31, 2015, was derived from the Company's audited financial statements as of December 31, 2015, 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, 2015, 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.

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, 2015. During the six months ended June 30, 2016, there have been no significant changes to the Company's significant accounting policies from those previously disclosed in its Annual Report on Form 10-K.

Recently Issued Accounting Standards

In March 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2016-09, *Compensation - Stock Compensation (Topic 718)*, which is part of the FASB's Simplification Initiative. The updated guidance simplifies the accounting for share-based payment transactions. The amended guidance is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016, with early adoption permitted. The Company is currently evaluating the impact of the adoption of this standard on its consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which establishes a new lease accounting model for lessees. The updated guidance requires an entity to recognize assets and liabilities arising from a lease for both financing and operating leases, along with additional qualitative and quantitative disclosures. 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 is currently evaluating the impact of the adoption of this standard on its consolidated financial statements.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers*, to provide guidance on revenue recognition. ASU No. 2014-09 requires a company to 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 doing so, companies will need to use more judgment and make more estimates than under today's guidance. These may include 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 separate performance obligation. In August 2015, the FASB issued ASU No. 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which provided for the adoption of the new standard for fiscal years beginning after December 15, 2017. Accordingly, ASU No. 2014-09 is effective for the Company in the first quarter of 2018. Early adoption up to the first quarter of 2017 is permitted. Upon adoption, ASU No. 2014-09 can be applied retrospectively to all periods presented or only to the most current period presented with the cumulative effect of changes reflected in the opening balance of retained earnings in the most current period presented. The FASB has also issued the following standards which clarify ASU No. 2014-09 and have the same effective date as the original standard:

ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net)*;

ASU No. 2016-10, *Identifying Performance Obligations and Licensing (Topic 606);*

ASU No. 2016-11, *Revenue Recognition (Topic 605) and Derivatives and Hedging (Topic 815): Rescission of SEC Guidance Because of Accounting Standards Updates 2014-09 and 2014-16 Pursuant to Staff Announcements at the March 3, 2016 EITF Meeting;* and

ASU No. 2016-12, *Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients*.

The Company is currently evaluating the method of adoption and the impact of adopting ASU No. 2014-09 on its results of operations, cash flows and financial position.

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, 2016			
	Amortized Cost	**Gross Unrealized Gains**	**Gross Unrealized Losses**	**Fair Value**
Cash and cash equivalents:				
Cash	$68,360	$ —	$ —	$68,360
U.S. government agency securities	29,434	6	—	29,440
Total cash and cash equivalents	97,794	6	—	97,800
Marketable securities:				
U.S. government agency securities	1,000	—	—	1,000
Total marketable securities	1,000	—	—	1,000
Total cash, cash equivalents and investments	$98,794	$ 6	$ —	$98,800

	As of December 31, 2015			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$83,112	$ —	$ —	$83,112
U.S. government agency securities	24,809	1	—	24,810
Total cash and cash equivalents	107,921	1	—	107,922
Marketable securities:				
U.S. government agency securities	5,544	—	(2)	5,542
Total marketable securities	5,544	—	(2)	5,542
Total cash, cash equivalents and investments	$113,465	$ 1	$ (2)	$113,464

As of June 30, 2016 and December 31, 2015, 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, 2016 or December 31, 2015. 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, 2016 and 2015.

As of June 30, 2016 and December 31, 2015, the contractual maturity of all investments held was less than one year.

Fair Value Measurement

The Company's financial instruments consist of Level I and Level II assets and Level III liabilities. Level I securities include highly liquid money market funds and are valued based on quoted market prices. 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. As of June 30, 2016 and December 31, 2015, the Company held, in addition to Level I and Level II assets, a contingent put option liability associated with the Company's Amended and Restated Loan and Security Agreement, or the Amended Loan Agreement, with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., collectively referred to as Hercules, which amends and restates the loan and security agreement with Hercules dated as of June 29, 2011, or the Original Loan Agreement, and which was classified as a Level III liability. See Note 6 "Long-Term Debt" for further description. 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, 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. As of June 30, 2016 and December 31, 2015, 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. For a detailed description, see Note 8 "Warrants." The PIPE warrants are considered a liability and are valued using the Black-Scholes option-pricing model, the inputs for which include 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 can have a significant impact to the estimated fair value of the PIPE warrants. 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, 2016			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$26	$ 26	$—	$—
U.S. government agency obligations	30,414	—	30,414	—
Total assets measured at fair value	$30,440	$ 26	$30,414	$—
Liabilities				
PIPE warrants	$440	—	—	$440
Contingent put option liability	165	—	—	165
Total liabilities measured at fair value	$605	$ —	$—	$605

	As of December 31, 2015			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$2	$ 2	$—	$—
U.S. government agency obligations	30,352	—	30,352	—
Total assets measured at fair value	$30,354	$ 2	$30,352	$—
Liabilities				
PIPE warrants	$913	—	—	$913
Contingent put option liability	266	—	—	266
Total liabilities measured at fair value	$1,179	$ —	$—	$1,179

The following table sets forth the assumptions used in the Black-Scholes option-pricing model to estimate the fair value of the PIPE warrants as of June 30, 2016:

Market price	$2.69
Exercise price	$3.40
Risk-free interest rate	0.45%
Expected volatility	85.0%
Expected life (in years)	1.42
Expected dividend yield	0.0 %

The following table sets forth the assumptions used in the Black-Scholes option-pricing model to estimate the fair value of the PIPE warrants as of December 31, 2015:

Market price	$3.85
Exercise price	$3.40
Risk-free interest rate	1.06%
Expected volatility	80.0%
Expected life (in years)	1.92
Expected dividend yield	0.0 %

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, 2016 and 2015 (in thousands):

	Three Months Ended June 30, 2016	Six Months Ended June 30, 2016
Fair value—beginning of period	$ 804	$ 1,179
Change in fair value of PIPE warrants	(142)	(473)
Change in fair value of contingent put option associated with Original Loan Agreement with Hercules	(57)	(101)
Fair value—end of period	$ 605	$ 605

	Three Months Ended June 30, 2015	Six Months Ended June 30, 2015
Fair value—beginning of period	$ 1,155	$ 5,859
Change in fair value of PIPE warrants	68	(4,661)
Change in fair value of contingent put option associated with Original Loan Agreement with Hercules	(56)	(31)
Fair value—end of period	$ 1,167	$ 1,167

3. Inventories

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

Balance as of	
June 30, 2016	December 31, 2015

Raw materials	$675	$ 140
Work-in-process	278	181
Finished goods	375	145
Total	$1,328	$ 466

4. U.S. Department of Defense Contract

On May 11, 2015, the Company 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 the Company in order to support the development of the Company's product candidate, ARX-04 (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. The DoD Contract supports development of ARX-04 to perform Phase 3 clinical trials and manufacturing activities in order to submit an NDA to the FDA. Under the terms of the contract, the DoD will reimburse the Company for costs incurred for development, manufacturing and clinical costs outlined in the contract, including reimbursement for certain personnel and overhead expenses. The period of performance under the contract began on May 11, 2015. The contract gives the DoD the option to extend the term of the contract and provide additional funding for the research. On March 2, 2016, the Company entered into an amendment to the award contract with the DoD in which the DoD agreed to approve enrollment of additional patients in the SAP302 study, approve the addition of the SAP303 study, and extend the 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 will be absorbed within the current contract value. All other terms and conditions remain unchanged. If ARX-04 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 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 services performed under the DoD Contract, recorded as contract and other revenue in the condensed consolidated statements of comprehensive loss, was $3.2 million and $4.4 million for the three and six months ended June 30, 2016, respectively, and $1.4 million for the three and six months ended June 30, 2015.

5. Collaboration Agreement

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 in the Territory, for human use in the Field. The Company retains rights with respect to the Product in countries outside the Territory, including the United States, Asia and Latin America. 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 entered into amendments to the License Agreement, or the License Amendment, and together with the License Agreement, the

Amended License Agreement, and the MSA, or the MSA Amendment, and together with the MSA, the Amended MSA, between the Company and Grünenthal, each effective as of July 17, 2015, and together, the Amended Agreements.

In the Amended Agreements, the parties amended the Product supply configurations and packaging of Product components and accessories, and associated pricing therefor, which the Company will manufacture and supply to Grünenthal for the Territory. The parties agreed to increase the pricing of the Product components and accessories in exchange for a reduction of $5.5 million in the total milestone payments due from Grünenthal contingent upon achieving specified net sales targets from a total of $171.5 million to $166.0 million. The parties also updated the development plan for the Product in the Territory, providing for additional near-term development services to be rendered by AcelRx in exchange for payments by Grünenthal of $0.7 million. In accordance with the terms of the Amended MSA, AcelRx also received a binding Product forecast from Grünenthal for approximately $3.7 million.

Amended License Agreement

Under the terms of the Amended License Agreement, Grünenthal has the exclusive right to commercialize the Product in the Field in the Territory. The Company retains control of clinical development, while Grünenthal and the Company will be responsible for certain development activities pursuant to a development plan as agreed between the parties. The Company will not receive separate payment for such development activities, apart from the $0.7 million included under the Amended Agreements. Grünenthal is exclusively responsible for marketing approval applications and other regulatory filings relating to the sufentanil sublingual tablet drug cartridge for the Product in the Field in the Territory, while the Company is responsible for the CE Mark and other regulatory filings relating to device portions of the Product. In July 2014, Grünenthal submitted an MAA to the European Medicines Agency, or EMA, for Zalviso (15 micrograms sufentanil sublingual tablets) for the management of acute moderate-to-severe post-operative pain in adult patients. A CE Mark for Zalviso was obtained in the fourth quarter of 2014 which specifies AcelRx as the device design authority and manufacturer. In September 2015, the European Commission approved the MAA for Zalviso for the 28 European Union member states as well as for the EEA. In April 2016, Grünenthal completed the first commercial sale of Zalviso.

The Company received an upfront non-refundable cash payment of $30.0 million in December 2013, and 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 upon the European Commission, or EC, approval of the MAA for Zalviso, which was approved in September 2015. 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 7 “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. Grünenthal shall purchase from AcelRx, during the first five years after the effective date of the MSA, 100% and thereafter 80% of Grünenthal's and its sublicensees' and distributors' requirements of Product for use in the Field for the Territory. 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.

The Company identified the following four significant non-contingent performance deliverables under the original Agreements: 1) intellectual property (license), 2) the obligation to provide research and development services, 3) the significant and incremental discount on the manufacturing of Zalviso for commercial purposes, and 4) the obligation to participate on the joint steering committee.

At the time the Amended Agreements were executed, with the exception of the intellectual property license, these obligations remained partially undelivered. Additionally, the Company identified the following three performance deliverables under the License Amendment and the MSA Amendment: 1) the obligation to provide additional research and development services, 2) the obligation to provide Zalviso demonstration device systems, and 3) the obligation to manufacture and deliver Product under the binding forecast. The Company determined that the License Amendment and MSA Amendment are modifications to the original Agreements.

The Company considered the provisions of the multiple-element arrangement guidance in determining whether the deliverables outlined above have standalone value and thus should be treated as separate units of accounting. The Company's management determined that the license under the original License Agreement had standalone value and represented a separate unit of accounting because the rights conveyed permitted Grünenthal to perform all efforts necessary to commercialize and begin selling the product upon regulatory approval. In addition, Grünenthal has the appropriate development, regulatory and commercial expertise with products similar to the product licensed under the agreement and has the ability to engage third parties to manufacture the product allowing Grünenthal to realize the value of the license without receiving any of the remaining deliverables. Grünenthal can also sublicense its license rights to third parties. Also, the Company's management determined that the research and development services, Zalviso demonstration device systems, joint steering committee participation, the significant and incremental discount on the manufacturing of Zalviso, and the obligation to manufacture and deliver Products each represent individual units of accounting, as Grünenthal could perform such services and/or could acquire these on a separate basis.

The Company believes that none of the deliverables have vendor-specific objective evidence, or VSOE, or sufficient third-party evidence, or TPE, of selling price, as none of them have been sold separately by the Company, and as there is only limited information about third party pricing for similar deliverables. Accordingly, the Company developed best estimates of selling prices, or ESP, for each deliverable in order to allocate the noncontingent arrangement consideration to the units of accounting, based on current information available as of the modification date.

The Company's management determined the best estimate of selling price for the license based on Grünenthal's estimated future cash flows arising from the arrangement. Embedded in the estimate were significant assumptions regarding regulatory expenses, revenue, including potential customer market for the product and product price, costs to manufacture the product and the discount rate. The Company's management determined the best estimate of selling price of the research and development services and committee participation based on the nature and timing of the services to be performed and in consideration of personnel and other costs incurred in the delivery of the services. For the discount on manufacturing services, the Company's management estimated the selling price based on the market level of contract manufacturing margin it could have received if it were engaged to supply products to a customer in a separate transaction, the estimated cost of manufacturing, and the anticipated volume of Grünenthal's orders over the

course of the agreement, to which the discount would apply. For the Zalviso demonstration devices and the obligation to manufacture and deliver Product, the Company's management estimated the selling price based on the binding volume of such devices and Products, the estimated cost of manufacturing, and the market level of contract manufacturing margin. ESP of the license, research and development and committee participation services and the discount on manufacturing services were updated at the time the Amended Agreements were executed for purposes of allocating the amended arrangement consideration.

The Amended Agreements entitle the Company to receive additional payments upon the achievement of certain development and sales milestones. Based on ASC Topic 605-28, *Revenue Recognition — Milestone Method*, the Company evaluates contingent milestones at inception or modification of the agreement, and recognizes consideration that is contingent upon the achievement of a milestone in its entirety as revenue in the period in which the milestone is achieved only if the milestone is considered substantive in its entirety. Milestones are events which have the following characteristics: (i) they can be achieved based in whole or in part on either the Company's performance or on the occurrence of a specific outcome resulting from the Company's performance, (ii) there was substantive uncertainty at the date the agreement was entered into that the event would be achieved and, (iii) they would result in additional payments due to the Company. A milestone is considered substantive if the following criteria are met: (i) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item (s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (ii) the consideration relates solely to past performance and, (iii) the consideration is reasonable relative to all of the other deliverables and payment terms, including other potential milestone consideration, within the arrangement.

The substantive milestone payments will be recognized as revenue in their entirety upon the achievement of each substantive milestone. Based on the criteria noted above, the identified substantive milestones in the original Agreements pertain to post approval product enhancements, expanded market opportunities and manufacturing efficiencies for Zalviso. Each of these potential achievements is based primarily on the Company's performance and involves substantive uncertainty as achievement of these milestones requires future research, development and regulatory activities, which are inherently uncertain in nature. The Company determined that the consideration for each milestone was commensurate with the Company's performance to achieve the milestone, including future research, development, manufacturing and regulatory activities and that the consideration is reasonable relative to all of the other deliverables and payments within the arrangement. Aggregate potential payments for these milestones total $28.5 million.

In addition to substantive milestones, two milestones associated with the original Agreements were deemed not to be substantive. These milestones pertain to regulatory developments for Zalviso in Europe, which the Company's management deemed to be not substantive due to the high likelihood of achievement, both at inception of the original Agreements and at the time the Amended Agreements were executed. Aggregate potential payments for these milestones totaled $20.0 million. In July 2014, Grünenthal submitted an MAA to the EMA for Zalviso for the management of acute moderate-to-severe post-operative pain in adult patients, triggering the first of these two milestones, a cash payment of $5.0 million. In September of 2015, the MAA was approved by the European Commission, triggering the second of these two milestones, a cash payment of $15.0 million. Amounts received under these non-substantive milestones were allocated to performance deliverables based on the relative selling price method and recognized as appropriate for such deliverables.

The Amended Agreements also include milestone payments related to specified net sales targets, totaling $166.0 million. These milestones do not meet the definition of a milestone under ASU 2010-17 because the achievement of these milestones is solely dependent on counter-party performance and not on any performance obligations of the Company.

At the time the Amended Agreements were executed, approximately $33.3 million of revenue had been recognized, and $1.7 million remained unrecognized from the aggregate to-date consideration of $35.0 million received under the original Agreements. Upon execution of the Amended Agreements, the Company updated the allocation of this arrangement consideration, along with the consideration owed under the Amended Agreements totaling $54.4 million, consisting of $0.7 million related to research and development services and the demonstration device systems, and $3.7 million related to the Product binding purchase forecast, to all of the identified deliverables in the arrangement (both delivered and undelivered) using their relative selling prices. Further, the $15.0 million non-substantive milestone achieved in September of 2015 was also allocated to the deliverables in the same manner. As a result of such allocations, additional amounts of $13.2 million and $0.5 million were allocated to the previously delivered license and research and development and committee participation services, respectively. A total of $4.4 million was allocated to the significant and incremental discount on manufacturing services, and is expected to be recognized over the period such discount is made available to Grünenthal, beginning in February 2016, on a straight-line basis over the estimated period through 2029. An additional $0.2 million has been allocated to committee participation services and is recognized on a straight-line basis over the performance obligation period extending through 2018. A total of $2.3 million was allocated to manufacturing services for the binding forecast of Products. The remaining $0.5 million was allocated to the additional research and development services under the Amended License Agreement and demonstration device systems, and manufacturing and delivery of the Products, and will be recognized as those services are performed or as the devices are delivered, as applicable.

Below is a summary of revenue recognized under the Amended Agreements during the three and six months ended June 30, 2016 and 2015 (in thousands):

	Three Months	**Six Months Ended**

	Ended June 30,		June 30,	
	2016	2015	2016	2015
Product sales	$1,302	$—	$2,702	$—
Joint steering committee and research and development services	12	486	405	667
Total	$1,314	$486	$3,107	$667

As of June 30, 2016, the Company had current and noncurrent portions of the deferred revenue balance under the Amended Agreements of $1.0 million and $3.1 million, respectively.

6. Long-Term Debt

Hercules Loan and Security Agreements

In June 2011, AcelRx entered into the Loan and Security Agreement, or the Loan Agreement, between the Company and with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., together, the Lenders, under which AcelRx borrowed $20.0 million in two tranches of $10.0 million each, represented by secured convertible term promissory notes. The Company's obligations associated with the agreement are secured by a security interest in substantially all of its assets, other than its intellectual property and those assets sold under the Royalty Monetization.

The Company borrowed the first tranche of $10.0 million upon the closing of the transaction on June 29, 2011 and borrowed the second tranche of $10.0 million in December 2011. The Company used a portion of the proceeds from the first tranche to repay the remaining obligations under that certain loan and security agreement between the Company and Pinnacle Ventures, L.L.C., or Pinnacle Ventures, dated September 16, 2008. The interest rate for each tranche was 8.50%. In connection with the loan, the Company issued Hercules seven-year warrants to purchase an aggregate of 274,508 shares of common stock at a price of $3.06 per share. See Note 8 “Warrants,” for further description.

On December 16, 2013, AcelRx entered into an Amended and Restated Loan and Security Agreement with the Lenders, or the Amended Loan Agreement, under which the Company may borrow up to $40.0 million in three tranches. The loans are represented by secured convertible term promissory notes, collectively, the Notes. The Amended Loan Agreement amends and restates the Loan Agreement between the Company and the Lenders dated as of June 29, 2011. The Company borrowed the first tranche of $15.0 million upon closing of the transaction on December 16, 2013, and the second tranche of $10.0 million on June 16, 2014. The Company used approximately $8.6 million of the proceeds from the first tranche to repay its obligations under the Loan and Security Agreement with the Lenders. The Company recorded the new debt at an estimated fair value of $24.9 million as of December 31, 2014.

On September 24, 2014, the Company entered into Amendment No. 1 to the Amended Loan Agreement with Hercules. Amendment No. 1 extended the time period under which the Company could draw down the third tranche, of up to $15.0 million, from March 15, 2015 to August 1, 2015, subject to the Company obtaining approval for Zalviso from the FDA. The Company did not receive FDA approval of Zalviso by August 1, 2015 and as such, did not have access to the third tranche.

On September 18, 2015, concurrently with the closing of the Royalty Monetization, the Company entered into a Consent and Amendment No. 2, or Amendment No. 2, to the Amended Loan Agreement with the Lenders. Amendment No. 2 includes an interest only period from October 1, 2015 through March 31, 2016, with further extension to September 30, 2016 upon satisfaction of certain conditions. These conditions were satisfied in the third quarter of 2015 and the interest only period was extended through September 30, 2016. Loans under the Amended Loan Agreement mature on October 31, 2017. In connection with Amendment No. 2, the Company reduced the exercise price of the warrants already held by the Lenders, which are exercisable for an aggregate of 176,730 shares of Common Stock, from the previous exercise price of $6.79 per share to $3.88 per share, or the Warrant Amendments.

The interest rate for each tranche will be calculated at a rate equal to the greater of either (i) 9.10% plus the prime rate as reported from time to time in The Wall Street Journal minus 5.25%, and (ii) 9.10%. Payments under the Amended Loan Agreement were interest only until April 1, 2015, followed by equal monthly payments of principal and interest through September 30, 2015, to be followed by an interest only period from October 1, 2015 through September 30, 2016, and by equal monthly payments of principal and interest from October 1, 2016 through the scheduled maturity date on October 1, 2017, or the Loan Maturity Date. In addition, a final payment equal to $1.7 million will be due on the Loan Maturity Date, or such earlier date specified in the Amended Loan Agreement. The Company’s obligations

under the Amended Loan Agreement are secured by a security interest in substantially all of its assets, other than its intellectual property and those assets sold under the Royalty Monetization.

If the Company prepays the Amended Loan Agreement prior to maturity, it will pay Hercules a prepayment charge, based on a percentage of the then outstanding principal balance, or 1% if the prepayment occurs after December 16, 2015.

Subject to certain conditions and limitations set forth in the Amended Loan Agreement, the Company has the right to convert up to $5.0 million of scheduled principal installments under the Notes into freely tradeable shares of the Company's common stock, or Common Stock. The number of shares of Common Stock that would be issued upon conversion of the Amended Notes would be equal to the number determined by dividing (x) the product of (A) the principal amount to be paid in shares of Common Stock and (B) 103%, by (y) $9.30 (subject to certain proportional adjustments as provided for in the Amended Loan Agreement).

The Amended Loan Agreement includes customary affirmative and restrictive covenants, but does not include any financial maintenance covenants, and also includes standard events of default, including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of Hercules' security interest or in the value of the collateral, and events relating to bankruptcy or insolvency. Upon the occurrence of an event of default, a default interest rate of an additional 5% may be applied to the outstanding loan balances, and Hercules may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Amended Loan Agreement.

In connection with the Amended Loan Agreement, the Company issued a warrant to each Lender which, collectively, are exercisable for an aggregate of 176,730 shares of common stock and each carried an exercise price of $6.79 per share. As mentioned above, in connection with Amendment No. 2, the Company reduced the exercise price of these warrants from the previous exercise price of $6.79 per share to $3.88 per share. See Note 8 "Warrants," for further description.

Upon an event of default, including a change of control, Hercules has the option to accelerate repayment of the Amended Loan Agreement, including payment of any applicable prepayment charges, which range from 1%-3% of the outstanding loan balance and accrued interest, as well as a final payment fee of $1.7 million. This option is considered a contingent put option liability, as the holder of the loan may exercise the option in the event of default, and is considered an embedded derivative, which must be valued and separately accounted for in the Company's financial statements. As the Amended Loan Agreement entered into on December 16, 2013 was considered an extinguishment, the contingent put option liability associated with the Loan Agreement, which had an estimated fair value of $32,000 at the time of the amendment, was written off as a part of the loss on extinguishment, and a new contingent put option liability was established. As of June 30, 2016 and December 31, 2015, the estimated fair value of the contingent put option liability was $165,000 and $266,000, respectively, which was determined by using a risk-neutral valuation model, wherein the fair value of the underlying debt facility is estimated both with and without the presence of the default provisions, holding all other assumptions constant. The resulting difference between the two estimated fair values is the estimated fair value of the default provisions, or the contingent put option. The fair value of the underlying debt facility is estimated by calculating the expected cash flows in consideration of an estimated probability of default and expected recovery rate in default, and discounting such cash flows back to the reporting date using a risk-free rate. The contingent put option liability was recorded as a debt discount to the loan and consequently a reduction to the carrying value of the loan. The contingent put option liability is revalued at the end of each reporting period and any change in the fair value is recognized in interest income and other income (expense), net in the condensed consolidated statements of comprehensive loss.

The Company performed an analysis of Amendment No. 2 to determine if it was a modification or extinguishment of the debt under the Amended Loan Agreement. The Company assumed immediate prepayment of both the pre-modification debt and post-modification debt, including the change in the fair value due to the Warrant Amendments, and concluded that Amendment No. 2 was a modification rather than an extinguishment of the debt.

The balance due under the Amended Loan Agreement was $21.3 million at June 30, 2016 and $20.9 million at December 31, 2015. Interest expense related to the Amended Loan Agreement was $0.7 million and $1.4 million for the three and six months ended June 30, 2016, respectively, and $0.8 million and $1.6 million for the three and six months June 30, 2015, respectively.

7. Liability Related to Sale of Future Royalties

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

milestones of $43.5 million, including the $15.0 million payment for the approval of the Zalviso MAA.

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

The Company has significant continuing involvement in the Royalty Monetization primarily due to an obligation to act as the intermediary for the supply of Zalviso to Grünenthal. Under the relevant accounting guidance, because of its significant continuing involvement, the Royalty Monetization has been accounted for as a liability that will be amortized using the interest method over the life of the arrangement. In order to determine the amortization of the liability, the Company is required to estimate the total amount of future royalty and milestone payments to be received by PDL and payments the Company is required to make to PDL, up to a capped amount of $195.0 million, over the life of the arrangement. The sum of the capped amount of $195.0 million, less the $61.2 million of net proceeds the Company received will be recorded as interest expense over the life of the liability. Consequently, the Company imputes interest on the unamortized portion of the liability and records interest expense. The Company’s estimate of the interest rate under the arrangement is based on the amount of royalty and milestone payments expected to be received by PDL over the life of the arrangement. The Company’s estimate of this total interest expense resulted in an effective annual interest rate of approximately 14%.

The Company will periodically assess the expected royalty and milestone payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than our initial estimates or the timing of such payments is materially different than our original estimates, the Company will prospectively adjust the amortization of the liability and the interest rate.

The following table shows the activity within the liability account during the six months ended June 30, 2016 (in thousands):

Liability related to sale of future royalties—beginning balance as of December 31, 2015	$63,612
Non-cash interest expense recognized	4,520
Payments from AcelRx to PDL	—
Total liability related to sale of future royalties as of June 30, 2016	68,132
Less: current portion	(357)
Liability related to sale of future royalties, less current portion	$67,775

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

8. Warrants

Series A Warrants

As of June 30, 2016, warrants to purchase 3,425 shares of common stock had not been exercised and were still outstanding. These warrants expire in March 2017.

Hercules Warrants

In connection with the Amended Loan Agreement, executed in December 2013, the Company issued warrants to Hercules which were exercisable for an aggregate of 176,730 shares of common stock with an exercise price of $6.79 per share, or the Warrants. In connection with Amendment No. 2 to the Amended Loan Agreement, the Company reduced the exercise price of the warrants already held by the Lenders from the previous exercise price of $6.79 per share to $3.88 per share, or the Warrant Amendments. Each Warrant may be exercised on a cashless basis. The Warrants are exercisable for a term beginning on the date of issuance and ending on the earlier to occur of five years from the date of issuance or the consummation of certain acquisitions of the Company as set forth in the Warrants. The number of shares for which the Warrants are exercisable and the associated exercise price are subject to certain proportional adjustments as set forth in the Warrants. The Company estimated the fair value of these Warrants as of the issuance date to be $1.1 million, which was used in the estimating the fair value of the amended debt instrument and was recorded as equity. The fair value of the Warrants was calculated using the Black-Scholes option-valuation

model, and was based on the original strike price of $6.79, the stock price at issuance of $9.67, the five-year contractual term of the warrants, a risk-free interest rate of 1.55%, expected volatility of 71% and 0% expected dividend yield. The Company estimated the fair value of the modification of the Warrants, or the Warrant Amendments, as of the issuance date to be $0.1 million, which was used in estimating the fair value of the amended debt instrument and was recorded as equity.

As of June 30, 2016, warrants to purchase 176,730 shares of common stock issued to Hercules had not been exercised and were still outstanding. These warrants expire in December 2018.

2012 Private Placement Warrants

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

Upon execution of the Purchase Agreement, the fair value of the PIPE warrants was estimated to be $5.8 million, which was recorded as a liability. As of June 30, 2016, the fair value of the PIPE warrants was estimated to be $0.4 million. The change in fair value for the three months ended June 30, 2016, which was recorded as other income, was $0.2 million, while the change in fair value for the three months ended June 30, 2015, which was recorded as other expense, was $0.1 million. The change in fair value for the six months ended June 30, 2016 and 2015, which was recorded as other income, was $0.5 million, and $2.1 million, respectively.

During the three months ended March 31, 2015, PIPE warrants to purchase 847,058 shares were net exercised for 527,101 shares of common stock. As of June 30, 2016, PIPE warrants to purchase 512,456 shares of common stock issued in connection with the Private Placement had not been exercised and were outstanding. These warrants expire in November 2017.

9. Stockholders' Equity

Common Stock

Public Offerings

On July 23, 2013, AcelRx completed an underwritten public offering of 4,370,000 shares of common stock, at a price of $11.65 per share to the public. The total gross proceeds of this offering were $50.9 million with net proceeds to AcelRx of $47.9 million after deducting underwriting discounts and commissions and other expenses payable by AcelRx.

Private Placement Offering

On June 1, 2012, or the Issuance Date, the Company issued an aggregate of 2,922,337 shares of common stock and warrants to purchase up to 2,630,103 shares of common stock, or the PIPE warrants, for aggregate gross proceeds of $10.0 million, or the Private Placement. Costs related to the offering were $0.9 million. The shares of common stock and PIPE warrants issued in the Private Placement were sold pursuant to a Securities Purchase Agreement, or Purchase Agreement, dated May 29, 2012, between the Company and certain purchasers, including certain entities affiliated with Mark Wan and Stephen J. Hoffman, members of the Company's Board of Directors. Pursuant to the Purchase Agreement, AcelRx sold shares of common stock and PIPE warrants to purchase common stock in immediately separable "Units," with each Unit consisting of (i) one share of common stock and (ii) a PIPE warrant to purchase 0.9 of a share of common stock. The per share exercise price of the PIPE warrants was $3.40. The offering

price per Unit was $3.40 for non-affiliated investors, and $3.5125 for affiliated investors, which equals the sum of (i) $3.40, the closing consolidated bid price of the Company's common stock on May 29, 2012, plus (ii) $0.1125 (which is equal to $0.125 per PIPE warrant share, multiplied by 0.9), for an aggregate amount of $10.0 million. The PIPE warrants issued in the Private Placement became exercisable six months after the Issuance Date, and expire on the five year anniversary of the initial exercisability date.

In connection with the Private Placement, the Company filed a registration statement with the U.S. Securities and Exchange Commission, or SEC, registering for resale the shares of common stock and shares of common stock issuable upon exercise of the warrants sold in the Private Placement. The registration statement was declared effective by the SEC in July 2012.

2016 ATM Agreement

On June 21, 2016, the Company entered into a Controlled Equity Offering^{SM} Sales Agreement, or the Sales Agreement, or 2016 ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent, pursuant to which the Company may offer and sell, from time to time through Cantor, shares of the Company's common stock, or the Common Stock having an aggregate offering price of up to $40.0 million, or the Shares. The Company is not obligated to make any sales of common stock under the Sales Agreement. The offering of Shares pursuant to the Sales Agreement will terminate upon the earlier of (a) the sale of all of the Shares subject to the Sales Agreement or (b) the termination of the Sales Agreement by Cantor or the Company, as permitted therein. The Company will pay Cantor a commission rate in the low single digits on the aggregate gross proceeds from each sale of Shares and have agreed to provide Cantor with customary indemnification and contribution rights. As of June 30, 2016, the Company has not sold any shares of common stock pursuant to the 2016 ATM Agreement.

Stock Plans

2006 Stock Plan

In August 2006, the Company established the 2006 Plan in which 342,000 shares of common stock were originally reserved for the issuance of incentive stock options, or ISOs, and nonstatutory stock options, or NSOs, to employees, directors or consultants of the Company. In February 2008, an additional 375,000 shares of common stock were reserved for issuance under the 2006 Plan and, in November 2009, an additional 1,376,059 shares of common stock were reserved for issuance under the 2006 Plan. Per the 2006 Plan, the exercise price of ISOs and NSOs granted to a stockholder who at the time of grant owns stock representing more than 10% of the voting power of all classes of the stock of the Company could not be less than 110% of the fair value per share of the underlying common stock on the date of grant. Effective upon the execution and delivery of the underwriting agreement for the Company's IPO, no additional stock options or other stock awards may be granted under the 2006 Plan.

18

2011 Equity Incentive Plan

In January 2011, the Board of Directors adopted, and the Company's stockholders approved, the 2011 Equity Incentive Plan, or 2011 Incentive Plan, as a successor to the 2006 Plan. The 2011 Incentive Plan became effective immediately upon the execution and delivery of the underwriting agreement for the IPO on February 10, 2011. As of February 10, 2011, no more awards may be granted under the 2006 Plan, although all outstanding stock options and other stock awards previously granted under the 2006 Plan will continue to remain subject to the terms of the 2006 Plan. The 51,693 shares reserved under the 2006 Plan that remained available for future grant at the time of the IPO were transferred to the share reserve of the 2011 Incentive Plan.

The initial aggregate number of shares of the Company's common stock that may be issued pursuant to stock awards under the 2011 Incentive Plan is 1,875,000 shares, which number was the sum of (i) 51,693 shares remaining available for future grant under the 2006 Plan at the time of the execution and delivery of the underwriting agreement for the Company's IPO, and (ii) an additional 1,823,307 new shares. The number of shares of common stock reserved for issuance under the 2011 Incentive Plan will automatically increase on January 1st each year, starting on January 1, 2012 and continuing through January 1, 2020, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or such lesser number of shares of common stock as determined by the Board of Directors. The term of the option is determined by the Board of Directors on the date of grant but shall not be longer than 10 years. Options under the 2011 Equity Incentive Plan generally vest over four years, and all options expire after 10 years. The Company issues new shares for settlement of vested restricted stock units and exercises of stock options. The Company does not have a policy of purchasing its shares relating to its share-based programs.

2011 Employee Stock Purchase Plan

Additionally, in January 2011, the Board of Directors adopted, and the Company's stockholders approved, the 2011 Employee Stock Purchase Plan, or the ESPP, which also became effective immediately upon the execution and delivery of the underwriting agreement for the IPO.

Initially, 250,000 shares of the Company's common stock were authorized for issuance under the ESPP pursuant to purchase rights granted to the Company's employees or to employees of any of its designated affiliates. The number of shares of the Company's common stock reserved for issuance will automatically increase on January 1st each year, starting January 1, 2012 and continuing through January 1, 2020, in an amount equal to the lower of (1) 2% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or (2) a number of shares of common stock as determined by the Board of Directors. If a purchase right granted under the ESPP terminates without having been exercised, the shares of the Company's common stock not purchased under such purchase right will be available for issuance under the ESPP.

10. Stock-Based Compensation

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Cost of goods sold	$77	$—	$148	$—
Research and development	586	629	1,186	1,331
General and administrative	482	482	996	1,318
Total	$1,145	$1,111	$2,330	$2,649

As of June 30, 2016, there were 2,677,349 shares available for grant, 6,405,808 options outstanding and no restricted stock units outstanding under the Company's 2011 Equity Incentive Plan and 1,157,690 shares available for grant under the ESPP.

11. 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.

During the three months ended June 30, 2016 and the six months ended June 30, 2016, the PIPE warrants were out-of-the-money, and therefore antidilutive. During the three months ended June 30, 2015, the PIPE warrants were also antidilutive due to an increasing average market share price during the period; however, during the six months ended June 30, 2015, the PIPE warrants had a dilutive impact to net loss per share due to a lower average share price during the period as compared to the closing share price at December 31, 2014. The decrease in share price created a lower Black-Scholes value and lower liability for the PIPE warrants, which resulted in other income during the three months ended June 30, 2016 and the six months ended June 30, 2016 and 2015, respectively. The calculation of diluted net loss per share requires that, to the extent the average market price of the underlying shares for the reporting period exceeds the exercise price of the PIPE warrants and the presumed exercise of such securities are dilutive to loss per share for the period, adjustments to net loss used in the calculation are required to remove the change in fair value of the PIPE warrants for the period. Likewise, adjustments to the denominator are required to reflect the related dilutive shares. As the average market prices during the three and six months ended June 30, 2016, respectively, did not exceed the exercise price of the PIPE warrants, no such adjustments were made.

The following table sets forth the computation of the Company's basic and diluted net loss per share of common stock during the three and six months ended June 30, 2016 and 2015 (in thousands, except for share and per share amounts):

	Three Months Ended June 30,		**Six Months Ended June 30,**	
	2016	**2015**	**2016**	**2015**
	(in thousands, except share and per share amounts)			
Numerator				
Net loss used to compute net loss per share:				
Basic	$(11,092)	$(8,896)	$(22,073)	$(18,922)
Adjustments for change in fair value of warrant liability	—	—	—	(2,117)
Diluted	$(11,092)	$(8,896)	$(22,073)	$(21,039)
Denominator				
Weighted average shares outstanding used to compute net loss per share:				
Basic	45,312,242	44,343,270	45,299,560	44,109,488
Dilutive effect of warrants	—	—	—	287,983
Diluted	45,312,242	44,343,270	45,299,560	44,397,471
Net loss per share — basic	$(0.24)	$(0.20)	$(0.49)	$(0.43)
Net loss per share — diluted	$(0.24)	$(0.20)	$(0.49)	$(0.47)

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,	
	2016	2015
ESPP and stock options to purchase common stock	6,537,180	5,907,881
Restricted stock units	—	—
Convertible debt into common stock	553,763	553,763
Common stock warrants	180,155	692,611

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 AcelRx's product candidates, ARX-04 (sufentanil sublingual tablet, 30 mcg) and Zalviso® (sufentanil sublingual tablet system), including the ARX-04 clinical trial results; ability to fund ARX-04 development from the contract with the Department of Defense; anticipated submission of the New Drug Application, or NDA, for ARX-04 to the U.S. Food and Drug Administration, or FDA; AcelRx's pathway forward towards gaining approval of Zalviso in the U.S.; the anticipated timing, design and results of the IAP312 clinical trial for Zalviso; anticipated resubmission of the Zalviso NDA to the FDA including the scope of the resubmission and the timing of the resubmission, and FDA review time; the status of the Collaboration and License Agreement with Grünenthal GmbH, a company organized under the laws of Germany, or Grünenthal, or any other future potential collaborations, including potential milestones and royalty payments under the Grünenthal agreement; and the therapeutic and commercial potential of AcelRx's product candidates, including potential market opportunities for ARX-04 and Zalviso. These forward-looking statements are based on AcelRx Pharmaceuticals' current expectations and inherently involve significant risks and uncertainties. AcelRx Pharmaceuticals' actual results and timing of events could differ materially from those anticipated in such forward-looking statements, and as a result of these risks and uncertainties, which include, without limitation, risks related to AcelRx Pharmaceuticals' ability to complete Phase 3 clinical development of ARX-04 and support ARX-04 development under the contract with the Department of Defense; AcelRx's ability to successfully execute the pathway towards a resubmission of the Zalviso NDA to the FDA, including the initiation and completion of the IAP312 clinical study for Zalviso; any delays or inability to obtain and maintain regulatory approval of its product candidates, including ARX-04 in the United States and Europe, and Zalviso in the United States; AcelRx's ability to receive any milestones or royalty payments under the Grünenthal agreement and the timing thereof; ability to manufacture and supply sufficient quantities of Zalviso to Grünenthal on a timely basis; the commercial success of Grünenthal's launch of Zalviso in the European Union, or EU; the uncertain clinical development process, including adverse events; the risk that planned clinical trials may not begin on time, have an effective clinical design, enroll a sufficient number of patients, or be initiated or completed on schedule, if at all; the success, cost and timing of all development activities and clinical trials, including the Phase 3 ARX-04 SAP302 and SAP303 trials, and the additional clinical trial for Zalviso, IAP312; the fact that the FDA may dispute or interpret differently clinical results obtained to date from the Phase 3 SAP301 study of ARX-04; the market potential for AcelRx's product candidates; the accuracy of AcelRx's estimates regarding expenses, capital requirements and the need for financing. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including the risks faced by us and described in Part II, Item 1A of this Quarterly Report on Form 10-Q and our other filings with the SEC. You should not place undue reliance on these forward-looking statements, which apply 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.

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, 2015.

About AcelRx Pharmaceuticals

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute pain. Our lead product candidates, ARX-04 and Zalviso®, utilize sublingual sufentanil, delivered via a non-invasive route of administration. We intend to commercialize our product candidates in the United States and license the development and commercialization rights to our product candidates for sale outside of the United States through strategic partnerships and collaborations. We may also consider the option to enter into strategic partnerships for our product candidates in the United States.

ARX-04 (sufentanil sublingual tablet, 30 mcg)

ARX-04 is an investigational product candidate consisting of a single tablet delivered via a disposable, pre-filled, single-dose applicator, or SDA. We are developing ARX-04 for the treatment of moderate-to-severe acute pain to be administered by a healthcare professional to a patient in medically supervised settings of acute pain. If approved, examples of potential patient populations and settings in which ARX-04 could be used include: emergency room patients; patients who are recovering from short-stay or ambulatory surgery and do not require more long-term patient-controlled analgesia; post-operative patients who are transitioning from the operating room to the recovery floor; patients being treated and transported by paramedics; and for battlefield casualties.

In October 2015, we initiated an open-label Phase 3 study, SAP302, of ARX-04 for the treatment of adult patients who present in the emergency room with moderate-to-severe acute pain associated with trauma or injury. The primary efficacy endpoint is the summed pain intensity difference, or SPID, over 1-hour, or SPID-1. Safety endpoints, such as adverse events and vital signs will also be assessed, as will the patients' and healthcare providers' satisfaction with the method of pain control. The initial phase of SAP302 treated 40 patients, who each received a single dose of ARX-04. Patients treated with one dose of ARX-04 experienced a mean decrease from baseline pain intensity difference, or PID-1, of 2.7 points on a 0 – 10 point numeric rating scale for pain intensity one hour after dosing. Based on published literature, a PID-1 of 1.3 points has been shown to be the minimal clinically significant difference in pain. The most frequently reported adverse events, nausea and somnolence, were each reported in two of the 40 patients. Based on discussions with the FDA, we initiated the extension phase of the SAP302 study of ARX-04 in March 2016. In the extension phase, an additional 36 patients have been treated, each of whom may have received multiple doses of ARX-04, given hourly as needed for pain, for up to four doses.

We held a pre-NDA meeting with the FDA in December 2015 to review plans for an NDA for ARX-04. Based on discussions with the FDA, we expanded the clinical program for ARX-04 by 176 additional patients to include individuals from specific populations and settings, in order to increase the ARX-04 safety database. Enrollment in the SAP302 open-label study in the emergency room was increased as described above, and a new study, known as SAP303, was initiated in March 2016 in post-operative patients with moderate-to-severe acute pain. SAP303 treated 140 patients 40 years of age and older who had moderate-to-severe acute pain following a surgical procedure with general anesthesia or spinal anesthesia (except those who received intrathecal opioids). SAP303 allowed for administration of ARX-04 for up to 12 hours.

Both the SAP302 and SAP303 trials have had their last patient visits and data are currently being analyzed. Top-line results for both studies are expected to be available in the third quarter of 2016, and pending successful results of these two open-label studies, we anticipate submitting the NDA for ARX-04 by the end of 2016.

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 ARX-04, referred to as the DoD Contract. Under the terms of the contract, the DoD will reimburse us for costs incurred for development, manufacturing, regulatory and clinical costs outlined in the contract in order to submit an NDA to the FDA, including reimbursement for certain personnel and overhead expenses. The period of performance under the DoD Contract began on May 11, 2015. The contract gives the DoD the option to extend the term of the contract 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 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 will be absorbed within the current contract value. If ARX-04 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 contract.

We have also held various meetings with Health Authorities in Europe to discuss the submission of a Marketing Authorization Application, or MAA, for ARX-04. Based on feedback from these discussions, we intend to submit for a label indication for ARX-04 in the EU for acute moderate-to-severe pain following surgery, or as a result of trauma. At the time of the anticipated submission of the MAA, we will have only completed one study in the emergency room for acute pain patients, in addition to three Phase 3 post-operative pain studies. We may need an additional controlled study in the emergency department with ARX-04 to obtain a label that includes both post-operative pain and trauma-related pain. In addition, we anticipate that we may need comparator studies in the EU to ensure premium reimbursement in certain countries. Assuming successful completion of the studies, we anticipate submitting the MAA for ARX-04 in the first half of 2017.

The Market Opportunity for ARX-04

United States

According to the Nationwide Emergency Department Sample, or NEDS, there were more than 104 million adult emergency room visits in the United States during 2011, of which we estimate more than 48 million were associated with moderate-to-severe acute pain. Based on the National Survey of Ambulatory Surgery, in 2006, an estimated 27 million adult patients underwent outpatient surgical procedures in the United States, of which we estimate more than 11 million patients experienced moderate-to-severe acute pain. According to the National Inpatient Sample, in 2013, more than 15 million adult patients in the United States underwent surgical procedures in an inpatient setting, of which we estimate more than 7 million resulted in moderate-to-severe acute pain. At peak sales, assuming a 2016 price of $20 per unit, taking into account standard price increases, we believe the market opportunity for ARX-04 to be approximately $1.3 billion in the United States.

Europe

According to recent EU5 (France, Germany, Italy, Spain, and the United Kingdom) national health statistics, 142 million patients are represented across the ARX-04 target segments annually. Each year, there are an estimated 110 million emergency attendances and 32 million surgical procedures performed each year. It is anticipated that there are 51 million patients in emergency medicine with moderate-to-severe acute pain and 16 million with moderate-to-severe acute pain following surgery each year. Using the published priced benchmarks of Penthrox (methoxyflurane) and branded fentanyl products, £17.89 (UK) and €8.04 (Germany), respectively, we believe that ARX-04 could achieve a €15 price per unit. A micro-costing literature review is in process to determine the total cost per patient necessary to administer IV opioids in the emergency department as further support for premium pricing. Based on this information, we believe peak year sales in emergency medicine and post-operative pain across Europe are expected to be approximately €700 million, assuming ARX-04 achieves a €15 price point; however, there can be no assurance that ARX-04 will be able to achieve a €15 price per unit. Oligo-analgesia or under-treatment of pain is a recognized issue throughout Europe, and supports growth in treatment of acute pain with the introduction of ARX-04.

Zalviso (sufentanil sublingual tablet system)

Our product candidate, Zalviso, is intended for the management of moderate-to-severe acute pain in hospitalized adult patients. Zalviso consists of sufentanil sublingual tablets, 15 mcg, delivered by the Zalviso System, a needle-free, handheld, patient-administered, pain management system, or together, Zalviso.

Zalviso is a pre-programmed, non-invasive, system to allow hospital patients with moderate-to-severe acute pain to self-dose with sufentanil sublingual tablets, 15 mcg, to manage their pain. Zalviso is designed to help address certain problems associated with post-operative intravenous patient-controlled analgesia. Zalviso allows patients to self-administer sufentanil sublingual tablets via a pre-programmed, secure system designed to eliminate the risk of programming errors.

On December 16, 2013, AcelRx and Grünenthal GmbH, a company organized under the laws of Germany, or 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, the Company’s novel sublingual patient-controlled analgesia, or PCA, system, or the Product, in the countries of the European Union, 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. The Company retains rights with respect to the Product in countries outside the Territory, including the United States, Asia and Latin America. 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 entered into amendments to the License Agreement, or the License Amendment, and together with the License Agreement, the Amended License Agreement, and the MSA, or the MSA Amendment, and together with the MSA, the Amended MSA, between the Company and Grünenthal, each effective as of July 17, 2015, and together, the Amended Agreements. For additional information on the Amended Agreements,

see Note 5 “Collaboration Agreement” in the accompanying notes to the condensed consolidated financial statements.

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

In April 2016, Grünenthal completed the first commercial sale of Zalviso. Grünenthal continues to sell Zalviso initially in a limited number of hospitals in Germany under a pilot program, whereby the hospital will use Zalviso in a small number of post-operative patients. The pilot program, which is expected to last approximately two months at each institution, is being made available to additional hospitals in Germany over the next several months. Pending success with the pilot program, Grünenthal expects to make the product widely available in Germany. With similar methodology, Grünenthal has also initiated the sale of Zalviso in France, the United Kingdom, Italy and Belgium, and intends to launch Zalviso in the Netherlands, Ireland and Portugal by the end of 2016.

On September 18, 2015, we sold a portion of the expected royalty stream and commercial milestones from the sales of Zalviso in the EU by Grünenthal to PDL, or the Royalty Monetization. AcelRx received gross proceeds of $65.0 million in 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), subject to the capped amount of $195.0 million. For additional information on the Royalty Monetization with PDL, see Note 7 “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, which the FDA accepted for filing in December 2013. On July 25, 2014, the FDA issued a Complete Response Letter, or CRL, for the Zalviso NDA. The CRL contains 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 optical system errors, changes to address inadvertent dosing, among other items, and submission of additional data to support the shelf life of the product. Although there were no requests for additional clinical studies in the CRL, 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 modifications to the Zalviso device.

Our IAP312 study is designed to evaluate the effectiveness of changes made to enhance performance of the Zalviso device and takes into account comments from the FDA on the protocol. The IAP312 study is expected to include approximately 315 post-operative patients and collect information requested by the Division of Anesthesia, Analgesia, and Addiction Products, or the Division, of the FDA to supplement the three positive Phase 3 trials already completed. While the Company estimates that it may be able to begin the IAP312 study in September 2016, it does not intend to initiate the study until final supplies have been received and tested and clinical sites are ready. These activities may or may not occur in time to initiate the trial in September 2016. Timing of the completion of the IAP312 study will be dependent on the actual initiation date and other timing including, but not limited to, study enrollment.

The Market Opportunity for Zalviso

According to the 2014 Decision Resources Acute Pain Report, or 2014 DR Report, the acute pain market (represented by treatments for post-operative pain, acute musculoskeletal pain and cancer breakthrough pain) in the United States, Europe and Japan realized 2013 revenues of $12.7 billion, and is expected to reach approximately $13.3 billion by 2023. Opioid analgesic use remains a standard in the management of acute pain, representing 44% of the 2013 market, and is projected to grow to 46% of the 2023 market. Post-operative acute pain treatment in the United States is projected to grow significantly in the 2013 to 2023 period, from management of 8.9 million procedures in 2013 to 10.3 million procedures in 2023, a 1.5% Compound Annual Growth Rate.

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 activities and pre-commercialization activities. As a result, we expect to continue to incur negative cash flows. Although Zalviso has been approved for sale in the European Union, 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 pursue development of our product

candidates, including regulatory review and potential commercial development, subject to FDA approval, of our product candidates, we expect the business aspects of our company to become more complex. In the future, we plan to add personnel and incur additional costs related to the maturation of our business and the potential commercialization of ARX-04 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 DoD.

Our revenues since inception have consisted primarily of revenues from our Amended License Agreement with Grünenthal and our research contracts with the DoD. As mentioned above, in May 2015, the DoD agreed to provide us up to $17.0 million to support the development of ARX-04. Under the terms of the contract, the DoD will reimburse us for costs incurred for development, manufacturing, regulatory and clinical costs outlined in the contract in order to submit an NDA to the FDA, including reimbursement for certain personnel and overhead expenses.

There can be no assurance that we will enter into other collaborative agreements or receive research-related contract awards in the future. We expect revenues to continue to fluctuate from period-to-period. There can be no assurance that our relationship with our existing commercial partner, Grünenthal, will continue beyond the initial term, or that we will be able to meet the milestones specified in the Amended License Agreement, or that the funding provided by the DoD Contract will be sufficient for an NDA submission for ARX-04, or that we will obtain marketing approval for any of our product candidates outside of Zalviso in the EU and EEA 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, 2016 was $11.1 million and $22.1 million, respectively, compared to net losses of $8.9 million and $18.9 million for the three and six months ended June 30, 2015, respectively. As of June 30, 2016, we had an accumulated deficit of $225.3 million. As of June 30, 2016, we had cash, cash equivalents and investments totaling $98.8 million compared to $113.5 million as of December 31, 2015.

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, 2015. There have been no significant changes in our critical accounting policies and estimates during the three and six months ended June 30, 2016 from those previously disclosed in our Annual Report on Form 10-K.

Recently Issued Accounting Standards

In March 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2016-09, *Compensation - Stock Compensation (Topic 718)*, which is part of the FASB's Simplification Initiative. The updated guidance simplifies the accounting for share-based payment transactions. The amended guidance is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016, with early adoption permitted. We are currently evaluating the impact of the adoption of this standard on our consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which establishes a new lease accounting model for lessees. The updated guidance requires an entity to recognize assets and liabilities arising from a lease for both financing and operating leases, along with additional qualitative and quantitative disclosures. The amended guidance is effective for fiscal years, and interim periods within those years, beginning after December 15, 2018, with early adoption permitted. We are currently evaluating the impact of the adoption of this standard on our consolidated financial statements.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers*, to provide guidance on revenue recognition. ASU No. 2014-09 requires a company to 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 doing so, companies will need to use more judgment and make more estimates than under today's guidance. These may include 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 separate performance obligation. In August 2015, the FASB issued ASU No. 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which provided for the adoption of the new standard for fiscal years beginning after December 15, 2017. Accordingly, ASU No. 2014-09 is effective for the Company in the first quarter of 2018. Early adoption up to the first quarter of 2017 is permitted. Upon adoption, ASU No. 2014-09 can be applied retrospectively to all periods presented or only to the most current period presented with the cumulative effect of changes reflected in the opening balance of retained earnings in the most current period presented. The FASB has also issued the following standards which clarify ASU No. 2014-09 and have the same effective date as the original standard:

ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net)*;

ASU No. 2016-10, *Identifying Performance Obligations and Licensing (Topic 606)*;

and ASU No. 2016-11, *Revenue Recognition (Topic 605) and Derivatives and Hedging (Topic 815): Rescission of SEC Guidance Because of Accounting Standards Updates 2014-09 and 2014-16 Pursuant to Staff Announcements at the March 3, 2016 EITF Meeting;* and

ASU No. 2016-12, *Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients*.

We are currently evaluating the method of adoption and the impact of adopting ASU No. 2014-09 on our consolidated financial statements.

Results of Operations

Three and Six Months Ended June 30, 2016 and 2015

Revenue

In September 2015, the European Commission, or EC, granted marketing approval for Zalviso in the European Union to our commercial partner, Grünenthal. In April 2016, Grünenthal completed the first commercial sale of Zalviso. Grünenthal continues to sell Zalviso initially in a limited number of hospitals in Germany under a pilot program, whereby the hospital will use Zalviso in a small number of post-operative patients. The pilot program, which is expected to last approximately two months at each institution, is being made available to additional hospitals in Germany over the next several months. Pending success with the pilot program, Grünenthal expects to make the product widely available in Germany. With similar methodology, Grünenthal has also initiated the sale of Zalviso in France, the United Kingdom, Italy and Belgium, and intends to launch Zalviso in the Netherlands, Ireland and Portugal by the end of 2016. We anticipate that royalty revenues and non-cash royalty revenues from the commercial sale of Zalviso in 2016 will be minimal. Revenue during the three months ended June 30, 2016, was $4.5 million, including $1.3 million in collaboration agreement revenue recognized under our Amended Agreements with Grünenthal, plus $3.2 million in revenue for services performed under the DoD Contract.

Revenue for the three and six months ended June 30, 2015, was $1.9 million and $2.1 million, respectively, the majority of which was generated from our contract for ARX-04 with the DoD.

Collaboration Agreement Revenue

Below is a summary of revenue recognized under the Amended Agreements during the three and six months ended June 30, 2016 and 2015 (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	**2015**	**2016**	**2015**
Product sales	$1,302	$—	$2,702	$—

Joint steering committee, research and development services and demonstration devices	12	486	405	667
Collaboration agreement revenue	$1,314	$486	$3,107	$667

In support of the launch of Zalviso in Europe by our licensee, Grünenthal, we recognized $1.3 million and $2.7 million in product sales in the three and six months ended June 30, 2016, respectively, consisting of Zalviso devices, drug product and accessories. Delivery of the Zalviso cartridges ordered by Grünenthal is behind schedule at Patheon. The inability to deliver cartridges to the schedule ordered by Grünenthal may have a negative impact on their future sales including the timing of their launch in certain countries. We are working with Patheon to resolve these issues; however, there can be no assurance that the issues will be resolved in a timely fashion, or that we will be able to meet Grünenthal's needs in such a way as to not impact their future sales.

The first commercial sale of Zalviso occurred in April 2016; however, we did not recognize any royalty revenue or non-cash royalty revenue in the second quarter of 2016 from the sales in the EU by Grünenthal. Beginning in the third quarter of 2016, we will receive quarterly royalty reports from Grünenthal for the prior quarter. As the royalty amounts are not currently reasonably estimable without the royalty reports, we will recognize royalty revenue and non-cash royalty revenue on a quarterly basis, one quarter in arrears beginning in the third quarter of 2016.

As of June 30, 2016, we had current and non-current portions of the deferred revenue balance under the Amended Agreements of $1.0 million and $3.1 million, respectively. Our long-term deferred revenue balance increased during the six months ended June 30, 2016 from $0.6 million to $3.1 million. 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 peak at approximately $4.0 million, as we complete invoicing Grünenthal in connection with the Amended Agreements in 2016, and 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, 2016, AcelRx recognized revenue of $3.2 million and $4.4 million, respectively, for services performed under the DoD contract for ARX-04.

Cost of goods sold

Total cost of goods sold was $3.0 million and $6.6 million for the three and six months ended June 30, 2016, respectively. As mentioned above, the EC approved Zalviso in late September 2015. 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. We may not be able to 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. The indirect costs to manufacture include internal personnel and related costs for purchasing, supply chain, quality assurance, depreciation and related expenses. Prior to the initiation of commercial production in October 2015, these costs were included in research and development expenses as period costs.

Research and Development Expenses

Conducting research and development is central to our business model. The majority of our operating expenses to date have been for research and development activities related to Zalviso; however, in 2016 we anticipate that research and development expenses for ARX-04 will be greater than those for Zalviso. 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.

Product candidates in late stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of late stage clinical trials. We will incur substantial future research and development expenditures as we seek to continue development of ARX-04 and Zalviso, including the expenses associated with the anticipated submission of the NDA for ARX-04, in addition to preparing for and conducting IAP312, the additional clinical trial for Zalviso.

We track external development expenses on a program-by-program basis. Our development resources are shared among all of our programs. Compensation and benefits, facilities, depreciation, stock-based compensation, and development support services are not allocated specifically to projects and are considered research and development overhead. Below is a summary of our research and development expenses during the three and six months ended June 30, 2016 and 2015:

	Three Months Ended June 30,				**Six Months Ended June 30,**			
Drug Indication/Description	**2016**	**2015**	**2016 vs. 2015 Increase/ (Decrease)**		**2016**	**2015**	**2016 vs. 2015 Increase/ (Decrease)**	
	(In thousands, except percentages)							
ARX-04	$3,365	$2,996	12	%	$4,520	$4,157	9	%
Zalviso	777	1,082	(28	)%	1,687	2,752	(39	)%
Overhead	2,138	3,232	(34	)%	4,244	6,707	(37	)%
Total research and development expenses	$6,280	$7,310	(14	)%	$10,451	$13,616	(23	)%

Due to the inherently unpredictable nature of product development, development timelines and the probability of success, development costs can differ materially from expectations. While we are currently focused on advancing ARX-04 and the continued development of Zalviso, our future research and development expenses will depend on the clinical success of each product candidate as well as ongoing assessments of the commercial potential of our product candidates. 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.

Research and development expenses during the three months ended June 30, 2016, as compared to the three months ended June 30, 2015, decreased by $1.0 million primarily due to a $1.1 million reduction in overhead costs, predominantly as a result of the cost reduction plan implemented in March 2015 and the allocation of certain personnel and related expenses to cost of goods sold. In addition, Zalviso-related expenses decreased by $0.3 million due to the slowing of development activities as we clarified the development path forward with the FDA, while ARX-04-related spending increased incrementally by $0.4 million due to increased spending on the SAP302 and SAP303 studies, partially offset by the completion of the SAP301 study in 2015.

The $3.2 million decrease in research and development expenses during the six months ended June 30, 2016, as compared to the six months ended June 30, 2015, was primarily attributable to a $2.5 million reduction in overhead costs, predominantly as a result of the cost reduction plan implemented in March 2015 and the allocation of certain personnel and related expenses to cost of goods sold. In addition, during the first half of 2016, Zalviso-related expenses decreased by $1.1 million while ARX-04-related spending increased by a $0.4 million, as compared to the first half of 2015.

General and Administrative Expenses

General and administrative expenses consisted primarily of salaries, benefits and stock-based compensation for personnel in administration, finance, pre-commercialization and business development activities. Other significant expenses included legal expenses related to litigation and patent protection of our intellectual property, allocated facility costs and professional fees for general legal, audit and consulting services. We expect general and administrative expenses for the remainder of 2016 to remain comparable to 2015 expenses, as we focus our efforts on further development and seeking marketing approval for ARX-04, and the continued development of Zalviso.

Total general and administrative expenses for the three and six months ended June 30, 2016 and 2015 were as follows:

	Three Months Ended June 30,				Six Months Ended June 30,			
	2016	2015	Change	%	2016	2015	Change	%

	(In thousands, except percentages)								
General and administrative expenses	$ 3,597	$ 2,735	$ 862	32	%	$ 7,374	$ 7,256	$ 118	2 %

The $0.9 million increase in general and administrative expenses during the three months ended June 30, 2016, as compared to the three months ended June 30, 2015, was primarily due to $0.5 million in ARX-04-related market research activities, and an incremental increase of $0.4 million in other general and administrative expenses.

The $0.1 million increase in general and administrative expenses during the six months ended June 30, 2016, as compared to the six months ended June 30, 2015, was primarily due to $0.9 million in ARX-04-related market research activities, partially offset by decreases of $0.5 million in headcount-related expenses, including a $0.3 million decrease in stock-based compensation expense, and net decreases in other general and administrative expenses of $0.3 million.

Restructuring Costs

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 CRL, a clinical trial would be needed to assess the risk of inadvertent dispensing and overall risk of dispensing failures. On March 19, 2015, our Board of Directors, in connection with our efforts to reduce operating costs, conserve capital, focus the Company's financial and development resources on working with the FDA to seek marketing approval for Zalviso, and continuing development of ARX-04, implemented a cost reduction plan. The cost reduction plan reduced our workforce by 19 employees, approximately 36% of total headcount, in the first quarter of 2015.

	Three Months Ended June 30,				Six Months Ended June 30,			
	2016	2015	Change	%	2016	2015	Change	%
	(In thousands, except percentages)							
Restructuring costs	$—	$ 2	$ (2)	-%	$—	$756	$ (756)	-%

Restructuring costs in the three and six months ended June 30, 2015 consisted of employee termination benefit costs of $0.8 million which has been fully disbursed.

Other (Expense) Income

Total other (expense) income for the three and six months ended June 30, 2016 and 2015 was as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2016	2015	2016	2015
Interest expense	$(687)	$(777)	$(1,367)	$(1,583)
Interest income and other income (expense), net	241	4	660	2,184
Non-cash interest expense on liability related to sale of future royalties	(2,324)	—	(4,520)	—
Total other (expense) income	$(2,770)	$(773)	$(5,227)	$601

Interest expense consisted primarily of interest accrued or paid on our debt obligation agreements and amortization of debt discounts. Interest expense for all periods pertains to interest on our Loan and Security Agreement with Hercules. In December 2013, we entered into the Amended Loan Agreement with Hercules, which amends and restates the Loan

and Security Agreement. The overall debt facility was increased to $40.0 million, and the maturity was extended to October 1, 2017. On June 16, 2014, we borrowed the second tranche of $10.0 million. We did not have access to the third tranche, of up to $15.0 million, as we did not receive FDA approval of Zalviso by August 1, 2015. As a result of the lower principal balance in the three and six months ended June 30, 2016 as compared to the three and six months ended June 30, 2015, the amount of interest expense incurred decreased. As of June 30, 2016, the balance due to Hercules was $21.3 million.

On September 18, 2015, concurrently with the closing of the Royalty Monetization, the Company entered into a Consent and Amendment No. 2, or Amendment No. 2, to the Amended Loan Agreement. Amendment No. 2 provided for an interest only period from October 1, 2015 through March 31, 2016, with further extension to September 30, 2016 upon satisfaction of certain conditions, which have since been satisfied.

Interest income and other income (expense), net, during the three and six months ended June 30, 2016 and 2015, consisted primarily of the change in the fair value of our warrants, or PIPE warrants, issued in connection with our private placement of our common stock, which was completed in June 2012.

The decrease in interest income and other income (expense), net, during the three and six months ended June 30, 2016 as compared to the three and six months ended June 30, 2015, was primarily attributable to fewer PIPE warrants outstanding at June 30, 2016, as compared to June 30, 2015. During the three months ended June 30, 2016, our stock price decreased resulting in other income for the revaluation of the PIPE warrants, while during the three months ended June 30, 2015, our stock price increased, resulting in other expense during the second quarter of 2015. In the six months ended June 30, 2016 as compared to the six months ended June 30, 2015, there was a smaller decrease in our stock price, which is a primary driver in the Black-Scholes valuation model used to estimate the fair value of the PIPE warrants.

The increase in non-cash interest expense on liability related to the Royalty Monetization during the three and six months ended June 30, 2016 as compared to the three and six months ended June 30, 2015, is attributable to the royalty sale transaction 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 an additional $4.9 million in non-cash interest expense related to the Royalty Monetization in the year ended December 31, 2016, for a total of $9.4 million in 2016.

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 2016 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 sales of Zalviso by Grünenthal, and our contracts with the DoD.

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, or the Shares. For a detailed description, see Note 9 "Stockholders' Equity."

As of June 30, 2016, we had cash, cash equivalents and investments totaling $98.8 million compared to $113.5 million as of December 31, 2015. The decrease was primarily due to cash required to fund our continuing operations, as we continue our research and development activities. We anticipate that our existing capital resources will permit us to meet our capital and operational requirements through at least the first half of 2017. While we believe we have sufficient capital to meet our operational requirements through at least the first half of 2017, our expectations may change depending on a number of factors. For example, based on their review of the protocol we have submitted for the requested clinical trial for Zalviso, the FDA may in the future, require a scope or design change that is beyond what our current and estimated future capital resources can support. We believe that together with the support from the DoD Contract, we have sufficient resources to complete the Phase 3 development program for ARX-04 through submission of the NDA to the FDA. However, our existing capital resources will not be sufficient to fund our operations until such time as we may be able to generate sufficient revenues to sustain our operations.

On September 18, 2015, we sold a portion of the expected royalty stream and commercial milestone payments from the sales of Zalviso in the EU by Grünenthal to PDL. As mentioned above, we received net proceeds of $61.2 million in 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), subject to the capped amount of $195.0 million. We are entitled to receive all remaining amounts under the Amended License Agreement which include 25% of the European royalties, 20% of the first four commercial milestones, 100% of the remaining commercial milestones and all development milestones of $43.5 million, including the $15.0 million payment for the EC approval of the MAA for Zalviso, which we received in the fourth quarter of 2015. The total liability related to sale of future royalties to PDL as of June 30, 2016 was $68.1 million.

On December 16, 2013, AcelRx and Grünenthal entered into 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, or the Product, in the Territory for human use in the Field. We retain rights with respect to the Product in countries outside the Territory, including the United States, Asia and Latin America. On July 22, 2015, the Company entered into amendments to the License Agreement, or the License Amendment, and together with the License Agreement, the Amended License Agreement, and the MSA, or the MSA Amendment, and together with the MSA, the Amended MSA, between the Company and Grünenthal, each effective as of July 17, 2015, and together, the Amended Agreements.

Under the terms of the Amended Agreements, 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 December 16, 2013, AcelRx entered into an Amended and Restated Loan and Security Agreement with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., together, the Lenders, or the Amended Loan Agreement, under which AcelRx may borrow up to $40.0 million in three tranches. The loans are represented by secured convertible term promissory notes, collectively, the Notes. The Amended Loan Agreement amends and restates the Loan and Security Agreement between AcelRx and the Lenders dated as of June 29, 2011. We borrowed the first tranche of $15.0 million upon closing of the transaction on December 16, 2013, and the second tranche of $10.0 million on June 16, 2014. We used approximately $8.6 million of the proceeds from the first tranche to repay our obligations under the Loan and Security Agreement with the Lenders. We recorded the new debt at an estimated fair value of $24.9 million as of December 31, 2014.

On September 24, 2014, we entered into Amendment No. 1 to the Amended Loan Agreement with Hercules. Amendment No. 1 extended the time period under which we could draw down the third tranche, of up to $15.0 million, from March 15, 2015 to August 1, 2015, subject to AcelRx obtaining approval for Zalviso from the FDA. We did not receive FDA approval of Zalviso by August 1, 2015 and as such, did not have access to the third tranche.

On September 18, 2015, concurrently with the closing of the Royalty Monetization, we entered into a Consent and Amendment No. 2, or Amendment No. 2, to the Amended Loan Agreement with the Lenders. Amendment No. 2 includes an interest only period from October 1, 2015 through March 31, 2016, with further extension to September 30, 2016 upon satisfaction of certain conditions, which have since been satisfied. Loans under the Amended Loan Agreement mature on October 31, 2017. As of June 30, 2016, the balance due to Hercules was $21.3 million.

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 March 31,	
	2016	2015
Net cash used in operating activities	$(14,467)	$(21,438)
Net cash provided by (used in) investing activities	4,224	(977)
Net cash provided by (used in) financing activities	121	(1,781)

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, ARX-04 and 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 revaluation of our PIPE warrant liability and the contingent put option liability.

Cash used in operating activities of $14.5 million during the six months ended June 30, 2016, reflected a net loss of $22.1 million, partially offset by aggregate non-cash charges of $7.7 million, and a net change of $0.1 million in our net operating assets and liabilities. Non-cash charges included $4.5 million in non-cash interest expense on the liability related to the royalty monetization and $2.3 million for stock-based compensation, and $1.0 million in depreciation expense, partially offset by $0.6 million for the change in fair value of our PIPE warrant liability and contingent put liability. The net change in our operating assets and liabilities included an increase in accounts payable of $1.4 million, primarily due to the timing of payments, partially offset by a decrease in accrued liabilities of $1.0 million, largely due to the payment of compensation-related expenses.

Cash used in operating activities of $21.4 million during the six months ended June 30, 2015, reflected a net loss of $18.9 million, partially offset by aggregate non-cash charges of $1.3 million, and a net change of $3.8 million in our net operating assets and liabilities. Non-cash charges included $2.6 million for stock-based compensation, and $1.0 million for depreciation and amortization of our fixed assets, partially offset by $2.1 million for the change in fair value of our PIPE warrant liability and contingent put liability. The net change in our operating assets and liabilities included a $1.4 million increase in prepaid expenses and other assets, primarily due to the timing of payments, and a decrease in accrued liabilities of $0.9 million, largely due to payment of compensation-related expenses.

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, 2016, cash provided by investing activities of $4.2 million was primarily a result of $5.5 million in proceeds from maturity of investments, offset by $1.0 million for purchases of investments and $0.3 million for purchases of property and equipment.

During the six months ended June 30, 2015, cash used in investing activities of $1.0 million was primarily as a result of $5.5 million for purchases of investments and $0.9 million for purchases of property and equipment, partially offset by $5.4 million in proceeds from maturity of investments.

Cash Flows from Financing Activities

During the six months ended June 30, 2016, cash provided by financing activities of $0.1 million as a result of stock purchases made under our 2011 Employee Stock Purchase Plan.

During the six months ended June 30, 2015, cash used in financing activities of $1.8 million was primarily due to payments on our Loan and Security Agreement with Hercules.

Operating Capital and Capital Expenditure Requirements

We expect our rate of cash usage to increase in the future, in particular to support our product development activities, including continued development of ARX-04, Zalviso and the potential commercialization of our product candidates, if approved outside of the Grünenthal Territory. Our future cash needs anticipate the receipt of reimbursement for qualified expenses under the DoD Contract. We anticipate that our existing capital resources will permit us to meet our capital and operational requirements through at least the first half of 2017. Our current operating plan includes the continued development of ARX-04, specifically the filing of the NDA by the end of 2016. These assumptions may change as a result of many factors. For example, based on feedback from the FDA, we expanded the planned clinical program for ARX-04 by 176 additional patients to include individuals from specific populations and settings. As a result, the completion of the Phase 3 clinical program for ARX-04 was extended and our clinical trial expenses have increased. In addition, although the FDA has provided feedback on both the ARX-04 clinical program and reviewed the protocol for IAP312, the additional clinical trial for Zalviso, pending the results of these clinical trials, the FDA may in the future require us to complete additional work to submit the NDA for ARX-04 and/or to resubmit the NDA for Zalviso. We have delayed the initiation of the IAP312, originally planned for the first quarter of 2016. If we are unable to initiate the IAP312 study before the end of 2016, we may not have sufficient resources to complete the study and resubmit the Zalviso NDA. We will continue to evaluate the work necessary to gain approval of ARX-04 and Zalviso in the U.S. 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 forward looking factors, including but not limited to the following:

- the outcome, timing and cost of regulatory approvals for ARX-04 and Zalviso;

- the initiation, progress, timing and completion of clinical trials for our product candidates, including ARX-04 and Zalviso;
- expenditures related to the activities required in support of the anticipated NDA submission for ARX-04;
- expenditures related to the activities required in support of our resubmission of the Zalviso NDA, including an additional clinical trial for Zalviso, as requested by the FDA;
- expenditures related to our commercialization preparation of ARX-04;
- future manufacturing, selling and marketing costs related to ARX-04 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 ARX-04 and Zalviso, if approved outside of the Grünenthal Territory;
- manufacture and market our product candidates;
- conduct preclinical and clinical testing of our product candidates, and;
- conduct research and development programs.

Our existing capital resources may 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.

Contractual Obligations

During the six months ended June 30, 2016, there were no material changes to our contractual obligations, other than the fulfillment of existing obligations in the ordinary course of business, described under Management's Discussion and Analysis of Financial Condition and Results of Operations contained in Part II, Item 7 of our Annual Report on Form 10-K for our fiscal year ended December 31, 2015.

Off-Balance Sheet Arrangements

Through June 30, 2016, 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, 2016, consisted primarily of money market funds and U.S. government agency securities. We do not have any auction rate securities on our 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, 2016, 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, as appropriate, 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.

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, 2015.

Risks Related to Clinical Development and Regulatory Approval

We depend substantially on the success of ARX-04, which may not receive regulatory approval in the United States or in Europe.*

Since our inception in 2005, we have focused primarily on development of our product candidate, Zalviso®; however, given the delay in the potential approval of Zalviso in the United States, we believe the importance of ARX-04 (sufentanil sublingual tablet, 30 mcg) to our future success has increased. ARX-04 is a non-invasive investigational product candidate consisting of a single tablet delivered sublingually via a disposable, pre-filled, single-dose applicator, or SDA.

As part of our development program, we met with the United States Food and Drug Administration, or FDA, in December 2015 to review plans for a New Drug Application, or NDA, for ARX-04. We have also held various meetings with Health Authorities in Europe to discuss the submission of a Marketing Authorization Application, or MAA, for ARX-04. Based on feedback from the FDA, we expanded the clinical program for ARX-04 by 176 additional patients to include individuals from specific populations and settings, in order to increase the ARX-04 safety database. As a result, the completion of the Phase 3 clinical program for ARX-04 has been extended and our clinical trial expenses have increased. Based on feedback from discussions with the Health Authorities in Europe, we intend to submit for a label indication for acute moderate-to-severe pain following surgery, or as a result of trauma. At the time of submission of the MAA we will have only completed one open-label study in the emergency room for acute pain patients, in addition to three Phase 3 post-operative pain studies. We may need an additional controlled study in the emergency department setting with ARX-04 to obtain a label that includes both post-operative pain and trauma-related pain. In addition, we anticipate we may need comparator studies in the European Union, or EU, to ensure premium reimbursement in certain countries. With these modifications, and assuming successful completion of the studies, we anticipate submitting the NDA for ARX-04 by the end of 2016 and the MAA in the first half of 2017. However, while we have announced positive top-line results from SAP301, SAP302 and SAP303 may not achieve positive results. Even if we believe the results from SAP301, SAP302 and SAP303 support an NDA and MAA submission for ARX-04, the FDA and European Medicines Agency, or EMA, may not agree, or may interpret the study results differently, which would delay the timing of our commercialization of ARX-04 and adversely affect our business operations. If ARX-04 is not approved for sale in the United States or Europe, it could have a significant impact on our ability to generate cash flows from product sales or to enter into a collaboration agreement. If we are

not able to receive approval to commercialize ARX-04 in the United States, we would be required to find alternative sources of capital to continue operations. If ARX-04 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 under our current operating plan.

Any disagreement with the FDA or EMA as to the results from SAP301, SAP302, and SAP303, and therefore any additional requirements imposed by the FDA or EMA prior to our ability to submit an NDA or MAA, as well as any delay in approval by the FDA or EMA of the ARX-04 NDA or MAA, if and when it is submitted, may negatively impact our stock price and harm our business operations. If and when the ARX-04 NDA is submitted, the FDA may hold an Advisory Committee meeting to obtain committee input on the safety and efficacy of ARX-04. 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 ARX-04. Any delay in obtaining, or inability to obtain, regulatory approval would prevent us from commercializing ARX-04 in the United States or Europe, generating revenues and potentially achieving profitability. If any of these events occur, we may be forced to delay or abandon our development efforts for ARX-04, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We depend substantially on the success of Zalviso, which may not receive regulatory approval in the United States.*

While ARX-04's importance has increased for our future success, Zalviso remains an important product candidate for us. Zalviso consists of sufentanil sublingual tablets, 15 mcg, delivered by the Zalviso System, a needle-free, handheld, patient-administered, pain management system, or together, Zalviso. The success of our business depends, in part, upon our ability to develop, receive regulatory approval in the United States for, and commercialize Zalviso for the management of moderate-to-severe acute pain in adult patients in the hospital setting.

To date, our Phase 3 program for Zalviso has 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. On July 25, 2014, the FDA issued a Complete Response Letter, or CRL, for our NDA for Zalviso. The CRL contains 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 optical system 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 CRL, a clinical trial is needed to assess the risk of inadvertent dispensing and overall risk of dispensing failures. Based on the results of the Type C meeting with FDA, which took place in September 2015, we submitted a protocol to the FDA for a clinical study in post-operative patients designed to evaluate the effectiveness of changes made to enhance Zalviso device performance. We completed the protocol review with the FDA and have postponed the start of IAP312, originally planned for the first quarter of 2016. If we are unable to initiate the IAP312 study before the end of 2016, we may not have sufficient resources to complete the study and resubmit the Zalviso NDA. While we estimate that we may be able to begin the IAP312 study in September 2016, we do not intend to initiate the IAP312 study until final supplies have been received and tested and clinical sites are ready. These activities may or may not occur in time to initiate the trial in September 2016. Timing of the completion of the IAP312 study will be dependent on the actual initiation date and other timing including, but not limited to, study enrollment.

There is no guarantee that the additional work we perform 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 trial might not meet its objectives or the FDA could 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 submission 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. 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 the EU. 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 first Phase 3 clinical trial for ARX-04, or SAP301, the interim analysis from SAP302, each of our three Zalviso Phase 3 clinical trials completed to date, in addition to all of our Phase 2 clinical trials for ARX-04 and Zalviso. However, even if we believe that the data 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. Any such determination by the FDA would delay the timing of our commercialization plan for ARX-04 and Zalviso, or further development of our other product candidates, and adversely affect our business operations. For example, although we had achieved the primary endpoints in each of our three Phase 3 clinical trials for Zalviso which were included in our NDA filed in 2013, in March 2015, we received correspondence from the FDA stating that in addition to the bench testing and two Human Factors studies we had performed in response to the issues identified in the CRL, a clinical trial is needed to assess the risk of inadvertent dispensing and overall risk of dispensing failures.

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 ARX-04, three Phase 3 clinical trials for Zalviso, and several Phase 2 clinical trials both for ARX-04 and 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 June 2014, we completed a pharmacokinetic study in support of the ARX-04 development program. In this study of healthy volunteers, it was shown that two sublingual administrations of a Zalviso sufentanil sublingual tablet, 15 mcg, dosed 20 minutes apart

were equivalent to one sublingual administration of a sufentanil sublingual tablet, 30 mcg. Based on the pharmacokinetic equivalency of two Zalviso tablets to one ARX-04 tablet, the FDA has agreed to accept 323 Zalviso patients into the ARX-04 safety database; however, the FDA also required that the ARX-04 safety database comprise 350 patients dosed with at least one dose of ARX-04. Based on this feedback from the FDA, we expanded the clinical program for ARX-04 by 176 additional patients to include individuals from specific populations and settings, in order to increase the ARX-04 safety database. In addition, a new study, known as SAP303, was initiated in March 2016 in post-operative patients with moderate-to-severe acute pain. As a result, the completion of the Phase 3 clinical program for ARX-04 was extended and our clinical trial expenses increased. Finally, we have postponed the start of IAP312, originally planned for the first quarter of 2016. We are planning to initiate IAP312 once final supplies have been received and tested and clinical sites are ready, in order to support our NDA resubmission, which will delay our development timeline for Zalviso even further. While we estimate that we may be able to begin the IAP312 study in September 2016, we do not intend to initiate the IAP312 study until final supplies have been received and tested and clinical sites are ready. These activities may or may not occur in time to initiate the trial in September 2016. Timing of the completion of the IAP312 study will be dependent on the actual initiation date and other timing including, but not limited to, study enrollment. If we are unable to initiate the IAP312 study before the end of 2016, we may not have sufficient resources to complete the study and resubmit the Zalviso NDA.

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 not yet responded to the Zalviso Complete Response Letter nor resubmitted the Zalviso NDA. Activities that we undertake to address issues raised in the 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 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 CRL. In response to discussions with the FDA, we have agreed to complete an additional open-label study with Zalviso in post-operative patients, known as IAP312. We have completed the protocol review for IAP312 and we are planning to initiate this trial once final supplies have been received and tested and clinical sites are ready, in order to support our NDA resubmission. These activities may or may not occur in time to initiate the trial in September 2016. Timing of the completion of the IAP312 study will be dependent on the actual initiation date and other timing including, but not limited to, study enrollment. If we are

unable to initiate the IAP312 study before the end of 2016, we may not have sufficient resources to complete the study and resubmit the Zalviso NDA. There is no guarantee that the trial results, even if successful, 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 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 CRL, and designed the protocol for the additional Zalviso clinical trial to further address these issues, there is no guarantee that 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, even if we believe that the test results from our bench testing and Human Factors studies are positive, and we are able to conduct and achieve positive results from the IAP312 study, 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 which 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. In our Phase 3 active comparator clinical trial (IAP309), 7.9% of Zalviso-treated patients dropped out of the trial prematurely due to an AE, and we observed one serious adverse event, or SAE, that was assessed as possibly or probably related to Zalviso. In our Phase 3, double-blind, placebo-controlled, abdominal surgery trial (IAP310), adverse events reported in the trial were generally mild or moderate in nature and similar in both placebo and treatment groups. In addition, one patient in the trial, who was in the sufentanil sublingual tablet group, experienced an SAE, which was determined to be unrelated to the trial drug. In our Phase 3, double-blind, placebo-controlled, orthopedic surgery trial (IAP311), treatment-emergent adverse events were generally mild-to-moderate in nature and similar for the majority of adverse events between sufentanil sublingual tablet- and placebo-treated patients. Two patients (one each in the sufentanil sublingual tablet group and placebo group) experienced a serious adverse event considered possibly or probably related to the trial drug by the investigator.

In our Phase 2 ARX-04 trial, two serious adverse events, or SAEs, both in the 20 mcg dose group, occurred one week after the study (surgical infections) and were deemed unrelated to study drug. All but two adverse events reported in the study were mild-to-moderate in nature with 58 patients (58%) reporting a total of 135 adverse events. The most frequently reported adverse events for all patients were nausea (30%), vomiting (17%), dizziness (14%) and somnolence (11%). Two patients discontinued treatment, one unrelated to study drug (anxiety/chest pain) and the other probably related to study drug (somnolence/respiratory depression); however, both patients recovered without medical intervention.

Phase 2 clinical trials we have conducted with Zalviso did generate some AEs, but no SAEs, related to the trial drug.

Further, if any of our future products, including Zalviso or ARX-04 cause serious or unexpected side effects after receiving marketing approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified Risk Evaluation and Mitigation Strategy, 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 ARX-04 and Zalviso because they are drug/device combination products.*

ARX-04 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

ARX-04 and Zalviso. As a result, we have in the past, and may in the future, experience delays in the development and commercialization of Zalviso due to regulatory uncertainties in the product development and approval process, in particular as it relates to a drug/device combination product approval under an NDA, and we may experience similar delays and regulatory uncertainties when, and if, we submit the NDA for ARX-04.

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 ARX-04 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 ARX-04. Based on feedback from the FDA, we expanded the clinical program for ARX-04 by 176 additional patients to include individuals from specific populations and settings, in order to increase the ARX-04 safety database. As a result, the completion of the Phase 3 clinical program for ARX-04 was extended and our clinical trial expenses increased. We have also held various meetings with Health Authorities in Europe to discuss the submission of an MAA for ARX-04. Based on feedback from discussions with the Health Authorities in Europe, we intend to submit for a label indication for acute moderate-to-severe pain following surgery, or as a result of trauma. At the time of submission of the MAA we will have only completed one open-label study in the emergency room for acute pain patients, in addition to three Phase 3 post-operative pain studies. We may need an additional controlled study in the emergency department setting with ARX-04 to obtain a label that includes both post-operative pain and trauma-related pain. In addition, we anticipate we may need comparator studies in the European Union to ensure premium reimbursement in certain countries. These additional studies will delay commercialization and any associated future revenues from ARX-04 in these countries.

In September 2015, the European Commission, or EC, approved Grünenthal's, MAA for Zalviso for post-operative pain; however, we cannot predict the commercial success of Zalviso. We received a CRL for Zalviso 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 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 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 enhance the Zalviso device. We have completed the protocol review and while we estimate that we may be able to begin the IAP312 study in September 2016, we do not intend to initiate the IAP312 study until final supplies have been received and tested and clinical supplies are ready, in order to support our NDA resubmission. These activities may or may not occur in time to initiate the trial in September 2016. Timing of the completion of the IAP312 study will be dependent on the actual initiation date and other timing including, but not limited to, study enrollment. Although the FDA has provided feedback on the ARX-04 clinical program and reviewed the protocol for IAP312, and we have incorporated feedback from Health Authorities in Europe concerning the submission of the MAA for ARX-04, pending the results of our clinical trials, the FDA or EMA may in the future require us to complete additional clinical work prior to submitting the NDA for ARX-04, resubmitting the NDA for Zalviso or submitting the MAA for ARX-04. 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.

The FDA and other foreign regulatory agencies, such as 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 commercial sales of Zalviso in the EU.

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 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 intend to submit the MAA for ARX-04 for a label indication for

acute moderate-to-severe pain following surgery, or as a result of trauma. We may need an additional controlled study in the emergency department setting with ARX-04 to obtain a label that includes both post-operative pain and trauma-related pain. 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 Federal Food, Drug and Cosmetic Act, or 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. 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 ARX-04, 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 ARX-04, Zalviso and our other product candidates, if approved, will likely include restrictions on use due to the opioid nature of sufentanil.

ARX-04, Zalviso and our other product candidates, if approved 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 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 approval in Europe, we may never obtain approval for, or commercialize, 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 European Commission 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.

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 in all territories. In addition, we lack the personnel, expertise and capabilities to gain regulatory approval of our product candidates on a global basis without a commercial partner. With Zalviso's approval for sale in Europe, we are substantially dependent on Grünenthal to successfully commercialize it. While Grünenthal does have products approved in international markets, we do not have any product candidates approved for sales in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. Grünenthal's experience in international markets does not guarantee regulatory approval or compliance with regulatory requirements in international markets. If we 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.

ARX-04, 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. 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 United States launch may be delayed, the costs to commercialize Zalviso may increase substantially and the potential commercial market could be restricted. ARX-04, if approved, will also require REMS programs that may significantly increase our costs to commercialize these product candidates. Furthermore, risks of sufentanil that are not adequately addressed through proposed REMS for our future product candidates, if approved, may also prevent or delay their approval for commercialization.

Existing and future legislation may increase the difficulty and cost for us to commercialize ARX-04, 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 the EU, or our other product candidates, including ARX-04, restrict or regulate post-approval activities for ARX-04 and Zalviso, and affect our ability to profitably sell any products for which we obtain marketing approval.

In the 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 Health Care Reform Law (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 Health Care Reform Law that may impact our business include:

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

The Health Care Reform Law 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.

In addition, other legislative changes have been proposed and adopted in the United States since the Health Care Reform Law 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 2024 unless Congressional action is taken. The American Tax Payer Relief Act further reduced Medicare payments to several providers, including hospitals.

41

Moreover, the Drug Supply Chain Security Act of 2013 imposes new 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 payors 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 2016 and may continue to incur losses for the foreseeable future.*

Since our inception in 2005, we have focused primarily on development of our product candidate, Zalviso. While Zalviso remains an important asset to the Company, ARX-04 has become a focus. In September 2015, we announced that a pivotal Phase 3 study of ARX-04, SAP301, met all primary and secondary endpoints and in October 2015, we initiated SAP302, a Phase 3 study of ARX-04 in the emergency room. Based on feedback from the FDA, we expanded the clinical program for ARX-04 by 176 additional patients to include individuals from specific populations and settings, in order to increase the ARX-04 safety database. Accordingly, we initiated the extension phase of the SAP302 study of ARX-04 in March 2016. In addition, a new study, known as SAP303, was also initiated in March 2016 in post-operative patients with moderate-to-severe acute pain. As a result, the completion of the Phase 3 clinical program for ARX-04 was extended and our clinical trial expenses increased. In addition, the FDA has requested an additional clinical trial for Zalviso, IAP312, prior to resubmission of the Zalviso NDA which will increase our development costs for the Zalviso program. We have incurred significant net losses in each year since our inception in July 2005, and as of June 30, 2016, we had an accumulated deficit of $225.3 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 continue our research and development activities for our product candidates, including addressing issues raised by the FDA related to regulatory review of Zalviso, as well as to support manufacturing and supply of Zalviso in Europe for Grünenthal. To date, none of our product candidates have been commercialized, and if ARX-04, 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 are substantially dependent on our commercial partner, Grünenthal, to successfully commercialize Zalviso in Europe.*

On December 16, 2013, we 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, with Grünenthal. On July 22, 2015, we entered into amendments to the License Agreement, or the License Amendment, and the MSA, or the MSA Amendment, with Grünenthal, each effective as of July 17, 2015, and together with the License Agreement, and the MSA, the Amended Agreements. The Amended Agreements grant rights to commercialize Zalviso in the European Union, or EU, Switzerland, Liechtenstein, Iceland, Norway and Australia, or the Territory, for human use in pain treatment within, or dispensed by, hospitals, hospices, nursing homes and other medically-supervised settings. In September 2015, the European Commission 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. Grünenthal continues to sell Zalviso initially in a limited number of hospitals in Germany under a pilot program, whereby the hospital will use Zalviso in a small number of post-operative patients. The pilot program, which is expected to last approximately two months at each institution, is being made available to additional hospitals in Germany over the next several months. With similar methodology, Grünenthal has also initiated the sale of Zalviso in France, the United Kingdom, Italy and Belgium, and intends to launch Zalviso in the Netherlands, Ireland and Portugal by the end of 2016. Pending success with the pilot program, Grünenthal expects to make the product widely available in Germany; however, there is no guarantee that Grünenthal will achieve commercial success in its Zalviso launches in Germany, France and the United Kingdom or anywhere in the European Union. 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. Even if Grünenthal is successful in the commercialization of Zalviso in the EU, 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 ARX-04 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.

42

We have never generated 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 ARX-04, Zalviso or our other product candidates in the United States. While we have a collaboration with Grünenthal for commercialization of Zalviso in Europe and Australia, we may not achieve all of the development milestones associated with the collaboration, and 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 portion 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 ARX-04 and/or Zalviso in the United States and/or in Europe;
- launching and commercializing ARX-04 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; and
- completing the clinical development of, obtaining regulatory approval for, and launching and commercializing ARX-04 and Zalviso, which may require additional funding or corporate partnership resources.

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 ARX-04 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 have a limited operating history that may make it difficult to predict our future performance or evaluate our business and prospects.

We were incorporated in 2005. Since inception, our operations have been primarily limited to organizing and staffing our company, 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 ARX-04 and Zalviso in the United States. We have not yet obtained regulatory approval of any of our product candidates in the United States. 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, including conducting ARX-04 Phase 3 clinical trials, development activities associated with ARX-04, including regulatory costs in support of the potential NDA submission, and the remaining development activities associated with Zalviso, to respond to issues raised by the FDA. While we believe we have sufficient capital resources to continue planned operations through at least the first half of 2017, we may need additional capital to continue development and commercialization of ARX-04, and Zalviso will need additional capital to potentially pursue commercialization of any of our product candidates.

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. Any further development activities can be time consuming and costly. We submitted a protocol to the FDA for a clinical study in post-operative patients designed to evaluate the effectiveness of changes made to enhance Zalviso device performance. We received comments from the FDA on the protocol for the study, known as IAP312, and while we estimate that we may be able to begin the IAP312 study in September 2016, we do not intend to initiate the IAP312 study until supply and production testing is complete and clinical sites are ready. These activities may or may not occur in time to initiate the trial in September 2016. Timing of the completion of the IAP312 study will be dependent on the actual initiation date and other timing including, but not limited to, study enrollment. Clinical trials, regulatory reviews, and a potential launch of a commercial product are expensive activities. In addition, commercialization costs for ARX-04 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. To raise capital, we may seek to sell additional equity or debt securities, including under our Controlled Equity Offering^{SM} Sales Agreement, or the Sales Agreement, with Cantor Fitzgerald & Co., or 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.

We may sell additional equity or debt securities to fund our operations, which may result in dilution to our stockholders and 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. The incurrence of 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.

In December 2013, we entered into an amended loan and security agreement, or the Amended Loan Agreement, with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., collectively referred to as Hercules, under which we could have borrowed up to $40.0 million in three tranches, represented by secured convertible promissory notes. We drew the first tranche of $15.0 million at the closing of the new credit facility and the second tranche of $10.0 million on June 16, 2014. We did not have access to the third tranche of up to $15.0 million, as it was conditioned upon FDA approval to market Zalviso in the United States by August 1, 2015, which we did not obtain. We began making principal payments in April 2015. On September 18, 2015, we amended the Amended Loan Agreement with Hercules to extend an interest only period from October 1, 2015 through March 31, 2016, with further extension to September 30, 2016 upon satisfaction of certain conditions, which have since been satisfied. The scheduled maturity date is October 31, 2017.

We granted Hercules 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, we recently sold a portion of the royalties and first four commercial sales milestone payments we are entitled to receive under the Amended Agreements with Grünenthal to PDL, which will decrease future cash flows available to us to repay the Hercules 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.

We may not receive all of the funding from the Department of Defense for the advancement of ARX-04.*

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 ARX-04, referred to as the DoD Contract. Under the terms of the contract, the DoD will reimburse us for costs incurred for development, manufacturing, regulatory and clinical costs outlined in the contract in order to submit an NDA to the FDA, including reimbursement for certain personnel and overhead expenses. The period of performance under the contract began on May 11, 2015. The contract gives the DoD the option to extend the term of the 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 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 will be absorbed within the current contract value. Funding under this 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 contract. The lack of ARX-04 supportive funding, may adversely affect our ability to continue to advance the development of ARX-04.

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;
- 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.

45

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.

As mentioned above, we have entered into the Amended Agreements with Grünenthal under which we are obligated to manufacture and supply Zalviso for use in the EU 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.

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.

Currently, we use two established suppliers of sufentanil citrate for our tablets. We only have one supplier qualified for our manufacture of Zalviso. For each product candidate, only one of the two suppliers will be qualified as a vendor with the FDA. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. The alternative vendor would need to be qualified through an NDA supplement 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.

Early development and clinical trial manufacturing of Zalviso was conducted at Patheon in Toronto, Canada. Because the DEA requires that sufentanil be manufactured in the United States if our product candidates are marketed in the United States, we transferred our manufacturing capability in the third quarter of 2011 from Patheon in Toronto, Canada to Patheon's production facility in Cincinnati, Ohio, where we have built out a suite within their existing buildings 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 Patheon, Cincinnati. While we have produced a limited 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.

Delivery of the Zalviso cartridges ordered by Grünenthal is behind schedule at Patheon. The inability to deliver cartridges to the schedule ordered by Grünenthal may have a negative impact on their future sales including the timing of their launch in certain countries. AcelRx is working with Patheon to resolve these issues; however, there can be no assurance that the issues will be resolved in a timely fashion, or that we will be able to meet Grünenthal's needs in such a way as to not impact their future sales.

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. 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. In addition, in January 2013, we entered into an Amended and Restated Capital Expenditure and Equipment Agreement, or the Amended Capital Agreement, with Patheon, relating to the manufacture of sufentanil sublingual tablets. Under the terms of the Amended Capital Agreement, we have made and may make certain future modifications to Patheon's Cincinnati facility.

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 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 or other foreign regulatory agency approval for ARX-04 and Zalviso outside the EU. 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. As mentioned above, the CRL from the FDA contains a request for additional information on the Zalviso System to ensure proper use of the device. 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 CRL, a clinical trial is needed to assess the risk of inadvertent dispensing and overall risk of dispensing failures. 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 any resubmitted NDA. In early September 2015, we met with the FDA to discuss their request for an additional clinical trial and our planned response to the CRL. In the Type C meeting minutes, the FDA provided some additional details about the type of clinical data they would like us to provide, as a complement to the other data we already have provided, to assess the overall performance 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 enhance Zalviso device performance. We have completed the protocol review with the FDA for the study, known as IAP312, and while we estimate that we may be able to begin the IAP312 study in September 2016, we do not intend to initiate the IAP312 study until final supplies have been received and tested and clinical sites are ready. These activities may or may not occur in time to initiate the trial in September 2016. Furthermore, 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 completed the process validation for the device components and have manufactured launch supplies 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 ARX-04 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 would adversely impact our ability to supply our customers with ARX-04, if approved, and Zalviso, in the EU, and 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 ARX-04, we currently package the finished goods under a manual process at the Patheon facility. The capacity and cost to package the ARX-04 units under this manual process is not sufficient to support successful future sales of ARX-04. We will need to purchase, install and validate new equipment and processes to automate the ARX-04 manufacturing process. The purchase and subsequent installation of this equipment to automate the ARX-04 packaging process will require substantial resources and take several years. There is no assurance that we will be able to successfully purchase, install or validate the equipment necessary to automate the ARX-04 packaging process. 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 ARX-04, as well as our ongoing 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 ARX-04, Zalviso, and our 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 ARX-04 and Zalviso, or our other product candidates. As a result, our financial results and the commercial prospects for ARX-04, 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 ARX-04, and Zalviso outside the EU, if approved, as well as Zalviso in the EU, 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 ARX-04, and Zalviso outside the EU, if approved, as well as Zalviso in the EU, will depend on a number of factors, including:

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and health care payors;
- the use of ARX-04 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 the perception of sufentanil as a potentially unsafe drug due to its high potency;

- limitations or warnings contained in the FDA- or EMA-approved label for ARX-04 or Zalviso;
- restrictions or limitations placed on ARX-04 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 or reimbursement.

If our approved products do not achieve an adequate level of acceptance by physicians, nurses, patients and pharmacy and therapeutics committees, or 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 ARX-04 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, including ARX-04 and Zalviso; 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.

As a result of delays in the resubmission of the Zalviso NDA and obtaining FDA approval, our Board of Directors implemented a cost reduction plan that reduced our workforce by 19 employees, approximately 36% of total headcount, in the first quarter of 2015. As a result, the build out of our commercial capabilities, including internal sales, marketing, supply chain and medical affairs departments is currently on hold. 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. 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 our other product candidates, if approved, 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, including the United States, 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;

49

- 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 in the EU, and any future approvals of our product candidates outside of the United States, will result in a variety of risks associated with international operations and could materially adversely affect our business.

Our existing collaboration with Grünenthal for marketing Zalviso in European countries and Australia requires us to supply product to support the EU commercialization of Zalviso. In addition, if any of our currently unapproved product candidates are approved for commercialization outside the United States, we intend to enter into agreements with third parties to market our product candidates in those countries, which may also require us to supply products to the third party. 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 ARX-04, Zalviso, and our other product candidates 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.

50

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. More specifically, competitors for ARX-04 in the emergency department are likely to include generic injectable intravenous opioids such as morphine, hydromorphone and fentanyl. In this environment, ARX-04 may also compete with other branded non-invasive products or product candidates, such as Egalet Corporation's SPRIX, Hospira, Inc.'s DYLOJECT (Hospira, Inc. acquired by Pfizer, Inc. in September 2015), Acura Pharmaceuticals, Inc.'s OXAYDO, Depomed, Inc.'s NUCYNTA, Bristol-Myers Squibb Company's COMBUNOX, Purdue Pharma, L.P.'s OXYFAST, Endo Pharmaceuticals, Inc.'s OPANA, Medical Developments International Limited's PENTHROX (methoxyflurane) inhaler, CL-108, a bi-layered tablet, in development by Charleston Laboratories Inc., in collaboration with Daiichi Sankyo, or generic oral opioids which have moderate-to-severe acute pain labeling. In the short-stay or ambulatory surgery segment, ARX-04 will likely compete with these products in addition to generic injectable local anesthetics such as bupivacaine, or branded formulations thereof, including Pacira Pharmaceuticals, Inc.'s EXPAREL. Within the military environment, and in certain civilian settings, ARX-04 competitors may also include intramuscular morphine injections which are marketed by a variety of generic manufacturers.

We believe that Zalviso would compete with a number of opioid-based and non-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. (acquired by Pfizer, Inc.), 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.

Also available on the market is the Avancen Medication on Demand, or MOD, Oral PCA Device developed by Avancen MOD Corporation. Oral opioids and other agents can be used in this system. In addition, oral and parenteral opioids administered by the nurse are used to manage moderate-to-severe acute pain in the hospital, available both as branded and generic products. These oral opioids, as well as IV PCA opioids, are often used as part of a multi-modal analgesia approach, which might include, in addition to the opioid, NSAIDs, acetaminophen, gabapentanoids and other pain management modalities, as well as local anesthetic blocks to provide temporary blockage of the pain signal, either as a wound infiltration agent or as a nerve block. These local anesthetic agents such as bupivacaine can also utilize controlled-release formulations such as Pacira Pharmaceuticals, Inc.'s EXPAREL. In addition, Halyard Health, Inc. has developed a medical device, the ON-Q* Pain Relief System, which is a non-narcotic elastomeric pump that automatically and continuously delivers a regulated flow of local anesthetic to a patient's surgical site or in close proximity to nerves, providing targeted pain relief for up to five days.

Additional potential competitors for Zalviso include the fentanyl iontophoretic transdermal system, IONSYS, originally developed by ALZA Corporation and Ortho-McNeil Pharmaceutical, Inc., both Johnson & Johnson subsidiaries, and most recently by The Medicines Company. In April 2015, IONSYS was approved for marketing in the U.S. by the FDA, and in November 2015, it was approved for marketing in the EU by the EMA, providing a

potential first-to-market advantage for IONSYS. Cara Therapeutics, Inc. is developing a kappa opioid agonist, CR845, as an IV agent for the management of post-operative moderate-to-severe pain. Trevena, Inc. is developing TRV130, an intravenous G protein biased ligand that targets the mu opioid receptor for the treatment of moderate-to-severe acute pain where intravenous therapy is preferred, with a clinical development focus in acute post-operative pain. Trevena, Inc. initiated Phase 3 development of TRV130 in the first quarter of 2016. Recro Pharma, Inc. is developing an intranasal form of dexmedetomidine as a potential agent for the management of post-operative pain, for which it announced positive efficacy results in its Phase II clinical trial. Finally, Innocoll AG is developing XARACOLL a controlled-release resorbable implant containing bupivacaine, and Durect Corporation has been developing POSIDUR, a controlled-release bupivacaine product candidate utilizing Durect Corporation's Saber technology.

It is possible that any of these competitors could develop or improve technologies or products that would render our product candidates obsolete or non-competitive, which could adversely affect our revenue potential. Key competitive factors affecting the commercial success of our product candidates are likely to be efficacy, safety profile, reliability, convenience of dosing, price and reimbursement.

Many of our potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drug candidates, obtaining FDA and other regulatory approval of products and the commercialization of those products. Accordingly, our competitors may be more successful than we are in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' drugs or drug delivery systems may be more effective, have fewer adverse effects, be less expensive to develop and manufacture, or be more effectively marketed and sold than any product candidate we may commercialize. This may render our product candidates obsolete or non-competitive before we can recover our losses. We anticipate that we will face intense and increasing competition as new drugs enter the market and additional technologies become available. These entities may also establish collaborative or licensing relationships with our competitors, which may adversely affect our competitive position. Finally, the development of different methods for the treatment of moderate-to-severe acute pain (ARX-04 and Zalviso) could render our products non-competitive or obsolete. These and other risks may materially adversely affect our ability to attain or sustain profitable operations.

Formulary approval may not be available, or could be subject to certain restrictions for ARX-04 or Zalviso in the United States and our other product candidates, which could make it difficult for us to sell our products profitably.

Obtaining formulary approval can be an expensive and time-consuming process. We cannot be certain if and when we will obtain formulary approval to allow us to sell our products into our target markets. Failure to obtain timely formulary approval will limit our commercial success. If we are successful in obtaining formulary approval, we may need to complete evaluation programs whereby ARX-04 or Zalviso is used on a limited basis for certain patient types. Hospitals may seek to obtain ARX-04 or Zalviso devices at little or no cost during this evaluation period. Revenue generated from these hospitals during the evaluation period would be minimal. The evaluation period may last several months and there can be no assurance that use during the evaluation period will lead to formulary approval of ARX-04 or Zalviso. Further, even successful formulary approval may be subject to certain restrictions based on patient type or hospital protocol. Failure to obtain timely formulary approval for ARX-04 and/or Zalviso would materially adversely affect our ability to attain or sustain profitable operations.

Coverage and adequate reimbursement may not be available for ARX-04 or Zalviso, if approved in the United States, or ARX-04 in the EU, if approved, or Zalviso in the EU, which could make it difficult for us, or our partners, to sell our products profitably.

Our ability to commercialize ARX-04 or Zalviso, if approved in the United States, or ARX-04 in the EU, if approved, or Zalviso in the EU successfully will depend, in part, on the extent to which coverage and adequate reimbursement will be available from government payor programs at the federal and state levels, authorities, including Medicare and Medicaid, private health insurers, managed care plans and other third-party payors.

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

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell our products profitably. These legislative and/or regulatory changes may negatively impact the reimbursement for our products, following approval. The availability of numerous generic pain medications may also substantially reduce the likelihood of reimbursement for ARX-04, Zalviso or any of our other product candidates, if approved in the United

States, and ARX-04 or any of our other product candidates, if approved outside the United States, as well as Zalviso in the EU and elsewhere. The application of user fees to generic drug products may expedite the approval of additional pain medication generic drugs. We expect to experience pricing pressures in connection with the sale of Zalviso in the EU, and ARX-04, Zalviso outside of the EU and any of our other product candidates, if approved, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. If we fail to successfully secure and maintain reimbursement coverage for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and our business will be harmed.

Furthermore, market acceptance and sales of our product candidates, if approved, will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third party payors, such as private health insurers, hospitals and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that reimbursement will be available for ARX-04, Zalviso, or any of our other product candidates, if approved in the United States or ARX-04, or any of our other product candidates, if approved in the EU, or Zalviso in the EU. Also, reimbursement amounts may reduce the demand for, or the price of, our products. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize ARX-04, Zalviso, or any of product candidates, if approved in the United States, or ARX-04, or any of our other product candidates, if approved in the EU, or Zalviso in the EU.

Additionally, the regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues able to be generated from the sale of the product in that country. For example, although in September 2015 the European Commission approved the MAA for Grünenthal to market Zalviso in the 28 European Union member states as well as for the European Economic Area countries, Norway, Iceland and Liechtenstein, separate pricing and reimbursement approvals may impact their ability to successfully commercialize Zalviso. Adverse pricing limitations may hinder our ability to recoup our investment in ARX-04, Zalviso and/or our other drug candidates, even if/when those drug candidates obtain marketing approval.

Furthermore, even after initial price and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple factors, including reference pricing systems and publication of discounts by third party payors or authorities in other countries. In the EU, prices can be reduced further by parallel distribution and parallel trade, i.e. arbitrage between low-priced and high-priced countries. If any of these events occur, Zalviso, and any future approved product candidates would be negatively affected.

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

If we are found to have improperly promoted off-label uses of our product candidates, including ARX-04 and/or Zalviso, if approved in the United States, we may become subject to significant liability. Such enforcement has become more common in the industry. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription drug products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for our product candidates for our proposed indications, physicians may nevertheless use our products for their patients in a manner that is inconsistent with the approved label, if the physicians personally believe in their professional medical judgment it could be used in such manner. However, if the FDA determines that our promotional materials or training constitutes promotion of an off-label use, it could request that we modify our training or promotional materials or subject us to regulatory or enforcement actions, including the issuance of an untitled letter, a warning letter, injunction, seizure, civil fine or criminal penalties. It is also possible that other federal, state or foreign enforcement authorities might take action if they consider our promotional or training materials to constitute promotion of an off-label use, which could result in significant civil, criminal and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government-funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, increased losses and diminished profits and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. The FDA or other regulatory authorities could also request that we enter into a consent decree or a corporate integrity agreement, or seek a permanent injunction against us under which specified promotional conduct is monitored, changed or curtailed. If we cannot successfully manage the promotion of our product candidates, including ARX-04 and Zalviso in the United States, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Guidelines and recommendations published by government agencies, as well as non-governmental organizations, can reduce the use of our product candidates, including ARX-04 and Zalviso, if/when approved.*

Government agencies and non-governmental organizations promulgate regulations and guidelines applicable to certain drug classes that may include the product candidates that we are developing. Recommendations of government agencies or non-governmental organizations may relate to such matters as maximum quantities dispensed to patients, dosage, route of administration and use of concomitant therapies. Government agencies and non-governmental organizations have offered commentary and guidelines on the use of opioid-containing products. We are uncertain how these activities and guidelines may impact our product candidates and our ability to gain marketing approval.

Regulations or guidelines suggesting the reduced use of certain drug classes that may include the product candidates that we are developing or the use of competitive or alternative products as the standard of care to be followed by patients and healthcare providers could result in decreased use of our product candidates, or negatively impact our ability to gain market acceptance and market share.

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

Many end-users of pharmaceutical products have relationships with group purchasing organizations, or GPOs, whereby such GPOs provide such end-users access to a broad range of pharmaceutical products from multiple suppliers at competitive prices and, in certain cases, exercise considerable influence over the drug purchasing decisions of such end-users. Hospitals and other end-users contract with the GPO of their choice for their purchasing needs. We expect to derive revenue from end-user customers that are members of GPOs, if ARX-04 or Zalviso is approved by the FDA. Establishing and maintaining strong relationships with these GPOs will require us to be a reliable supplier, remain price competitive and comply with FDA regulations. The GPOs with whom we have relationships may have relationships with manufacturers that sell competing products, and such GPOs may earn higher margins from these products or combinations of competing products or may prefer products other than ours for other reasons. If we are unable to establish or maintain our GPO relationships, sales of our products and revenue could be negatively impacted.

We intend to rely on a limited number of pharmaceutical wholesalers to distribute our product candidates, including ARX-04 and Zalviso in the United States, if approved.

We intend to rely primarily upon pharmaceutical wholesalers in connection with the distribution of our product candidates, including ARX-04 and Zalviso in the United States, if approved. If we are unable to establish or maintain our business relationships with these pharmaceutical wholesalers on commercially acceptable terms, it could have a material adverse effect on our sales and may prevent us from achieving profitability.

Risks Related to Our Business Operations and Industry

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

Our sufentanil-based products are subject to extensive regulation by the DEA, due to their status as scheduled drugs. Sufentanil is a Schedule II opioid, considered to present a high risk of abuse. The manufacture, shipment, storage, sale and use of controlled substances are subject to a high degree of regulation, including security, record-keeping and reporting obligations enforced by the DEA and also by comparable state agencies. This high degree of regulation can result in significant costs in order to comply with the required regulations, which may have an adverse effect on the development and commercialization of our product candidates.

The DEA limits the availability and production of all Schedule II substances, including sufentanil, through a quota system. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. Our contract manufacturers have applied annually for a quota on our behalf. We will need significantly greater amounts of sufentanil to implement our commercialization plans for Zalviso in the EU, and any of our products that may be approved by the FDA in the future, including ARX-04 and Zalviso. Any delay or refusal by the DEA in establishing the procurement quota or a reduction in our quota for sufentanil or a failure to increase it over time to meet anticipated increases in demand could delay or stop the clinical development of any of our product candidates or the commercial sale of any approved products. This, in turn, could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

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

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

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

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

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

- the federal transparency law, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the Health Care Reform Law), and its implementing regulations, requires certain manufacturers of drugs, devices, biologicals and medical supplies to report to the U.S. Department of Health and Human Services information related to payments and other transfers of value provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- analogous state laws that may apply to our business practices, including but not limited to, state laws that require pharmaceutical companies to implement compliance programs and/or comply with the pharmaceutical industry's voluntary compliance guidelines; state laws that impose restrictions on pharmaceutical companies' marketing practices and require manufacturers to track and file reports relating to pricing and marketing information, which requires tracking and reporting gifts, compensation and other remuneration and items of value provided to healthcare professionals and entities; and

- the federal Foreign Corrupt Practices Act of 1977 and other similar anti-bribery laws in other jurisdictions generally prohibit companies and their intermediaries from providing money or anything of value to officials of foreign governments, foreign political parties, or international organizations with the intent to obtain or retain business or seek a business advantage. Recently, there has been a substantial increase in anti-bribery law enforcement activity by U.S. regulators, with more frequent and aggressive investigations and enforcement proceedings by both the Department of Justice and the U.S. Securities and Exchange Commission. A determination that our operations or activities are not, or were not, in compliance with United States or foreign laws or regulations could result in the imposition of substantial fines, interruptions of business, loss of supplier, vendor or other third-party relationships, termination of necessary licenses and permits, and other legal or equitable sanctions. Other internal or government investigations or legal or regulatory proceedings, including lawsuits brought by private litigants, may also follow as a consequence.

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

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

We underwent a Conformité Européenne approval process for the Zalviso device, more commonly known as a CE Mark approval process. We received CE Mark approval in December 2014, which permits the commercial sale of the Zalviso device in the European Union. In connection with the CE Mark approval, we were also granted International Standards Organization, or ISO, 13485:2003 certification of our quality management system in November 2014. This is an internationally recognized quality standard for medical devices. Certification of our quality management system was issued by the British Standards Institution, or BSI, a Notified Body. ISO 13485:2003 certification recognizes that consistent quality policies and procedures are in place for the development, design and manufacturing of medical devices. The certification indicates that we have successfully implemented a quality system that conforms to ISO 13485 standards for medical devices. Certification to this standard is one of the key regulatory requirements for a CE Mark in the EU and EEA, as well as to meet equivalent requirements in other international markets. The certification applies to the Redwood City, California location which designs, manufactures and distributes finished medical devices, and includes critical suppliers. In November 2015, AcelRx underwent a successful surveillance audit by the Notified Body for the Zalviso CE mark and for AcelRx's status as an ISO 13485 certified device manufacturer.

If we fail to remain in compliance with applicable European laws and directives, we would be unable to continue to affix the CE Mark to our Zalviso device, which would prevent Grünenthal from selling these devices within the EEA.

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

Our headquarters is located in the San Francisco Bay Area, near known earthquake fault zones and is vulnerable to significant damage from earthquakes. We are also vulnerable to other types of natural disasters and other events that could disrupt our operations. We do not carry insurance for earthquakes or other natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

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

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

In the future, we will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.*

As of June 30, 2016, we had 39 full-time employees. As our product candidates mature and approach potential commercialization in the United States, we plan to expand our employee base to increase our managerial, sales, marketing, operational, quality, engineering, financial and other resources and to hire more consultants and contractors. Future growth will impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be

reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize ARX-04, Zalviso and our other product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

Our current product liability insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. For example, with the recent approval of Zalviso in the EU, we have expanded our insurance coverage to include the sale of Zalviso to our commercial partner, Grünenthal. There can be no assurance that such coverage will be adequate to protect us against any future losses due to liability. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

56

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

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

Risks Related to Our Intellectual Property

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

To protect our proprietary technology, we rely on patents as well as other intellectual property protections including trade secrets, nondisclosure agreements, and confidentiality provisions. As of June 30, 2016, we are the owner of record of 52 issued patents worldwide. These issued patents cover AcelRx’s sufentanil sublingual tablet, medication delivery devices, packaging and other platform technology. These issued patents are expected to provide coverage through 2027 – 2031.

In addition, we are pursuing a number of U.S. non-provisional patent applications and foreign national applications directed to our product candidates. The patent applications that we have filed and have not yet been granted may fail

to result in issued patents in the United States or in foreign countries. Even if the patents do successfully issue, third parties may challenge the patents.

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

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

There is also no assurance that any patents issued to us will not become the subject of adversarial proceedings such as opposition, inter partes review, post-grant review, reissue, supplemental examination, re-examination or other post-issuance proceedings. For example, an anonymous third party filed an Opposition on October 7, 2015 against European patent EP2182902B1, which claims a dosage form related to ARX-03. Although the Opposition is currently pending, the European Patent Office has neither reviewed nor made any initial comments regarding the validity of the EP2182902B1 patent. There is also no assurance that the respective court or agency in such adversarial proceedings would not make unfavorable decisions, such as reducing the scope of a patent of ours, or determining that a patent of ours is invalid or unenforceable. There is also no assurance that any patents issued to us will provide us with competitive advantages, will not be challenged by any third parties, or that the patents of others will not prevent the commercialization of products incorporating our technology. Furthermore, there can be no guarantee that others will not independently develop similar products, duplicate any of our products, or design around our patents.

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

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

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

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

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

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

It is possible that we may in the future receive, particularly as a public company, communications from competitors and other companies alleging that we may be infringing their patents, trade secrets or other intellectual property rights,

offering licenses to such intellectual property or threatening litigation. In addition to patent infringement claims, third parties may assert copyright, trademark or other proprietary rights against us. We may need to expend considerable resources to counter such claims and may not be able to successful in our defense. Our business may suffer if a finding of infringement is established.

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

The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. The pharmaceutical patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. For example, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The United States Patent and Trademark Office has developed new regulations and procedures to govern the full implementation of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, that became effective March 16, 2013. We are uncertain what impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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

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

58

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Ownership of Our Common Stock

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

Since our initial public offering, or IPO, in February 2011, the trading price of our common stock has experienced significant volatility and is likely to be volatile in the future. For example, our stock price declined by more than 40% on July 28, 2014, the first trading day following the announcement of the receipt of the CRL from the FDA. In addition, our stock price dropped by 37% on March 9, 2015, the day we announced the correspondence we received from the FDA requesting a clinical trial to assess the risk of inadvertent dispensing and overall risk of dispensing failures for Zalviso. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- any delay in submitting the NDA for ARX-04 or resubmitting the NDA for Zalviso, and any adverse development or perceived adverse development with respect to the FDA’s review of any NDA;

- adverse results or delays in future clinical trials, including the Phase 3 clinical development program for ARX-04 and Zalviso;
- inability to obtain additional funding, including funding necessary for the planned potential commercialization and manufacturing of ARX-04 and Zalviso in the United States;
- failure to successfully develop and commercialize our product candidates;
- changes in laws or regulations applicable to our products;
- inability to obtain adequate product supply for our product candidates, or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or other significant transactions, including disposition transactions, or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;

- sales of our common stock by us or our stockholders in the future; and

- trading volume of our common stock.

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

Historically, our common stock has thinly traded, and in the future may continue to be thinly traded, and our stockholders may be unable to sell at or near asking prices, or at all if they need to sell their shares to raise money or otherwise desire to liquidate such shares.*

Historically, we have not had a high volume of daily trades in our common stock on NASDAQ. For example, the average daily trading volume in our common stock on NASDAQ during the six months ended June 30, 2016 and 2015 was approximately 370,000 and 640,000 shares per day, respectively. A more active market for our stock has only recently developed and may not be sustained. Our stockholders may be unable to sell their common stock at or near their asking prices, which may result in substantial losses to our investors.

The market for our common stock may be characterized by significant price volatility when compared to seasoned issuers, and we expect that our share price will be more volatile than a seasoned issuer for the indefinite future. As noted above, our common stock may be sporadically and/or thinly traded. As a consequence of this lack of liquidity, the trading of relatively small quantities of shares by our stockholders may disproportionately influence the price of those shares in either direction. The price for our shares could, for example, decline significantly in the event that a large number of our common stock are sold on the market without commensurate demand, as compared to a seasoned issuer that could better absorb those sales without adverse impact on its share price.

Our principal stockholders and management own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval.

Our executive officers and directors, together with the stockholders with whom our executive officers and directors are affiliated or associated, beneficially own a significant percentage of our voting stock. Therefore, these stockholders have the ability to influence us through this ownership position. These stockholders are able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, are able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We incur significant increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or Dodd-Frank Act, as well as the information and reporting requirements of the Exchange Act and other federal securities laws, and rules subsequently implemented by the SEC and NASDAQ, have imposed various requirements on public companies. The costs of compliance with the Sarbanes-Oxley Act and of preparing and filing annual and quarterly reports, proxy statements and other information with the SEC, the Dodd-Frank Act, and regulations promulgated under these statutes, are significant. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

As a public company, we are subject to the requirements of Section 404 of the Sarbanes-Oxley Act. If we are unable to comply with Section 404 in a timely manner, it may affect the reliability of our internal control over financial reporting. Assessing our staffing and training procedures to improve our internal control over financial reporting is an ongoing process.

We have been and will continue to be involved in a substantial effort to implement appropriate processes, document the system of internal control over key processes, assess their design, remediate any deficiencies identified and test their operation. If we fail to comply with the requirements of Section 404, it may affect the reliability of our internal control over financial reporting and negatively impact the quality of disclosure to our stockholders. If we, or our independent registered public accounting firm, identify and report a material weakness, it could adversely affect our stock price.

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

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. A significant number of shares of our common stock are held by some of our original pre-IPO venture investors. These investors have previously distributed, and may in the future distribute their shares of AcelRx to their limited partners. Historically, these limited partners have subsequently sold those shares on the open market following the distribution. Sales of substantial number of shares of our common stock following such distributions may lead to a decline in the price of our common stock.

We are unable to predict the effect that sales may have on the prevailing market price of our common stock. All of our shares of common stock outstanding are eligible for sale in the public market, subject in some cases to the volume limitations and manner of sale requirements of Rule 144 under the Securities Act. Sales of stock by our stockholders could have a material adverse effect on the trading price of our common stock.

In addition, certain holders of our securities are entitled to certain rights with respect to the registration of their shares of common stock under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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

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

Pursuant to the 2011 Incentive Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under our 2011 Incentive Plan will automatically increase each year by 4% of all shares of our capital stock outstanding as of

December 31 of the prior calendar year, subject to the ability of our Board of Directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under our 2011 Incentive Plan each year. If our Board of Directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

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

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

For example, on October 1, 2014, a securities class action complaint was filed in the U.S. District Court for the Northern District of California against AcelRx and certain of our current and former officers. On April 17, 2015, lead plaintiff filed an amended complaint. The amended complaint alleged that between September 30, 2013 and July 25, 2014, AcelRx and certain of our current and former officers violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 in connection with statements related to our lead drug candidate, Zalviso. On November 25, 2015, the Court granted our Motion to Dismiss. Plaintiffs had the opportunity to file an amended complaint within 30 days' which they declined to do. On January 18, 2016, the Court issued an order dismissing the case with prejudice.

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

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. The completion of the July 2013 public equity offering, together with our public equity offering in December 2012, our initial public offering, private placements and other transactions that have occurred, have triggered such an ownership change. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo further ownership changes in the future. In the year ended December 31, 2015, we used net operating losses to reduce our income tax liability. In the future, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset United States federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us.

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

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

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

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

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;

- limiting the removal of directors by the stockholders;
- a staggered Board of Directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to our Board of Directors or for proposing matters that can be acted upon at stockholder meetings.

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

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant, currently in effect.	8-K	001-35068	3.1	2/28/2011
3.2	Amended and Restated Bylaws of the Registrant, currently in effect.	S-1	333-170594	3.4	1/7/2011
4.1	Reference is made to Exhibits 3.1 through 3.2.				
4.2	Specimen Common Stock Certificate of the Registrant.	S-1	333-170594	4.2	1/31/2011
4.3	Second Amended and Restated Investors' Rights Agreement, among the Registrant and certain of its security holders, dated as of November 23, 2009.	S-1	333-170594	4.3	11/12/2010
4.4	Warrant to Purchase Common Stock of the Registrant, issued to Hercules Technology II, L.P., dated as of December 16, 2013.	10-K	001-35068	4.4	3/17/2014
4.5	Warrant to Purchase Common Stock of the Registrant, issued to Hercules Technology Growth Capital, Inc., dated as of December 16, 2013.	10-K	001-35068	4.5	3/17/2014
4.6	Form of Warrant issued to certain purchasers pursuant to the Securities Purchase Agreement dated May 29, 2012, between the Registrant and the purchasers identified therein.	8-K	001-35068	4.8	5/30/2012
4.7	Warrant Modification Agreement to Purchase Common Stock of the Registrant, issued to Hercules Technology II, L.P. dated as of September 17, 2015.	10-Q	001-35068	4.7	11/3/2015
4.8	Warrant Modification Agreement to Purchase Common Stock of the Registrant, issued to Hercules Technology Growth Capital, Inc. dated as of September 17, 2015.	10-Q	001-35068	4.8	11/3/2015
10.1+	Offer Letter between the Registrant and Howard B. Rosen, effective as of April 1, 2016.	10-Q	001-35068	10.3	5/2/2016
10.2	Controlled Equity OfferingSM Sales Agreement between the Registrant and Cantor Fitzgerald & Co., dated as of June 21, 2016.	8-K	001-35068	10.1	6/21/2016

10.3	Modification of Contract W81XWH-15-C-0046 between the Registrant and the U.S. Army Medical Research and Materiel Command, effective June 14, 2016.
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1	Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.*
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

+ Indicates management contract or compensatory plan.

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

SIGNATURES

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

Date: July 28, 2016 **AcelRx Pharmaceuticals, Inc.**
(Registrant)

/s/ Timothy E. Morris
Timothy E. Morris
Chief Financial Officer
(Duly Authorized and Principal Financial and Accounting Officer)

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