ACELRX PHARMACEUTICALS INC
Form 10-Q
August 11, 2014
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10-Q

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

For the quarterly period ended June 30, 2014

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 x 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 x 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 x
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 x

As of July 21, 2014, the number of outstanding shares of the registrant s common stock was 43,377,078.

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ACELRX PHARMACEUTICALS, INC.

QUARTERLY REPORT ON FORM 10-Q FOR THE QUARTER ENDED JUNE 30, 2014

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Unless the context indicates otherwise, the terms AcelRx, AcelRx Pharmaceuticals, we, us and our refer to AcelRx Pharmaceuticals, Inc. ACELRX , NANOTAB 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.

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

AcelRx Pharmaceuticals, Inc.

Condensed Balance Sheets

(In thousands, except share data)

	June 30, 2014 (Unaudited)	December 31, 2013[1]
Assets		
Current Assets:		
Cash and cash equivalents	$ 77,728	$ 88,401
Short-term investments	14,621	15,262
Prepaid expenses and other current assets	868	897
Total current assets	93,217	104,560
Property and equipment, net	6,820	5,179
Restricted cash	250	250
Other assets	87	42
Total Assets	$ 100,374	$ 110,031
Liabilities and Stockholders Equity		
Current Liabilities:		
Accounts payable	$ 2,798	$ 2,341
Accrued liabilities	2,958	3,904
Deferred revenue	776	623
Long-term debt, current portion	2,208	
Total current liabilities	8,740	6,868
Deferred rent	243	188
Long-term debt, net of current portion	22,429	14,364
Deferred revenue	1,687	2,007
Contingent put option liability	438	334
Warrant liability	11,288	13,111
Total liabilities	44,825	36,872
Stockholders Equity:		
Common stock, $0.001 par value 100,000,000 shares authorized as of June 30, 2014 and December 31, 2013; 43,373,116 and 43,050,580 shares issued and outstanding as of June 30, 2014 and December 31, 2013	43	43
Additional paid-in capital	221,166	218,568
Accumulated deficit	(165,659)	(145,453)
Accumulated other comprehensive income	(1)	1
Total stockholders equity	55,549	73,159
Total Liabilities and Stockholders Equity	$ 100,374	$ 110,031

(1) The condensed balance sheet as of December 31, 2013 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, 2013.

See notes to condensed financial statements.

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AcelRx Pharmaceuticals, Inc.

Condensed Statements of Comprehensive Loss

(Unaudited)

(In thousands, except share and per share data)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2013	2014	2013
Revenue:				
Collaboration agreement	$ 71	$	$ 166	$
Research grant		407		1,347
Total revenue	$ 71	$ 407	$ 166	$ 1,347
Operating expenses:				
Research and development	7,284	6,108	11,995	15,426
General and administrative	5,047	2,070	8,972	4,261
Total operating expenses	12,331	8,178	20,967	19,687
Loss from operations	(12,260)	(7,771)	(20,801)	(18,340)
Interest expense	(530)	(403)	(1,002)	(857)
Interest income and other income (expense), net	2,215	(9,273)	1,597	(11,012)
Net loss	(10,575)	(17,447)	(20,206)	(30,209)
Other comprehensive loss:				
Unrealized losses on available-for-sale securities	(2)		(2)	(2)
Comprehensive loss	$ (10,577)	$ (17,447)	$ (20,208)	$ (30,211)
Net loss per share of common stock, basic	$ (0.24)	$ (0.47)	$ (0.47)	$ (0.81)
Net loss per share of common stock, diluted	$ (0.30)	$ (0.47)	$ (0.50)	$ (0.81)
Shares used in computing net loss per share of common stock, basic	43,333,210	37,262,754	43,262,204	37,198,413
Shares used in computing net loss per share of common stock, diluted see Note 8	44,310,166	37,262,754	43,774,033	37,198,413

See notes to condensed financial statements.

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AcelRx Pharmaceuticals, Inc.

Condensed Statements of Cash Flows

(Unaudited)

(In thousands)

	Six Months Ended June 30,	
	2014	**2013**
Cash flows from operating activities:		
Net loss	$ (20,206)	$ (30,209)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	318	288
Amortization of premium/discount on investments, net	140	81
Interest expense related to debt financing	279	253
Stock-based compensation	1,869	1,559
Revaluation of put option and PIPE warrant liabilities	(1,719)	11,003
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(23)	697
Restricted cash		(45)
Accounts payable	457	(937)
Accrued liabilities	(871)	(1,731)
Deferred revenue	(167)	
Deferred rent	(20)	(55)
Net cash used in operating activities	(19,943)	(19,096)
Cash flows from investing activities:		
Purchase of property and equipment	(1,959)	(153)
Purchase of investments	(4,879)	(18,022)
Proceeds from maturity of investments	5,379	14,845
Net cash used in investing activities	(1,459)	(3,330)
Cash flows from financing activities:		
Proceeds from issuance of long-term debt	10,000	
Payment of long-term debt		(3,820)
Net proceeds from issuance of common stock through equity plans and exercise of warrants	729	233
Net cash provided by (used in) financing activities	10,729	(3,587)
Net decrease in cash and cash equivalents	(10,673)	(26,013)
Cash and cash equivalents Beginning of period	88,401	47,932
Cash and cash equivalents End of period	$ 77,728	$ 21,919

See notes to condensed financial statements.

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AcelRx Pharmaceuticals, Inc.

Notes to Condensed Financial Statements

(Unaudited)

1. Organization and Summary of Significant Accounting Policies

The Company

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

AcelRx is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough 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. On July 25, 2014, the U.S. Food and Drug Administration, or FDA, issued a Complete Response Letter, or CRL, for the Company s new drug application, or NDA, for Zalviso (sufentanil sublingual tablet system), formerly known as ARX-01. The proposed indication for Zalviso is for the management of moderate-to-severe acute pain in adult patients in the hospital setting. Zalviso consists of sufentanil tablets delivered by the Zalviso System, a needle-free, handheld, patient-administered, pain management system (together, Zalviso). The Company is currently reviewing the FDA s comments and requests contained in the CRL and plans to discuss these requests with the FDA. See Note 11 Subsequent Events, for further description.

In addition, in December 2013, the Company entered into a collaboration agreement with Grünenthal, a European-based pharmaceutical company, for the commercialization of Zalviso in Europe and Australia. The Marketing Authorization Application, or MAA, for Zalviso was filed by Grünenthal under the centralized procedure in the European Union, or EU, in July 2014.

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 in the future as it prepares for the commercial launch of Zalviso and continues its research and development activities. In previous years, prior to the commercial collaboration of Zalviso with Grünenthal, AcelRx was considered a development stage company.

The Company has one business activity, which is the development and commercialization of product candidates for the treatment of pain, and a single reporting and operating unit structure.

Basis of Presentation

The accompanying unaudited condensed 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, 2014, are not necessarily indicative of the results that may be expected for the year ending December 31, 2014. The condensed balance sheet as of December 31, 2013, was derived from the Company s audited financial statements as of December 31, 2013, 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, 2013, 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 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.

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Recently Issued Accounting Standards

In May 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2014-09, *Revenue from Contracts with Customers*, issued as a new Topic, Accounting Standards Codification (ASC) Topic 606. The new revenue recognition standard provides a five-step analysis of transactions to determine when and how revenue is recognized. The core principle of the guidance is that a Company should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. This ASU is effective for AcelRx beginning in fiscal 2017 and can be adopted by the Company either retrospectively or as a cumulative-effect adjustment as of the date of adoption. The Company is currently evaluating the effect that adopting this new accounting guidance will have 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, 2014			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 77,060	$	$	$ 77,060
Money market funds	668			668
Total cash and cash equivalents	77,728			77,728
Marketable securities:				
U.S. government agency securities	14,622		(1)	$ 14,621
Total marketable securities	14,622		(1)	$ 14,621
Total cash, cash equivalents and investments	$ 92,350	$	$ (1)	$ 92,349

	As of December 31, 2013			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 88,390	$	$	$ 88,390
Money market funds	11			11
Total cash and cash equivalents	88,401			$ 88,401
Marketable securities:				
U.S. government agency securities	15,261	1		15,262
Total marketable securities	15,261	1		$ 15,262
Total cash, cash equivalents and investments	$ 103,662	$ 1	$	$ 103,663

As of June 30, 2014 and December 31, 2013, 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, 2014 or December 31, 2013. 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, 2014 and 2013.

As of June 30, 2014 and December 31, 2013, the contractual maturity of all investments held was less than one year.

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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, 2014 and December 31, 2013, 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 5 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 (expense), net in the condensed 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, 2014 and December 31, 2013, the Company also held a Level III liability associated with warrants, or PIPE warrants, issued in connection with the Company s private placement equity offering, completed in June 2012. The PIPE warrants 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 the 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, 2014			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$ 668	$ 668	$	$
U.S. government agency obligations	14,621		14,621	
Total assets measured at fair value	$ 15,289	$ 668	$ 14,621	$
Liabilities				
PIPE warrants	$ 11,288			$ 11,288
Contingent put option liability	438			438
Total liabilities measured at fair value	$ 11,726	$	$	$ 11,726

	As of December 31, 2013			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$ 11	$ 11	$	$
U.S. government agency obligations	15,262		15,262	
Total assets measured at fair value	$ 15,273	$ 11	$ 15,262	$
Liabilities				
PIPE warrants	$ 13,111			$ 13,111
Contingent put option liability	$ 334			$ 334

Total liabilities measured at fair value	$ 13,445	$	$	$ 13,445

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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, 2014:

Market price	$ 10.25
Exercise price	$ 3.40
Risk-free interest rate	0.88%
Expected volatility	66.0%
Expected life (in years)	3.4
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, 2013:

Market price	$ 11.31
Exercise price	$ 3.40
Risk-free interest rate	1.27%
Expected volatility	69.0%
Expected life (in years)	3.92
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, 2014 and June 30, 2013 (in thousands):

	Three Months Ended June 30, 2014	Six Months Ended June 30, 2014
Fair value beginning of period	$ 14,091	$ 13,445
Change in fair value of PIPE warrants	(2,507)	(1,823)
Change in fair value of contingent put option associated with Amended Loan Agreement with Hercules	142	104
Fair value end of period	$ 11,726	$ 11,726

	Three Months Ended June 30, 2013	Six Months Ended June 30, 2013
Fair value beginning of period	$ 9,254	$ 7,500
Change in fair value of PIPE warrants	8,656	10,432
Change in fair value of contingent put option associated with Original Loan Agreement with Hercules	(21)	(43)
Fair value end of period	$ 17,889	$ 17,889

3. Research Grant Agreement

In May 2011, AcelRx received a grant from the US Army Medical Research and Materiel Command, or USAMRMC, in which the USAMRMC granted $5.6 million to the Company in order to support the development of a new product candidate, ARX-04, a sufentanil tablet for the treatment of moderate-to-severe acute pain. Under the terms of the grant, the USAMRMC reimbursed the Company for development, manufacturing and clinical costs necessary to prepare for and complete the planned Phase 2 dose-finding trial in a study of acute moderate-to-severe pain, and to prepare to enter Phase 3 development. The grant gives the USAMRMC the option to extend the term of the grant and provide additional funding for the research. As of December 31, 2013, the full amount of the grant, $5.6 million, had been received and recognized as revenue.

Revenue is recognized based on expenses incurred by AcelRx in conducting research and development activities set forth in the agreement. Revenue attributable to the research and development performed under the USAMRMC grant was $407,000 and $1.3 million for the three and six months ended June 30, 2013, respectively. There was no such revenue recognized for the three and six months ended June 30, 2014.

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4. Collaboration Agreement

On December 16, 2013, AcelRx and Grünenthal GmbH, or Grünenthal, entered into a Collaboration and License Agreement (the License Agreement) and related Manufacture and Supply Agreement (the Manufacturing Agreement and together with the License Agreement, the Grünenthal Agreements). The License Agreement grants Grünenthal rights to commercialize Zalviso in the EU, Switzerland, Liechtenstein, Iceland, Norway and Australia, for pain treatment within or dispensed by hospitals, hospices, nursing homes and other medically-supervised settings. Under the Supply Agreement, the Company will exclusively manufacture and supply Zalviso to Grünenthal for sale in their territories.

License Agreement

Under the terms of the License Agreement, Grünenthal has the exclusive right to commercialize Zalviso in their territories. The Company retains control of clinical development, and together with Grünenthal will be responsible for certain development activities. The Company will not receive separate payment for such development activities. Grünenthal is responsible for marketing approval applications and other regulatory filings relating to the sufentanil drug cartridge for Zalviso, while the Company is responsible for the CE Mark and other regulatory filings relating to the device portions.

The Company received an upfront non-refundable cash payment of $30.0 million, and is eligible to receive a milestone payment of $5.0 million related to the MAA submission, which occurred in July 2014. The Company is eligible to receive an additional $15.0 million milestone payment upon the approval of the MAA, if approved. If the MAA is approved, the Company is eligible to receive approximately $200.0 million in additional milestone payments, based upon successful regulatory and product development efforts ($28.5 million) and net sales target achievements ($171.5 million). Grünenthal will also make tiered royalty and supply and trademark fee payments in the mid-teens up to the mid-twenties percent range on net sales of Zalviso.

Unless earlier terminated, the 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 Zalviso to Grünenthal. The 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.

Manufacturing Agreement

Under the terms of the Manufacturing Agreement, the Company will manufacture and supply Zalviso exclusively for Grünenthal. The Company will supply Zalviso at the Company s fully burdened manufacturing cost (as defined in the Manufacturing Agreement). The Manufacturing Agreement requires the Company to use commercially reasonable efforts to enter stand-by contracts with third party contract manufacturers to ensure continual supply of Zalviso and under certain conditions permits Grünenthal to use a third party back-up manufacturer to manufacture Zalviso for commercial sale in their territories.

Unless earlier terminated, the Manufacturing Agreement 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 License Agreement. The Manufacturing Agreement is subject to earlier termination in connection with certain termination events in the 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 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. The Company developed best estimates of selling prices for each deliverable in order to allocate the non-contingent arrangement consideration to the four units of accounting.

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 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

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milestones at the inception 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 agreement 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 Agreements were deemed not to be substantive. These milestones pertain to regulatory developments for Zalviso in Europe, which Company s management deemed to be not substantive due to the level of performance associated with future achievement of these milestones. Aggregate potential payments for these milestones total $20.0 million. When achieved, the value of these milestones will be allocated to the four separate units of accounting based on estimated selling prices and recognized as revenue in the period of achievement to the extent the services underlying the separate units of accounting have been performed. In July 2014, Grünenthal submitted a Marketing Authorization Application, or MAA, to the European Medicines Authority, or EMA, for Zalviso for the management of moderate-to-severe acute pain in adult patients in a medically supervised environment. Under the terms of the License Agreement with Grünenthal, the Company is eligible to receive a cash payment of $5.0 million for the MAA submission and expects to receive such payment in the third quarter of 2014. The Company is eligible to receive an additional $15.0 million milestone payment upon the approval of the MAA.

The Agreements also include milestone payments related to specified net sales targets, totaling $171.5 million. The sales-based 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.

The Company allocated the $30.0 million upfront fee across the four deliverables based on estimated selling prices and for the quarter ended December 31, 2013, recognized $27.4 million attributable to the license. The remaining $2.6 million was recorded as deferred revenue at December 31, 2013, to be recognized in future periods to the extent services are performed related to the other non-contingent performance deliverables under the agreements.

The Company recognized $71,000 and $166,000, of previously deferred revenue related to research and development services under the collaboration agreement during the three and six months ended June 30, 2014, respectively. As of June 30, 2014, the Company had a deferred revenue balance of $2.5 million. There were no milestone payments received or recognized under these Agreements during the three and six months ended June 30, 2014.

5. Long-Term Debt

Hercules Loan and Security Agreements

In June 2011, AcelRx entered into a Loan and Security Agreement, or the Original Loan Agreement, with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., collectively referred to as Hercules, under which AcelRx borrowed $20.0 million in two tranches of $10.0 million each, represented by secured convertible term promissory notes, or collectively, the Original Notes. The Company s obligations associated with the agreement were secured by a security interest in substantially all of its assets, other than its intellectual property.

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 interest rate for each tranche was 8.50%. In connection with the Original Loan Agreement, 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 6 Warrants, for further description.

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On December 16, 2013, AcelRx entered into an Amended and Restated Loan and Security Agreement, or the Amended Loan Agreement, with Hercules, under which the Company may borrow up to $40.0 million in three tranches. These loans are represented by secured convertible term promissory notes, or collectively, the Amended Notes. The Amended Loan Agreement amends and restates the Original Loan Agreement, as noted above. 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 Original Loan Agreement. The Company recorded the new debt at an estimated fair value of $24.6 million and $14.3 million as of June 30, 2014 and December 31, 2013, respectively.

The second tranche of the Amended Loan Agreement of $10.0 million was drawn by the Company on June 16, 2014. The third tranche, of up to $15.0 million, can be drawn at any time between December 15, 2014 and March 15, 2015, but only if the Company has obtained approval for Zalviso from the U.S. Food and Drug Administration, or the Milestone. 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 are interest only until April 1, 2015 (which will be extended until January 1, 2016 if the Company achieves the Milestone on or before April 1, 2015) followed by equal monthly payments of principal and interest through the scheduled maturity date on October 1, 2017 (which would be extended until January 1, 2018 if the Company achieves the Milestone on or prior to April 1, 2015), 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.

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, equal to 3% if the prepayment occurs prior to December 16, 2014, 2% if the prepayment occurs after December 16, 2014, but prior to December 16, 2015, 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 carry an exercise price of $6.79. See Note 6 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 amendment of the loan agreement was considered an extinguishment, the contingent put option liability associated with the Original 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, 2014 and December 31, 2013, the estimated fair value of the contingent put option liability was $438,000 and $334,000, 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

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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 statements of comprehensive loss.

As of June 30, 2014 and December 31, 2013, the Company had outstanding borrowings under the Amended Loan Agreement of $25.0 million and $15.0 million, respectively. Interest expense related to the Amended Loan Agreement was $530,000 and $1.0 million for the three and six months ended June 30, 2014, respectively, $145,000 and $273,000 of which represented amortization of the debt discount for the three and six months ended June 30, 2014, respectively. Interest expense related to the Original Loan Agreement was $403,000 and $857,000 for the three and six months ended June 30, 2013, respectively, $97,000 and $205,000 of which represented amortization of the debt discount for the three and six months ended June 30, 2013, respectively.

6. Warrants

Series A Warrants

In March 2007, the Company entered into an equipment financing agreement in which the Company issued immediately exercisable and fully vested warrants to purchase 2,500 shares of its Series A convertible preferred stock, or the Series A warrants, with an exercise price of $10.00 per share. The fair value of the Series A warrants on the date of issuance was $1,000, as determined using the Black-Scholes option-pricing model. This fair value was recorded as a convertible preferred stock warrant liability and as a deferred financing cost in other assets. The fair value was remeasured at the end of each reporting period. In connection with the IPO, the Series A warrants were automatically converted into warrants to purchase 3,425 shares of common stock. As a result of the conversion, these common stock warrants were no longer recorded as liabilities and were, therefore, no longer remeasured as of the end of each reporting period.

As of June 30, 2014, warrants to purchase 3,425 shares of common stock had not been exercised and were still outstanding. These warrants expire in March 2017.

Pinnacle Warrants

In September 2008, the Company entered into a $12.0 million loan and security agreement with Pinnacle Ventures. In connection with this loan and security agreement, the Company issued immediately exercisable and fully vested warrants, or the Series B warrants, to purchase 56,250 shares of Series B convertible preferred stock with an exercise price of $16.00 per share which were ultimately converted into warrants to purchase 228,264 shares of common stock with an exercise price of $3.94 per share in connection with the Company s initial public offering in 2011.

In February 2013, warrants to purchase 228,264 shares were net exercised, for 58,580 shares of common stock. As of June 30, 2014, no warrants to purchase shares of common stock issued to Pinnacle were outstanding.

Hercules Warrants

In connection with the Amended Loan Agreement, executed in December 2013, the Company issued warrants to Hercules which are exercisable for an aggregate of 176,730 shares of Common Stock and each carry an exercise price of $6.79 (the Warrants). 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 recorded as equity. The fair value of the warrants was calculated using the Black-Scholes option-valuation model, and was based on the strike price of $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.

As of June 30, 2014, 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.

In connection with the Original Loan Agreement with Hercules, executed in June 2011, the Company issued warrants to Hercules to purchase an aggregate of 274,508 shares of common stock at a price of $3.06 per share.

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During June and July 2013, warrants to purchase 274,508 shares were net exercised, for 183,404 shares of common stock.

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 interest income and other income (expense), net in the condensed statements of comprehensive loss. The Black-Scholes assumptions used to value the PIPE warrants are disclosed in Note 2.

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, 2014, the fair value of the PIPE warrants was estimated to be $11.3 million. As of December 31, 2013, the fair value of the PIPE warrants was estimated to be $13.1 million. The change in fair value for the three and six months ended June 30, 2014, which was recorded as other income, was $2.5 million and $1.8 million, respectively. The change in fair value for the three and six months ended June 30, 2013, recorded as other expense, was $8.7 million and $10.5 million, respectively.

During the three and six months ended June 30, 2014, no warrants were exercised for shares of common stock. As of June 30, 2014, PIPE warrants to purchase 1,494,514 shares of common stock issued in connection with the Private Placement had not been exercised and were outstanding. These warrants expire in November 2017.

7. Stock-Based Compensation

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2013	2014	2013
Expenses:				
Research and development	$ 560	$ 411	$ 1,039	$ 766
General and administrative	334	391	830	793
Total stock-based compensation expense	$ 894	$ 802	$ 1,869	$ 1,559

As of June 30, 2014 there were 1,519,366 shares available for grant, 5,160,416 options outstanding and 0 restricted stock units outstanding under the Company s 2011 Equity Incentive Plan.

8. 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 and six months ended June 30, 2014, the PIPE warrants had a dilutive impact to net loss per share due to a lower share price at June 30, 2014, compared to the closing share price on March 31, 2014 and December 31, 2013. 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 and six months ended June 30, 2014. 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.

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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, 2014 and 2013 (in thousands, except for share and per share amounts):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2013	2014	2013
	(in thousands, except share and per share amounts)			
Numerator				
Net loss used to compute net loss per share:				
Basic	$ (10,575)	$ (17,447)	$ (20,206)	$ (30,209)
Adjustments for change in fair value of warrant liability	(2,507)		(1,823)	
Diluted	$ (13,082)	$ (17,447)	$ (22,029)	$ (30,209)
Denominator				
Weighted average shares outstanding used to compute net loss per share:				
Basic	43,333,210	37,262,754	43,262,204	37,198,413
Dilutive effect of warrants	976,956		511,829	
Diluted	44,310,166	37,262,754	43,774,033	37,198,413
Net loss per share basic	$ (0.24)	$ (0.47)	$ (0.47)	$ (0.81)
Net loss per share diluted	$ (0.30)	$ (0.47)	$ (0.50)	$ (0.81)

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,	
	2014	2013
Stock options to purchase common stock	5,160,416	5,045,417
Restricted stock units		65,765
Common stock warrants	180,155	2,674,502

9. Manufacturing Agreements

Patheon

In January 2013, the Company and Patheon Pharmaceuticals Inc., or Patheon, entered into a Manufacturing Services Agreement, or the Services Agreement, and a related Amended and Restated Capital Expenditure and Equipment Agreement, or the Capital Agreement, relating to the manufacture of sufentanil tablets, or the Product, for use with the Company s Zalviso drug product.

Under the terms of the Services Agreement, the Company has agreed to purchase, subject to Patheon s continued material compliance with the terms of the Services Agreement, all of its Product requirements for the United States, Canada and Mexico from Patheon during the Initial Term of the Services Agreement (as defined below), and at least eighty percent (80%) of its Product requirements for such territories after the Initial Term.

The term of the Services Agreement extends until December 31, 2017, or the Initial Term, and will automatically renew thereafter for periods of two years, unless terminated by either party upon eighteen months prior written notice; provided, however, that the Services Agreement may not be terminated without cause prior to the end of the Initial Term.

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The Company also entered into a Capital Expenditure and Equipment Agreement, or the Capital Agreement. Under the terms of the Capital Agreement, as amended in January 2014, the Company has made and continues to make certain modifications to Patheon s Cincinnati facility, the aggregate cost of which is expected to be less than $4.4 million and which is the responsibility of the Company. Property and equipment, net in the condensed balance sheet at June 30, 2014, includes $2.9 million related to certain modifications the Company is making at Patheon s Cincinnati facility under the terms of the Capital Agreement.

Expenditures associated with the aforementioned agreements are primarily driven by the potential commercial requirements and demand for the Company s products, none of which have been approved for commercialization; accordingly, the amounts and timing of such future expenditures cannot be determined at this time.

Grünenthal

On December 16, 2013, AcelRx and Grünenthal entered into a Collaboration and License Agreement (the License Agreement) and related Manufacture and Supply Agreement (the Manufacturing Agreement and together with the License Agreement, the Grünenthal Agreements). The License Agreement grants Grünenthal rights to commercialize Zalviso in the EU, Switzerland, Liechtenstein, Iceland, Norway and Australia, for pain treatment within or dispensed by hospitals hospices, nursing homes and other medically-supervised settings.

Under the terms of the Manufacturing Agreement, the Company will manufacture and supply Zalviso exclusively for Grünenthal. The Company will supply Zalviso at the Company s fully burdened manufacturing cost (as defined in the Manufacturing Agreement). The Manufacturing Agreement requires the Company to use commercially reasonable efforts to enter stand-by contracts with third party contract manufacturers to ensure a continual supply of Zalviso and under certain conditions permits Grünenthal to use a third party back-up manufacturer to manufacture Zalviso for commercial sale in their territories.

Unless earlier terminated, the Manufacturing Agreement 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 License Agreement. The Manufacturing Agreement is subject to earlier termination in connection with certain termination events in the 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.

Under the Supply Agreement, the Company will exclusively manufacture and supply Zalviso to Grünenthal for commercial sale in their territories.

Expenditures associated with the aforementioned agreements are primarily driven by the potential commercial requirements and demand for the Company s products, none of which have been approved for commercialization; accordingly, the amounts and timing of such future expenditures cannot be determined at this time.

10. Commitments and Contingencies

Operating Leases

In May 2014, the Company entered into an amendment, or the Lease Amendment, to that certain lease dated December 21, 2011, with Metropolitan Life Insurance Company, or the Existing Lease, for 13,787 square feet of space located at 301 Galveston Drive, Redwood City, California, or the Current Premises. Pursuant to the Lease Amendment, the term of the Existing Lease has been extended for a period of twenty (20) months and twenty-two (22) days and expiring January 31, 2018, or the Expiration Date, unless sooner terminated pursuant to the terms of the Existing Lease. In addition, the Lease Amendment included a new lease on an additional 12,106 square feet of office space, or the Expansion Space, which is adjacent to the current premises. The new lease for the Expansion Space has a term of 42 months commencing on August 1, 2014, and expiring on the Expiration Date. The Company has an option to extend the term of the Lease Amendment for an additional five years, which would commence upon the Expiration Date, at a market rate determined according to the Existing Lease.

Base rent payable under the Lease Amendment during the Extended Term for the Current Premises will be as follows:

Period from/to	Monthly Base Rent

May 9, 2016 to May 8, 2017	$ 35,961.55
May 9, 2017 to January 31, 2018	37,040.40

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Base rent payable under the Lease Amendment for the Expansion Space, commencing August 1, 2014, will be as follows:

Months of Lease Term	Monthly Base Rent
1-12	$ 23,001.40
13-24	23,691.44
25-36	24,402.18
37-42	25,134.25

In addition, the Company will pay the Landlord specified percentages of certain operating expenses and taxes related to the leased facility incurred by the Landlord.

11. Subsequent Events

In July 2014, Grünenthal submitted an MAA to the EMA for Zalviso for the management of moderate-to-severe acute pain in adult patients in a medically supervised environment. Under the terms of the License Agreement with Grünenthal, the Company is eligible to receive a cash payment of $5.0 million for the MAA submission, which the Company expects to receive in the third quarter of 2014.

On July 25, 2014, the FDA issued a CRL for the Company s NDA for Zalviso. Since the receipt of the CRL, the Company has been working on a reply and intends to meet with the FDA to discuss the items contained in the CRL.

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 the Instructions for Use for the device to address inadvertent dosing, among other items, and submission of additional data to support the shelf life of the product. The Company believes certain of the requests were addressed in amendments to the NDA that have been submitted prior to the receipt of the CRL but, as acknowledged by the FDA, have not yet been reviewed by the FDA. While the Company anticipates that additional bench testing and human factors testing may be required to address certain items in the CRL, there were no requests to conduct additional human clinical studies. The Company believes it can satisfy all of the FDA s requests contained in the CRL and resubmit the NDA by the end of 2014, although it will have more clarity on the process and timing after its discussion with FDA. However, there is no guarantee that the information previously provided, or to be provided, to the FDA will be adequate to address the issues in the CRL.

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 regarding: our new drug application, or NDA, submission to the U.S. Food and Drug Administration, or FDA, for Zalviso (sufentanil sublingual tablet system), and the Complete Response Letter, or CRL, the Company received from the FDA for Zalviso; our plans to address the issues raised in the CRL; our 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; any delays or inability to obtain and maintain regulatory approval of our product candidates, including Zalviso, in the United States and Europe; our ability to build an effective commercial organization; our ability to obtain sufficient financing to commercialize Zalviso and proceed with clinical development of ARX-04; the anticipated timing, therapeutic and commercial potential of our product candidates, including Zalviso; potential milestones and royalty payments under the Grünenthal agreement; our anticipated timing for initiation or completion of our clinical trials for any of our product candidates , including the planned initiation of the Phase 3 clinical trial for ARX-04; the implications of interim or final results of our clinical trials; the progress of our research programs, including clinical testing; the extent to which our issued and pending patents may protect our products and technology; our ability to identify new product candidates; the potential of such product candidates to lead to the development of commercial products; our future operating expenses; our future losses; our future expenditures for research and development; and the sufficiency of our cash resources. 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, 2013.

About AcelRx Pharmaceuticals

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. Our lead product candidate is Zalviso™, formerly known as ARX-01. Zalviso consists of sufentanil tablets delivered by the Zalviso System, a needle-free, handheld, patient-administered, pain management system (together, Zalviso).

On July 25, 2014, the U.S. Food and Drug Administration, or FDA, issued a Complete Response Letter, or CRL, for our NDA for Zalviso. Since the receipt of the CRL, we have been working on a reply and intend to meet with the FDA to discuss the items contained in the CRL.

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 the Instructions for Use for the device to address inadvertent dosing, among other items, and submission of additional data to support the shelf life of the product. We believe certain of the requests were addressed in amendments to the NDA that were submitted prior to the receipt of the CRL but, as acknowledged by the FDA, have not yet been reviewed by the FDA. While we anticipate that additional bench testing and human factors testing may be required to address certain items in the CRL, there were no requests to conduct additional human clinical studies. We believe we can satisfy all of the FDA s requests contained in the CRL and resubmit the NDA by the end of 2014, although we will have more clarity on the process and timing after our discussion with FDA. However, there is no guarantee that the information previously provided, or to be provided, to the FDA will be adequate to address the issues in the CRL.

Zalviso

Zalviso is an investigational pre-programmed, non-invasive, system to allow hospital patients with moderate-to-severe acute pain to self-dose with sublingual sufentanil tablets to manage their pain. Zalviso is designed to help address certain problems associated with post-operative intravenous patient-controlled analgesia, by offering:

A high therapeutic index opioid: Zalviso uses sufentanil, an opioid that has a high therapeutic index. The therapeutic index is the ratio of the effective dose versus the lethal or toxic dose. In animal studies, the therapeutic index for sufentanil was approximately 100 times larger than fentanyl and 300 times larger than morphine.

A non-invasive route of delivery: Zalviso utilizes a sufentanil tablet which allows for a sublingual (under the tongue) route of delivery. Sufentanil is highly lipophilic which provides for rapid absorption in the fatty cells (or mucosal tissue) found under the tongue, and for rapid transit across the blood-brain barrier to bind the mu-opioid receptors in the brain. The sublingual delivery used by Zalviso provides rapid onset of analgesia. The sublingual delivery system also eliminates the risk of IV-related analgesic gaps and IV complications, such as catheter-related infections. In addition, because patients do not require direct connection to an IV PCA infusion pump through IV tubing, Zalviso allows for ease of patient mobility.

A pre-programmed PCA solution: Zalviso allows patients to self-dose sufentanil sublingual tablets via a pre-programmed, secure system designed to eliminate the risk of programming errors.

Based on the successful results of our Phase 3 clinical program for Zalviso, we submitted an NDA for Zalviso in September 2013 and, in December 2013 we announced that the FDA accepted for filing the Zalviso NDA. As mentioned above, the FDA issued a CRL for Zalviso on July 25, 2014, and we are currently reviewing the FDA s comments and requests contained in the CRL and plan to discuss these requests with the FDA.

The 505(b)(2) NDA submission for Zalviso is based on a development program that includes data from seven Phase 1 studies, three Phase 2 clinical trials, and three Phase 3 clinical trials. The Phase 3 trial program included two placebo-controlled efficacy and safety trials and one open-label active comparator trial, in which Zalviso was compared to IV PCA with morphine. To date, the Zalviso safety database includes more than 600 patients. Zalviso successfully achieved the primary efficacy endpoints for each of these trials. A summary of the Phase 3 trials and results is as follows:

Active comparator trial (IAP 309) in November 2012, we reported top-line data demonstrating that Zalviso met its primary endpoint of non-inferiority in a Phase 3 open-label active comparator trial designed to compare the efficacy and safety of Zalviso (15 mcg/dose, 20 minute lock-out) to IV PCA with morphine (1mg/dose, 6 minute lock-out) for the treatment of moderate-to-severe acute post-operative pain immediately following major abdominal or orthopedic surgery.

Double-blind, placebo-controlled, abdominal surgery trial (IAP 310) in March 2013, we reported top-line data demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major open abdominal surgery. Adverse events reported in the trial were generally mild or moderate in nature and similar in both placebo and treatment groups. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 trial enrolled 178 adult patients at 13 U.S. sites.

Double-blind, placebo-controlled, orthopedic surgery trial (IAP 311) in May 2013, we reported top-line data demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major orthopedic surgery. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 trial enrolled 426 adult patients at 34 U.S. sites. Treatment-emergent adverse events were generally mild to moderate in nature and similar for the majority of adverse events between Zalviso and placebo-treated patients, despite the shorter duration of exposure in the placebo-treated patients caused by early termination due to inadequate analgesia.

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In December 2013, we announced a commercial collaboration with Grünenthal, covering the territory of the European Union, certain other European countries and Australia for Zalviso for use in the management of moderate-to-severe acute pain within a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the United States, Asia and Latin America.

In July 2014, Grünenthal filed a Marketing Authorization Application, or MAA, to the European Medicines Authority, or EMA, under the centralized procedure in the European Union, or EU, for Zalviso for the management of moderate-to-severe acute pain in adult patients in a medically-supervised environment.

Under the terms of the license agreement, we received an upfront cash payment of $30.0 million, and are eligible to receive a milestone payment of $5.0 million related to the MAA submission. We are eligible to receive an additional $15.0 million milestone payment upon the approval of the MAA. After approval, we are eligible to receive approximately $200.0 million in additional milestone payments, based upon successful regulatory and product development efforts and net sales target achievements. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the twenty percent range, on net sales of Zalviso in the Grünenthal territory.

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

ARX-04

We are also developing a Sufentanil Single-Dose Tablet, or ARX-04, for the treatment of moderate-to-severe acute pain to be administered by a healthcare professional to a patient in settings of acute pain, such as on the battlefield, in the emergency room or in ambulatory care facilities. In December 2013, we completed an End-of-Phase 2 Meeting with the FDA to identify a Phase 3 program pathway forward for evaluation of ARX-04. This definition of the Phase 3 program allows us to continue to refine Phase 3 protocols with the FDA, with the goal of initiating Phase 3 trials for ARX-04 before the end of 2014.

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 15mcg sufentanil tablet dosed 20 minutes apart were equivalent to one sublingual administration of an ARX-04 30mcg sufentanil tablet. The significance of this study is that we believe we can include approximately 300 patients from the Zalviso clinical program in the ARX-04 safety database. The ARX-04 safety database required by the FDA is 500 patients and, therefore, we believe this demonstration of dose equivalency will allow for a significant reduction in the number of patients necessary to enroll in the ARX-04 Phase 3 clinical program.

In April 2013, we reported top-line data showing that the primary endpoint was achieved in a placebo-controlled, dose-finding, Phase 2 clinical trial of ARX-04 for acute pain. This trial randomized 101 patients following bunionectomy surgery in a 2:2:1 ratio to 30 mcg sufentanil, 20 mcg sufentanil or placebo treatment arms. Ninety-one percent of patients entering the trial completed the 12-hour trial period.

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Results demonstrated that patients receiving 30 mcg sufentanil tablet doses, administered by a healthcare professional, no more frequently than once per hour, had significantly greater pain reduction as measured by Summed Pain Intensity Difference to baseline during the 12-hour trial period (SPID-12) than placebo-treated patients (p=0.003).

Adverse events, or AEs, reported in the trial were generally mild-to-moderate in nature, with two serious adverse events, or SAEs, of post-surgical infection reported, both of which were determined by the investigator to be unrelated to trial drug.

Research and development of ARX-04, including the Phase 2 trial and pre-Phase 3 development, was funded by a $5.6 million grant from the U.S. Army Medical Research and Materiel Command, or USAMRMC. As of December 31, 2013, we had recognized the full amount of the grant of $5.6 million.

ARX-02 and ARX-03

In addition to ARX-04, our product candidate pipeline consists of two other sufentanil-based product candidates. The Sufentanil Tablet Breakthrough Pain, or BTP, Management System, or ARX-02, is a pain management system for the treatment of cancer patients who suffer from BTP. The Sufentanil/Triazolam Tablet, or ARX-03, is a single, fixed-dose, combination drug product designed to provide mild sedation, anxiety reduction and pain relief for patients undergoing painful procedures in a physician s office. We have successfully completed Phase 2 clinical trials for ARX-02 and ARX-03. Future development of ARX-02 and ARX-03 is contingent on funding from a corporate partnership or other external funding source.

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 we pursue commercial development of our product candidates, including Zalviso, 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 Zalviso, our lead product candidate. 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 the 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 corporate collaboration and our research grants.

Our revenues to date have consisted primarily of revenues from our collaboration with Grünenthal and our research grant with the USAMRMC. We have recognized in full, as revenue, our $5.6 million grant from the USAMRMC as of December 31, 2013. There can be no assurance that we will produce other collaborative agreement revenues or receive additional funding from USAMRMC or other research-related grant awards in the future. We expect revenues to continue to fluctuate from period-to period. There can be no assurance that our existing collaboration with Grünenthal will continue beyond the initial term, or that we will be able to meet the milestones specified in this agreement or that we will obtain marketing approval for our product candidates and subsequently generate revenue from those products in excess of our operating expenses.

Our net loss for the three months and six months ended June 30, 2014 was $10.6 million and $20.2 million, respectively. As of June 30, 2014, we had an accumulated deficit of $165.7 million. As of June 30, 2014, we had cash, cash equivalents and investments totaling $92.3 million compared to $103.7 million as of December 31, 2013.

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 may borrow up to $40.0 million in three tranches, represented by secured convertible promissory notes. The Amended Loan Agreement amends and restates the loan and security agreement with Hercules dated as of June 29, 2011, or the Original Loan Agreement. We borrowed the first tranche of $15.0 million upon closing of the transaction on December 16, 2013 and used approximately $8.6 million of the proceeds from the first tranche to repay our obligations under the Original Loan Agreement with Hercules. On June 16, 2014, we borrowed the second tranche of $10.0 million, which we plan to use to provide additional funding for the commercialization of Zalviso, for clinical trials for other development programs in our pipeline and for general corporate purposes. The third tranche, of $15.0 million, can be drawn at any time between December 15, 2014 and March 15, 2015, but only if we have obtained approval for Zalviso from the FDA. The

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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 are interest only until April 1, 2015 (which will be extended until January 1, 2016, if we obtain Zalviso approval on or before April 1, 2015) followed by equal monthly payments of principal and interest through the scheduled maturity date on October 1, 2017 (which will be extended until January 1, 2018, if we obtain Zalviso approval on or prior to April 1, 2015), 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. Our obligations under the Amended Loan Agreement are secured by a security interest in substantially all of our assets, other than our intellectual property.

As of June 30, 2014, the outstanding principal owed to Hercules was $25.0 million.

Since our inception in July 2005, we have not generated any revenue from the sale of our products. As mentioned above, on July 25, 2014, the FDA issued a CRL for our NDA for Zalviso. We believe we can satisfy all of the FDA s requests in the CRL and resubmit the NDA by the end of 2014, although we will have more clarity on the process and timing after our discussion with FDA. Assuming approval of the NDA for Zalviso, we plan to prepare for the commercial launch of Zalviso in 2015; however, there is no guarantee that we will receive approval from the FDA on a timely basis, or at all, and there can be no guarantee that we will be able to produce product revenue in the foreseeable future, if ever.

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, 2013. There have been no significant changes in our critical accounting policies and estimates during the six months ended June 30, 2014 from those previously disclosed in our Annual Report on Form 10-K.

Recently Issued Accounting Standards

In May 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2014-09, *Revenue from Contracts with Customers*, issued as a new Topic, Accounting Standards Codification (ASC) Topic 606. The new revenue recognition standard provides a five-step analysis of transactions to determine when and how revenue is recognized. The core principle of the guidance is that a Company should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. This ASU is effective for AcelRx beginning in fiscal 2017 and can be adopted by us either retrospectively or as a cumulative-effect adjustment as of the date of adoption. We are currently evaluating the effect that adopting this new accounting guidance will have on our results of operations, cash flows and financial position.

Results of Operations

Three and Six Months Ended June 30, 2014 and 2013

Revenue

To date, we have not generated any commercial product revenue. We do not expect to receive any commercial sales revenue from any product candidates that we develop until we, or our collaborators, obtain regulatory approval and commercialize our products.

Collaboration Agreement

In December 2013, we announced a commercial collaboration with Grünenthal, covering the territory of the European Union, certain other European countries and Australia for Zalviso for potential use in pain treatment within or dispensed by a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the United States, Asia and Central and South America.

Under the terms of the agreement, we received an upfront cash payment of $30.0 million, and are eligible to receive a milestone payment of $5.0 million related to the MAA submission. This non-substantive, contingent milestone payment will be recognized as revenue in the third quarter of 2014, when the milestone was achieved. We are eligible to receive an additional $15.0 million milestone payment upon the approval of the MAA. After approval, we are eligible to receive approximately $200.0 million in additional milestone payments, based upon successful regulatory and product development efforts and net sales target achievements. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, on net sales of Zalviso in the Grünenthal territory.

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

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Research Grant

In May 2011, we received a grant award of $5.6 million from the USAMRMC for the development of ARX-04, a sufentanil tablet for the treatment of moderate-to-severe acute pain. Revenue related to this grant award was recognized as the related research and development expenses were incurred. As of December 31, 2013, we had completed all grant-supported research and development activities and the $5.6 million grant had been recognized in full.

Revenue for the three and six months ended June 30, 2014, was $71,000 and $166,000, respectively, all of which related to development work associated with our collaboration with Grünenthal. Revenue for the three and six months ended June 30, 2013, was $407,000 and $1.3 million, respectively, and was generated from our grant from the USAMRMC.

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. Research and development expenses included the following:

- expenses incurred under agreements with contract research organizations and clinical trial sites;
- employee- and consultant-related expenses, which include salaries, benefits and stock-based compensation;
- payments to third party pharmaceutical and engineering development contractors;
- payments to third party manufacturers; and
- 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.

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 expenditures as we seek to continue development of Zalviso, including the requisite activities associated with preparing for the potential commercialization of Zalviso. In addition, we plan to continue to incur significant research and development expenses, including the expenses associated with the continued development of ARX-04. We do not plan to continue development of ARX-02 and ARX-03, unless additional funding or corporate partnership resources are available to support these programs.

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, 2014 and 2013 (in thousands):

	Three Months Ended June 30,			Six Months Ended June 30,		
Drug Indication/Description	**2014**	**2013**	**2014 vs. 2013 Increase/ (Decrease)**	**2014**	**2013**	**2014 vs. 2013 Increase/ (Decrease)**
	(In thousands, except percentages)					
Zalviso	$ 3,578	$ 3,777	(5)%	$ 5,300	$ 10,155	(48)%

ARX-04	994	366	172%	1,700	1,261	35%
Overhead	2,712	1,965	38%	4,995	4,010	25%
Total research and development expenses	$ 7,284	$ 6,108	19%	$ 11,995	$ 15,426	(22)%

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 Zalviso and the continued development of ARX-04, 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.

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Total research and development expenses for the three and six months ended June 30, 2014 and 2013 were as follows (in thousands, except percentages):

	Three Months Ended June 30,				Six Months Ended June 30,			
	2014	2013	Change	%	2014	2013	Change	%
Research and development expenses	$ 7,284	$ 6,108	$ 1,176	19%	$ 11,995	$ 15,426	$ (3,431)	(22)%

The $1.2 million increase in research and development expenses during the three months ended June 30, 2014, as compared to the three months ended June 30, 2013, was primarily attributable to an increase of $0.7 million related to personnel related expenses, including stock-based compensation, and an increase of $0.6 million related to our ARX-04 development program.

The $3.4 million decrease in research and development expenses during the six months ended June 30, 2014, as compared to the six months ended June 30, 2013, was primarily attributable to a $4.9 million decrease related to our Zalviso Phase 3 clinical program, partially offset by an increase of $1.0 million related to personnel related expenses, including stock-based compensation, and an increase of $0.4 million related to our ARX-04 development program.

General and Administrative Expenses

General and administrative expenses consisted primarily of salaries, benefits and stock-based compensation for personnel in administration, finance, marketing and business development activities. Other significant expenses included legal expenses to pursue 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 to continue to increase as we continue to build our corporate infrastructure in support of a pre-commercial organization and continue the development of our product candidates.

Total general and administrative expenses for the three and six months ended June 30, 2014 and 2013 were as follows (in thousands, except percentages):

	Three Months Ended June 30,				Six Months Ended June 30,			
	2014	2013	Change	%	2014	2013	Change	%
General and administrative expenses	$ 5,047	$ 2,070	$ 2,977	144%	$ 8,972	$ 4,261	$ 4,711	111%

General and administrative expenses increased over both comparative periods primarily due to increased market research activities related to our Zalviso development program.

The $3.0 million increase in general and administrative expenses during the three months ended June 30, 2014, as compared to the three months ended June 30, 2013, was primarily due to an increase in market research and outside services of $2.0 million, primarily related to market research activities for Zalviso and an increase of $1.0 million, primarily in headcount-related expenses, including recruiting efforts, and consulting and professional services fees of $438,000.

The $4.7 million increase in general and administrative expenses during the six months ended June 30, 2014, as compared to the six months ended June 30, 2013, was primarily due to an increase in market research and outside services of $3.0 million, primarily related to market research activities for Zalviso, an increase of $1.7 million, primarily in headcount-related expenses, including recruiting efforts, and consulting and other professional fees of $759,000.

Interest Expense

Interest expense consisted primarily of interest accrued or paid on our debt obligation agreements and amortization of debt discounts. Total interest expense for the three and six months ended June 30, 2014 and 2013, was as follows (in thousands, except percentages):

	Three Months Ended June 30,				Six Months Ended June 30,			
	2014	2013	Change	%	2014	2013	Change	%

Interest expense	$ 530	$ 403	$ 127	32%	$ 1,002	$ 857	$ 145	17%

Interest expense for both 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 Original Loan Agreement. The

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overall debt facility was increased to $40.0 million, $25.0 million of which was outstanding as of June 30, 2014, and the maturity was extended to October 1, 2017. On June 16, 2014, we borrowed the second tranche of $10.0 million. As a result, the amount of interest expense incurred during the three and six months ended June 30, 2014, increased as compared to the three and six months ended June 30, 2013.

Interest Income and Other Income (Expense), net

Interest income and other income (expense), net, during the three and six months ended June 30, 2014 and 2013, 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.

Total interest income and other income (expense), net for the three and six months ended June 30, 2014 and 2013 was as follows (in thousands):

	Three Months Ended June 30,			Six Months Ended June 30,		
	2014	2013	Change	2014	2013	Change
Interest income and other income (expense), net	$ 2,215	$ (9,273)	$ 11,488	$ 1,597	$ (11,012)	$ 12,609

The increase in interest income and other income (expense), net, during the three and six months ended June 30, 2014, as compared to the three and six months ended June 30, 2013, of $11.5 million and $12.6 million, respectively, was primarily attributable to fewer PIPE warrants outstanding at June 30, 2014, compared to June 30, 2013, and a decrease in our stock price during the first half of 2014 as compared to a significant increase in our stock price in the first half of 2013, which is the primary driver in the Black-Scholes valuation model used to estimate the fair value of the PIPE warrants.

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 and negative cash flows in 2014 and may incur significant losses and negative cash flows for the foreseeable future. We have funded our operations primarily through the issuance of equity securities and debt financings, and more recently through our collaboration agreement with Grünenthal, which we entered into in December 2013.

As of June 30, 2014, we had cash, cash equivalents and investments totaling $92.3 million compared to $103.7 million as of December 31, 2013. The decrease was primarily attributable to cash required to fund our continuing operations, as we continue our research, development and pre-commercialization activities. We anticipate that our existing capital resources will permit us to meet our capital and operational requirements through at least 2015, excluding any potential proceeds from milestones associated with our collaboration with Grünenthal, additional cash available under our Amended Loan Agreement with Hercules conditioned upon FDA approval of Zalviso, additional financings or other corporate partnerships. We base this expectation on our current operating plan that assumes FDA approval of Zalviso and a Zalviso commercial launch in 2015. These assumptions may change as a result of many factors. For example, We may not be able to adequately address the issues raised by the FDA in the Zalviso CRL, we may be unable to resubmit the Zalviso NDA by the end of 2014, the FDA may further delay the approval of Zalviso or may never approve Zalviso. 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 if these delays are substantial.

In December 2013, we announced a commercial collaboration with Grünenthal, covering the territory of the European Union, certain other European countries and Australia for Zalviso for potential use in pain treatment within or dispensed by a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the United States, Asia and Latin America. Under the terms of the agreement, we received an upfront cash payment of $30.0 million, and are eligible to receive a milestone payment of $5.0 million related to the MAA submission, which occurred in July 2014. We are eligible to receive an additional $15.0 million milestone payment upon the approval of the MAA. After approval, we are eligible to receive approximately $200.0 million in additional milestone payments, based upon successful regulatory and product development efforts and net sales target achievements. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, on net sales of Zalviso in the Grünenthal territory.

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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 may borrow up to $40.0 million in three tranches, represented by secured convertible promissory notes. The agreement amends and restates the loan and security agreement with Hercules dated as of June 29, 2011, or the Original Loan Agreement. We borrowed the first tranche of $15.0 million upon closing of the transaction on December 16, 2013 and used approximately $8.6 million of the proceeds from the first tranche to repay our obligations under the Original Loan Agreement with Hercules. On June 16, 2014, we borrowed the second tranche of $10.0 million, which we plan to provide additional funding for the commercialization of Zalviso, as a potential source of funding for clinical trials for other development programs in our pipeline and for general corporate purposes. The third tranche of $15.0 million, can be drawn at any time between December 15, 2014 and March 15, 2015 but only if we have obtained approval of Zalviso from the FDA.

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 financial statements which are included elsewhere in this Form 10-Q (in thousands):

	Six Months Ended June 30,	
	2014	**2013**
Net cash used in operating activities	$ (19,943)	$ (19,096)
Net cash used in investing activities	(1,459)	(3,330)
Net cash provided by (used in) financing activities	10,729	(3,587)

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 lead product candidate, Zalviso. Our cash used for operating activities also reflected changes in our working capital and adjustments for non-cash charges, such as depreciation and amortization of our fixed assets, stock-based compensation, 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 $19.9 million during the six months ended June 30, 2014, reflected a net loss of $20.2 million, partially offset by aggregate non-cash charges of $887,000, and a net change of $623,000 in our net operating assets and liabilities. Non-cash charges included $1.9 million for stock-based compensation, partially offset by $1.7 million for the change in fair value of our PIPE warrant liability and contingent put liability.

Cash used in operating activities of $19.1 million during the six months ended June 30, 2013 reflected a net loss of $30.2 million, partially offset by aggregate non-cash charges of $13.2 million and a net change of $2.1 million in our net operating assets and liabilities. Non-cash charges primarily included $11.0 million for the increase in fair value of our PIPE warrant primarily due to a higher price of our common stock at June 30, 2013 compared to December 31, 2012, and $1.6 million for stock-based compensation. The net change in our operating assets and liabilities was primarily a result of a decrease in accrued liabilities of $1.7 million and a decrease in accounts payable of $0.9 million primarily related to the completion of our Phase 3 clinical trials for Zalviso.

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, 2014, cash used in investing activities of $1.5 million was primarily as a result of $4.9 million for purchases of investments and $2.0 million for purchases of property and equipment, partially offset by $5.4 million in proceeds from maturity of investments.

During the six months ended June 30, 2013, cash used in investing activities of $3.3 million was primarily as a result of $18.0 million for purchases of investments, partially offset by $14.8 million in proceeds from the maturity of investments.

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Cash Flows from Financing Activities

Cash flows from financing activities primarily reflect proceeds from the sale of our securities, proceeds from our debt financings and payments made on such debt financings. As of June 30, 2014, we had outstanding debt of $24.6 million, net of $0.4 million in amortized debt discounts.

During the six months ended June 30, 2014, cash provided by financing activities of $10.1 million was primarily due to the drawdown of the second tranche of the Hercules debt of $10.0 million.

During the six months ended June 30, 2013, cash used in financing activities of $3.6 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 the potential commercialization of Zalviso. We anticipate that our existing capital resources will permit us to meet our capital and operational requirements through at least 2015. We base this expectation on our current operating plan, which may change as a result of many factors. Our current operating plan includes continued preparation for the commercial launch of Zalviso in 2015. Our operating plan also includes the initiation of the Phase 3 clinical program and continued development of ARX-04. 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 technology and 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;
- expenditures related to our commercialization preparation of Zalviso;
- future manufacturing, selling and marketing costs related to Zalviso, if the product candidate is approved for marketing, including our contractual obligations to Grünenthal;
- the initiation, progress, timing and completion of clinical trials for our product candidates, including ARX-04;
- 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 initiation, progress, timing and completion of clinical trials for our product candidates and potential product candidates;

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 possible costs of litigation.

We will need substantial funds to:

commercialize any products we market, including Zalviso, if approved;

manufacture and market our product candidates;

conduct preclinical and clinical testing of our product candidates; and

conduct research and development programs.

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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 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 commercialization efforts of our product candidates or other operations;
- obtain funds through entering into collaboration agreements on unattractive terms; and/or
- delay, postpone or terminate planned clinical trials.

Off-Balance Sheet Arrangements

Through June 30, 2014, 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, 2014, consisted primarily of money market funds and U.S. government agency securities. We do not have any auction rate securities on our 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, 2014, 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.

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

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

From time to time we may be involved in legal proceedings arising in the ordinary course of business. We believe there is no litigation currently pending that could have, individually or in the aggregate, a material adverse effect on our results of operations or financial condition.

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, 2013.

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Risks Related to Clinical Development and Regulatory Approval

We depend substantially on the success of Zalviso, which may not receive regulatory approval or be successfully commercialized.

Since our inception in 2005, we have focused primarily on development of our lead product candidate, Zalviso™. Zalviso consists of sufentanil tablets delivered by the Zalviso System, a needle-free, handheld, patient-administered, pain management system (together, Zalviso). The success of our business depends primarily upon our ability to develop, receive regulatory approval for and commercialize Zalviso for the management of moderate-to-severe acute pain in adult patients in the hospital setting. We have not marketed, distributed or sold any products to date. Our Phase 3 program for Zalviso 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 on September 27, 2013, which the FDA then accepted for filing in December 2013.

On July 25, 2014, the U.S. Food and Drug Administration, or FDA, issued a Complete Response Letter, or CRL, for our NDA for Zalviso. Since the receipt of the CRL, we have been working on a reply and intend to meet with the FDA to discuss the items contained in the CRL. 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 the Instructions for Use for the device to address inadvertent dosing, among other items, and submission of additional data to support the shelf life of the product. We believe certain of the requests were addressed in amendments to the NDA that were submitted prior to the receipt of the CRL but, as acknowledged by the FDA, have not yet been reviewed by the FDA. While we anticipate that additional bench testing and human factors testing may be required to address certain items in the CRL, there were no requests to conduct additional human clinical studies. We believe we can satisfy all of the FDA s requests contained in the CRL and resubmit the NDA by the end of 2014, although we will have more clarity on the process and timing after our discussion with FDA. However, there is no guarantee that the information previously provided, or to be provided, to the FDA will be adequate to address the issues in the CRL. While we plan to resubmit the NDA for Zalviso, there is no guarantee that we will be successful in obtaining FDA approval of Zalviso. For example, the FDA could require us to complete further clinical, human factors, pharmaceutical, reprocessing or other studies, which could delay or preclude any approval of the NDA and would require us to obtain significant additional funding.

Our proposed trade name of Zalviso has been 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, may negatively impact our stock price and harm our business operations. 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. 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 efforts for Zalviso, which would have a material adverse effect on our business and could potentially cause us to cease operations. In addition, Grünenthal may never achieve regulatory approval for Zalviso in their licensed territories, including the EU and Australia, in which case, we would not receive development or sales milestones, or product royalties, which could have a material adverse effect on our business.

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 each of our three Zalviso Phase 3 clinical trials. However, even if we believe that the data from required Phase 3 clinical trials is positive, the FDA could analyze our data using alternative strategies and determine that the data from our trials was negative or inconclusive. Negative or inconclusive results of a Phase 3 clinical trial 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. Any such determination by the FDA would delay the timing of our commercialization plan for Zalviso and adversely affect our business operations.

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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 pre-commercial trials for Zalviso, and the Phase 2 clinical trial for ARX-04, potential future clinical trials, such as the planned ARX-04 Phase 3 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. 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 following an inspection of our clinical trial operations or trial sites by the FDA 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 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.

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 (IAP 309), 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 (IAP 310), 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 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 (IAP 311), treatment-emergent adverse events were generally mild-to-moderate in nature and similar for the majority of adverse events between sufentanil and placebo treated patients. Two patients (one each in the sufentanil 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 (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 conducted by us with our Zalviso, ARX-02, ARX-03 and ARX-04 product candidates have to date generated some AEs, but no SAEs, related to the trial drug.

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

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified 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 regulatory approval for Zalviso because it is a drug/device combination.

Zalviso is a combination product candidate with both drug and device. Zalviso is viewed as a combination product by the FDA, and both drug and device components were required for review as part of our NDA submission. There are very few examples of the FDA approval process for drug/device combination products such as 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. For example, the Zalviso CRL received from the FDA in July 2014 contains requests for additional information on the Zalviso System to ensure proper use of the device.

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After the completion of our clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize any of our product candidates, and we cannot, therefore, predict the timing of any future revenue.

We cannot commercialize any of our product candidates, including Zalviso, until the appropriate regulatory authorities, such as the FDA or the European Medicines Agency, or EMA, have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval for our product candidates. 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 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 the clinical trials submitted for a product candidate, including Zalviso, in support of an NDA were not conducted in full compliance with the applicable protocols for these trials, as well as with applicable regulations and standards, or if the FDA does not agree with our interpretation of the results of such trials, the FDA may reject the data from such trials. The FDA may audit some of our clinical trial sites to determine the integrity of our clinical data. Any rejection 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.

Regulatory authorities may not approve our product candidates even if they meet safety and efficacy endpoints in clinical trials.

The FDA and other foreign regulatory agencies, such as the EMA, can delay, limit or deny marketing approval for many reasons, including:

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

Part of the regulatory approval process includes compliance inspections of manufacturing facilities to ensure adherence to applicable regulations and guidelines. The regulatory agency may delay, limit or deny marketing approval of our product candidates as a result of such inspections.

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 their advisors may disagree with our trial design and our interpretations of data from preclinical trials 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. Our systems are designed to 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, 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.

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Even if we obtain regulatory approval for Zalviso and our other product candidates, 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 Zalviso and our other product candidates, if approved, will likely include restrictions on use due to the opioid nature of sufentanil.

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.

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Even if we obtain FDA approval for Zalviso or any of our product candidates in the United States, we may never obtain approval for or commercialize our 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, our collaborator, Grünenthal, and we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. In October 2012, we received notice from the EMA that Zalviso was eligible for centralized European review, and in July 2014, Grünenthal filed Marketing Authorization Application, or MAA, under the centralized procedure in the EU. 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. While Grünenthal does have products approved in international markets, we do not have any product candidates approved for sale 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.

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

The FDA Amendments Act of 2007 implemented safety-related changes to product labeling and require the adoption of REMS. Our product candidates, if approved, 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 information from the FDA regarding certain aspects of the 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, the launch may be delayed, the costs to commercialize Zalviso may increase substantially and the potential commercial market could be restricted. ARX-02, ARX-03 and 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.

***Recently enacted and future legislation may increase the difficulty and cost for us to commercialize our product candidates, and affect the prices we may obtain. **

In the United States and some foreign jurisdictions, the legislative landscape continues to evolve. There have been a number of legislative and regulatory changes and proposed changes regarding healthcare systems that could prevent or delay marketing approval of our product candidates, including Zalviso restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval.

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;
- new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extensions;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133.0% of the Federal Poverty Level beginning in 2014, 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;

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a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;

a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and

creation of the Independent Payment Advisory Board which, beginning in 2014, will have 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. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation s automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and will stay in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, the American Tax Payer Relief Act was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals.

Moreover, the recently enacted 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 Zalviso or any of our other 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.

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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 2014 and may continue to incur losses for the foreseeable future.*

Since our inception in 2005, we have focused primarily on development of our lead product candidate, Zalviso. We have three additional product candidates in development, the Sufentanil Tablet BTP Management System, or ARX-02, the Sufentanil/Triazolam Tablet, or ARX-03, and Sufentanil Single-Dose Acute Pain Tablet, or ARX-04. We have incurred significant net losses in each year since our inception in July 2005, and as of December 31, 2013, we had an accumulated deficit of $145.5 million. For the six months ended June 30, 2014, we had a net loss of $20.2 million and as of June 30, 2014 we had an accumulated deficit of $165.7 million.

We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. To date, we have financed our operations primarily through the sale of equity securities, debt, government grant funding and proceeds from our collaboration with 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 prepare for the potential commercialization of Zalviso and continue our research and development activities for our product candidates. To date, none of our product candidates, including Zalviso, have been commercialized, and if 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.

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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 do not anticipate generating revenues from sales of Zalviso in the United States until 2015, if ever. While we have a collaboration with Grünenthal for potential commercialization of Zalviso in Europe and Australia, we may never achieve the development milestones associated with the collaboration, and Grünenthal may never achieve regulatory approval or recognize commercial sales of Zalviso, for which we would receive sales milestone payments and product royalties. 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 Zalviso;
- launching and commercializing Zalviso, including building or contracting out, a hospital-directed sales force in the U.S. and collaborating 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, ARX-02 and ARX-03, 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. In addition, our expenses could increase beyond expectations if we are delayed in obtaining approval of, or launching Zalviso, or we are required by the FDA to perform trials in addition to those that we have 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 preclinical studies and clinical trials for our product candidates, and more recently, preparing for the potential commercialization of our lead product candidate, Zalviso. We have not yet obtained regulatory approval of any of our product candidates including Zalviso. Consequently, any predictions that are made about our future success, or viability, or evaluation of our business and prospects, may not be accurate.

***We may 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, particularly preparation for the potential commercialization of Zalviso and advancement of our other product candidates, including the ARX-04 Phase 3 clinical trials.

Future events and circumstances, including those beyond our control, may cause us to consume capital more rapidly than we currently anticipate. For example, if we are not able to launch Zalviso for sale in the United States in 2015, due to a delay in approval by the FDA, technical difficulties in our commercialization efforts or otherwise, or revenues or expenses associated with the commercialization of Zalviso are not as estimated, we will likely need to seek additional capital to continue operations. Such capital demands could be substantial. In addition, if we do not receive FDA approval to market Zalviso by March 15, 2015, we cannot draw the third tranche of $15.0 million associated with our Amended Loan Agreement with Hercules.

To raise capital, we may seek to sell additional equity or debt securities, 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;

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- 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 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 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 may borrow 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 million on June 16, 2014. The third tranche of up to $15.0 million is conditioned upon the approval of Zalviso by the FDA, and if approved, can be drawn at our option at any time between December 15, 2014 and March 15, 2015. The scheduled maturity date is October 1, 2017, which would be extended until January 1, 2018, if we obtain FDA approval of Zalviso on or prior to April 1, 2015.

We granted Hercules a first priority security interest in substantially all of our assets, with the exception of our intellectual property, 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. 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.

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 comply with cGMP and similar foreign standards;

the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;

termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;

the reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our product candidates in a timely fashion, in sufficient quantities or under acceptable terms;

the lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;

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operations of our third party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;

carrier disruptions or increased costs that are beyond our control; and

the failure to deliver our products under specified storage conditions and in a timely manner.

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

We 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. In addition, the Drug Enforcement Administration, or the DEA, may reduce, delay or refuse our quota for sufentanil, which would disrupt our supply of sufentanil citrate and cause delay in the development and commercialization of our product candidates, including Zalviso.

Manufacture of sufentanil tablets requires specialized equipment and expertise.

Ethanol, which is used in the manufacturing process for our sufentanil 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 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 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 stage development and manufacture of clinical supplies were 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 initially built out a suite within their existing buildings, and where we have conducted late stage development and manufacture of Zalviso registration stability lots, which were utilized in Phase 3 clinical trials. We have expanded, and continue to expand, the manufacturing facilities at Patheon in Cincinnati, Ohio in order to increase our production capabilities and these expansions require qualifications. Potential complications regarding the expansion of the facility and related qualifications could adversely impact our ability to produce commercial supplies in sufficient quantities, or at all. We have not yet produced commercial product out of this facility and we may encounter difficulties in production, which may adversely affect our commercial plans.

We have limited experience manufacturing the Zalviso device on a clinical scale, no experience on a commercial scale and do not own or operate a manufacturing facility.

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. The request includes provision of data demonstrating a reduction in the incidence of optical system errors which require premature drug cartridge change requirement. 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 our resubmitted NDA. We do not believe these design modifications would require additional Phase 3 clinical trials. If we are required to further modify the Zalviso device, we may incur higher costs and experience delays in the approval and ultimate commercialization of Zalviso. Furthermore, if the identified changes to the device are substantial, we may need to conduct further clinical trials in order to have the commercial device approved by the FDA.

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We have manufactured Zalviso devices and supplies on a small scale, including those needed for our Phase 3 clinical trials. We, however, have not yet manufactured Zalviso devices and supplies on a large scale, for commercial purposes. We will not begin commercial scale production of the device until after approval by the FDA. 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. 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 Zalviso devices with third party manufacturers, or may be unable to do so on acceptable terms. In addition, we may encounter production issues with our current or future contract manufacturers and other third party service providers, including the quality of the components produced, their inability to meet demand or other unanticipated delays including the scale-up and automation process, which would adversely impact our ability to supply our customers with Zalviso, if approved.

We may not be able to establish additional sources of supply for device manufacture. Such suppliers are subject to FDA regulations requiring that materials be produced under cGMPs or Quality System Regulations, or QSR, 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.

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 our Phase 3 clinical trials of Zalviso, the Phase 2 clinical trial of ARX-04, and our planned Phase 3 clinical program for ARX-04. 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 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 Zalviso, or our other product candidates. As a result, our financial results and the commercial prospects for Zalviso and 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.

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Risks Related to Commercialization of Our Product Candidates

The commercial success of Zalviso and our other product candidates, if approved, 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 Zalviso and our other product candidates, if approved, 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 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-approved label for Zalviso;
- restrictions or limitations placed on 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 hospital formulary approval;
- our ability to obtain and maintain sufficient third party coverage or reimbursement.

If Zalviso is approved, but does 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 from Zalviso 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 revenue. *

In order to commercialize any products that may be approved, including Zalviso, we must build our internal sales, marketing, distribution, managerial and other capabilities or make arrangements with third parties to perform these services. We are currently building out our commercial capabilities, including internal sales, marketing, supply chain and medical affairs departments and are active in the recruitment

process; however, if delays in, or the inability to, recruit and hire the appropriate individuals occurs, the potential success of approved product candidates, including Zalviso, could be adversely affected. In addition, we plan to enter into agreements with third parties for the distribution of approved product candidates, including 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.

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 will 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 strategy for Zalviso is to develop a hospital-directed sales force to promote the product to healthcare professionals and third-party payors in the United States. 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

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collaborations to enable the sale of Zalviso or 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;
- 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.

If we obtain approval to commercialize our products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If any of our product candidates, including Zalviso, are approved for commercialization, we intend to enter into agreements with third parties to market our product candidates outside the United States, which may require us to supply products to the third party such as our existing collaboration with Grünenthal for marketing Zalviso in European countries and Australia. We may be required to establish international operations in connection with those collaborations and in that regard 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;

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- 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 market for Zalviso and our other product candidates is characterized by intense competition and rapid technological advances. 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, academic institutions, government agencies and other public and private research organizations.

We believe that Zalviso would compete with a number of opioid-based treatment options that are currently available. 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., CareFusion Corporation, 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. Also available on the market is the Avancen Medication on Demand, or MOD, Oral PCA Device developed by Avancen MOD Corporation.

Additional potential competitors for Zalviso include products in development, including the fentanyl iontophoretic transdermal system, IONSYS, originally developed by ALZA Corporation and Ortho-McNeil Pharmaceutical, Inc., both Johnson & Johnson subsidiaries, and currently under development by The Medicines Company.

Our potential competitors for ARX-02 include products approved in the United States for cancer breakthrough pain, including: ACTIQ and FENTORA, currently manufactured by Teva Pharmaceuticals; Onsolis, currently manufactured by BioDelivery Sciences International, Inc.; Abstral, currently manufactured by ProStrakan Group plc; Lazanda, currently manufactured by Archimedes Pharma Limited; Subsys, currently manufactured by Insys Therapeutics, Inc., as well as products approved in Europe, including Instanyl, currently manufactured by Nycomed International Management GmbH. The active ingredient in all approved products for cancer breakthrough pain is fentanyl. Additional potential competitors for ARX-02 include products in late stage development for cancer breakthrough pain, such as Fentanyl TAIFUN, currently manufactured by Akela Pharma, Inc.

We are not aware of any approved or development stage non-IV sedative/analgesic products that would present competition to ARX-03. In the future, there may be products developed or approved for this market which could directly compete with ARX-03.

Competitors for ARX-04 within the military environment include intramuscular morphine injections which are marketed by a variety of generic manufacturers. Within the civilian environment, 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.

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

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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 or breakthrough pain could render Zalviso and ARX-02, respectively, non-competitive or obsolete. These and other risks may materially adversely affect our ability to attain or sustain profitable operations.

Hospital formulary approval may not be available for Zalviso 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.

Coverage and adequate reimbursement may not be available for Zalviso and our other product candidates, if approved which could make it difficult for us to sell our products profitably. *

Our ability to commercialize Zalviso, or any of our other drug candidates, if approved, 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. 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 Zalviso or any of our other product candidates, if approved. 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 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 Zalviso, or any of our other product candidates, if approved. 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 Zalviso, or any of our other product candidates, if approved.

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

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time periods, and negatively impact the revenues able to be generated from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in Zalviso and our other drug candidates, even if those drug candidates obtain marketing approval.

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

If we are found to have improperly promoted off-label uses of our product candidates, including Zalviso, if approved, 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 Zalviso, 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 can reduce the use of our product candidates, including Zalviso, if approved. *

Government agencies promulgate regulations and guidelines applicable to certain drug classes which may include the product candidates that we are developing. Recommendations of government agencies may relate to such matters as usage, dosage, route of administration and use of concomitant therapies. Regulations or guidelines suggesting the reduced use of certain drug classes which 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, or GPOs, any future revenues or future profitability could be jeopardized. *

Many end-users of pharmaceutical products have relationships with 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 a small number of GPOs if 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 Zalviso, if approved. *

We intend to rely upon pharmaceutical wholesalers in connection with the distribution of our product candidates, including Zalviso, 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.

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Risks Related to Our Business Operations and Industry

Failure to 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 the highest 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 any of our products that may be approved by the FDA in the future, including 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 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; and

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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.

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.

We have not yet produced commercial supplies of Zalviso and we may encounter difficulties in production, which may adversely affect our commercial plans it Zalviso is approved for sale in the United States.

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 will serve as a manufacturing facility for clinical and commercial supplies of sufentanil tablets. Late stage development and manufacture of registration stability lots, which were utilized in clinical trials, were manufactured at Patheon, Cincinnati. However, we have not yet produced commercial supplies at this facility and we may encounter difficulties in production at the new facility, which may adversely affect our clinical and commercial plans.

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 regulatory agencies. In addition, in January 2013, we entered into a Capital Expenditure and Equipment Agreement, or the Capital Agreement, with Patheon, relating to the manufacture of sufentanil tablets. Under the terms of the Capital Agreement, we have made and plan to make certain future modifications to Patheon s Cincinnati facility.

If Patheon cannot provide us with an adequate supply of sufentanil 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. 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 tablets must be approved by the FDA before commercial distribution from such manufacturers occurs. We do not fully control the manufacturing process of sufentanil tablets and are completely dependent on these third party manufacturing partners for compliance with the FDA 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 s strict regulatory requirements, they will not be able to secure FDA approval for their manufacturing facilities. If the FDA does not approve these facilities for the commercial manufacture of sufentanil tablets, we will need to find alternative suppliers, which would result in significant delays in obtaining FDA approval for Zalviso. These challenges may have a material adverse impact on our business, results of operations, financial condition and prospects.

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

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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 may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive or key employee might impede the progress of our research, development and commercialization objectives.

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

As of June 30, 2014, we had 44 full-time employees. We are planning for commercial launch of Zalviso, and we are expanding our employee base to increase our managerial, scientific and engineering, operational, sales, marketing, financial and other resources and to hire more consultants and contractors. Current and future growth 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 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. 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.

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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. We are the owner of record of over 25 issued patents worldwide. These issued patents cover AcelRx s sufentanil tablet, medication delivery devices and 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 sufentanil formulation patents against third party challenges and expanding our existing formulation patent portfolio to provide additional layers of patent protection, as well as extending patent protection to our proprietary delivery devices. 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 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, re-examination or other post-issuance proceedings, 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.

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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 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 or be required to pay the owner of the patent for the right to license the patented technology. 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 Office has developed new and untested 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. It is too early to tell what, if any, 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. Further, if any patents 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 be required 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

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

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

- we were the first to make the inventions covered by each of our pending patent applications;
- 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 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.

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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. 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 our NANOTAB mark in the United States, Hong Kong and Singapore, and our ACCELERATE. INNOVATE. ALLEVIATE. tagline in the United States. We have additionally applied for registration of our ZALVISO mark in the United States on an intent-to-use basis and that application has been allowed. 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. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- any delay in resubmitting the NDA for Zalviso, submitting an NDA for any of our other product candidates and any adverse development or perceived adverse development with respect to the FDA s review of any NDA;
- any adverse development or perceived adverse development with respect to the FDA s regulatory review of Zalviso;
- adverse results or delays in future clinical trials;
- inability to obtain additional funding, including funding necessary for the planned potential commercialization and manufacturing of Zalviso in the United States and advancement of clinical trials for other product candidates;
- 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 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.

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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.

Until this year 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. *

Until this year, we had a low 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 first half of 2013 was approximately 275,000 shares per day. A more active market for our stock has only recently developed and may not be sustained. For example, the average daily trading volume in our common stock on NASDAQ during the first half of 2014 was approximately 600,000 shares per day. 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, as well as rules subsequently implemented by the SEC and NASDAQ, have imposed various requirements on public companies. 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

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

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. Recently, we registered for resale 3,070,000 shares of our common stock held by certain selling stockholders on a shelf registration statement that became effective on June 12, 2014. 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 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, 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.

We are at risk of securities class action litigation.

In the past, securities 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 pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management s attention and resources, which could harm 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. As a result, 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.

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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

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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
10.1	First Amendment to Lease between Metropolitan Life Insurance Company and the Registrant, dated May 2, 2014.	8-K	001-35068	10.1	5/7/2014
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				

* 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.

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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: August 11, 2014

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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