ZOGENIX, INC.
Form 10-Q
November 08, 2012
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2012

OR

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

For the transition period from to

Commission file number: 001-34962

Zogenix, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**20-5300780**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
12400 High Bluff Drive, Suite 650	
San Diego, California	**92130**
(Address of Principal Executive Offices)	**(Zip Code)**

858-259-1165

(Registrant s Telephone Number, Including Area Code)

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. x Yes ¨ No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes 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.

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer x (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 Rule 12b-2 of the Exchange Act). ¨ Yes x No

The number of outstanding shares of the registrant s common stock, par value $0.001 per share, as of November 1, 2012 was 100,666,197.

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ZOGENIX, INC.

FORM 10-Q

For the Quarterly Period Ended September 30, 2012

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PART I FINANCIAL INFORMATION

Item 1. Financial Statements

Zogenix, Inc.

Consolidated Balance Sheets

(In Thousands)

	September 30, 2012 (Unaudited)	December 31, 2011
Assets		
Current assets:		
Cash and cash equivalents	$ 49,552	$ 56,525
Trade accounts receivable, net	5,504	4,913
Inventory, net	13,705	16,251
Prepaid expenses and other current assets	2,600	2,210
Total current assets	71,361	79,899
Property and equipment, net	13,673	14,590
Other assets	6,273	6,151
Total assets	$ 91,307	$ 100,640
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	$ 4,876	$ 5,168
Accrued expenses	12,200	10,748
Common stock warrant liabilities	24,915	345
Accrued compensation	3,803	3,805
Revolving credit facility	0	5,081
Long-term debt, current portion	0	9,758
Deferred revenue, current portion	0	8,462
Total current liabilities	45,794	43,367
Long-term debt, less current portion	28,413	42,070
Other long-term liabilities	3,811	5,891
Commitments and contingencies		
Stockholders equity		
Common stock	101	65
Additional paid-in capital	341,936	291,252
Accumulated deficit	(328,748)	(282,005)
Total stockholders equity	13,289	9,312
Total liabilities and stockholders equity	$ 91,307	$ 100,640

See accompanying notes.

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Zogenix, Inc.

Consolidated Statements of Operations

(In Thousands, except Per Share Amounts)

(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2012	2011	2012	2011
Revenue:				
Net product revenue	$ 8,453	$ 8,835	$ 26,368	$ 24,986
Contract revenue	0	1,563	8,462	4,688
Total revenue	8,453	10,398	34,830	29,674
Operating expenses:				
Cost of sales	4,249	5,482	13,478	14,333
Royalty expense	325	343	997	972
Research and development	3,660	10,134	16,005	27,540
Selling, general and administrative	10,857	14,701	37,574	42,642
Total operating expenses	19,091	30,660	68,054	85,487
Loss from operations	(10,638)	(20,262)	(33,224)	(55,813)
Other income (expense):				
Interest income	11	2	40	21
Interest expense	(3,463)	(2,470)	(8,730)	(4,984)
Change in fair value of warrant liabilities	(3,569)	546	(3,611)	546
Change in fair value of embedded derivatives	(202)	137	166	137
Other income (expense)	(1,421)	16	(1,379)	(86)
Total other income (expense)	(8,644)	(1,769)	(13,514)	(4,366)
Net loss before income taxes	(19,282)	(22,031)	(46,738)	(60,179)
Provision for income taxes	0	(7)	(5)	(20)
Net loss	$ (19,282)	$ (22,038)	$ (46,743)	$ (60,199)
Net loss per share, basic and diluted	$ (0.21)	$ (0.59)	$ (0.63)	$ (1.71)
Weighted average shares outstanding, basic and diluted	90,370	37,320	73,790	35,127

See accompanying notes.

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Zogenix, Inc.

Consolidated Statements of Cash Flows

(In Thousands)

(Unaudited)

	Nine Months Ended September 30,	
	2012	**2011**
Operating activities:		
Net loss	$ (46,743)	$ (60,199)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	4,538	3,502
Depreciation and amortization	1,172	1,192
Amortization of debt issuance costs and non-cash interest	1,898	1,289
Change in fair value of warrant liabilities	3,611	(546)
Change in fair value of embedded derivatives	(166)	(137)
Changes in operating assets and liabilities:		
Trade accounts receivable	(591)	(1,473)
Inventory, net	2,546	1,089
Prepaid expenses and other current assets	(469)	(181)
Other assets	(286)	213
Accounts payable and accrued expenses	(805)	(529)
Deferred rent	49	(44)
Deferred revenue	(8,462)	(8,411)
Net cash used in operating activities	(43,708)	(64,235)
Investing activities:		
Purchases of property and equipment	(255)	(426)
Net cash used in investing activities	(255)	(426)
Financing activities:		
Proceeds from revolving credit facility	9,900	34,353
Payments on borrowings of debt	(40,051)	(6,094)
Proceeds from exercise of common stock options	27	92
Proceeds from issuance of common stock and common stock warrants	67,114	57,985
Net cash provided by financing activities	36,990	86,336
Net (decrease) increase in cash and cash equivalents	(6,973)	21,675
Cash and cash equivalents at beginning of period	56,525	49,172
Cash and cash equivalents at end of period	$ 49,552	$ 70,847

See accompanying notes.

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Zogenix, Inc.

Notes to Consolidated Financial Statements

1. Organization and Basis of Presentation

Zogenix, Inc. (the Company) is a pharmaceutical company commercializing and developing products for the treatment of central nervous system disorders and pain. The Company s first commercial product, Sumavel® DosePro® (*sumatriptan* injection) Needle-free Delivery System, offers fast-acting, easy-to-use, needle-free subcutaneous delivery of *sumatriptan* for the acute treatment of migraine and cluster headache in a pre-filled, single-use delivery system. Sumavel DosePro was approved by the U.S. Food and Drug Administration (FDA) on July 15, 2009 and was launched in the United States in January 2010.

The Company was incorporated in the state of Delaware on May 11, 2006 as SJ2 Therapeutics, Inc. and commenced operations on August 25, 2006. On August 28, 2006, the Company changed its name to Zogenix, Inc.

The Company has incurred significant net losses since inception and has relied on its ability to fund its operations through equity financings, debt financings, revenues from the sale of its product Sumavel DosePro and proceeds from business collaborations. As the Company continues to incur losses, successful transition to profitability is dependent upon achieving a level of revenues adequate to support the Company s cost structure. This may not occur and, unless and until it does, the Company will continue to need to raise additional cash.

On July 27, 2012, the Company completed a public offering (Offering) of common stock and warrants for net proceeds of $65,363,000 (including over-allotment purchase), after deducting underwriting discounts and commissions of $4,205,000 and offering expenses of $549,000. The Company sold a total of 32,500,000 shares of its common stock and warrants to purchase 14,625,000 shares of common stock (excluding over-allotment purchase) in the Offering, at a purchase price of $1.99 per share of common stock and $0.01 per share underlying each warrant. The underwriters were granted a 30-day option to cover over-allotments, if any, to purchase up to an additional 4,875,000 shares of common stock and warrants to purchase 2,193,750 shares of common stock. The underwriters exercised their option to purchase over-allotment warrants for 1,151,235 shares of common stock concurrent with the July 27, 2012 public offering at a purchase price of $0.01 per warrant and then exercised their option with respect to 2,558,300 shares of common stock at a purchase price of $1.99 per share on a subsequent date. The warrants will be exercisable beginning on July 27, 2013 at an exercise price of $2.50 per share and will expire on July 27, 2017, which is five years from the date of issuance.

Management expects operating losses and negative cash flows to continue for at least the next several years as the Company continues to incur costs related to the continued development of its product candidates and commercialization of its approved product. Management may pursue additional opportunities to raise additional capital through public or private equity offerings, debt financings, receivables financings or through collaborations or partnerships with other companies if required to further support its planned operations. There can be no assurance that the Company will be able to obtain any source of financing on acceptable terms, or at all.

2. Summary of Significant Accounting Policies

Financial Statement Preparation and Use of Estimates

The unaudited consolidated financial statements contained in this Quarterly Report on Form 10-Q have been prepared by Zogenix, Inc. according to the rules and regulations of the Securities and Exchange Commission (SEC) and, therefore, certain information and disclosures normally included in financial statements prepared in accordance with U.S. generally accepted accounting principles (GAAP) have been omitted.

In the opinion of management, the accompanying unaudited consolidated financial statements for the periods presented reflect all adjustments, which are normal and recurring, necessary to fairly state the financial position, results of operations and cash flows. These unaudited consolidated financial statements should be read in conjunction with the audited financial statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2011 filed with the SEC on March 12, 2012.

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results may differ from those estimates.

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Principles of Consolidation

The unaudited interim consolidated financial statements include the accounts of Zogenix, Inc. and its wholly owned subsidiary Zogenix Europe Limited, which was incorporated under the laws of England and Wales in June 2010. All intercompany transactions and investments have been eliminated in consolidation. Zogenix Europe Limited s functional currency is the U.S. dollar, the reporting currency of its parent.

Fair Value Measurements

The carrying amount of financial instruments consisting of cash, trade accounts receivable, prepaid expenses and other current assets, accounts payable, accrued expenses, accrued compensation, borrowings under the revolving credit facility, and current portion of long-term debt, included in the Company s consolidated financial statements are reasonable estimates of fair value due to their short maturities. Based on the borrowing rates currently available to the Company for loans with similar terms, management believes the fair value of long-term debt approximates its carrying value. The long-term liability for the two annual tail payments due to Astellas Pharma US, Inc. (Astellas) (See Note 4) for the termination of the Company s co-promotion agreement were measured at fair value using a present value technique, which incorporated the Company s own credit risk as measured by the most recent round of debt financing with Healthcare Royalty Partners (Healthcare Royalty) (formerly Cowen Healthcare Royalty Partners II, L.P.).

Authoritative guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices in active markets;

Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly; and

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

We classify our cash equivalents within Level 1 of the fair value hierarchy because we value our cash equivalents using quoted market prices. We classify our common stock warrant liabilities and embedded derivative liabilities within Level 3 of the fair value hierarchy because they are valued using valuation models with significant unobservable inputs. Assets and liabilities measured at fair value on a recurring basis at September 30, 2012 and December 31, 2011 are as follows (in thousands):

	Fair Value Measurements at Reporting Date Using			
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
At September 30, 2012				
Assets				
Money market fund shares[1]	$ 45,592	0	0	$ 45,592
Liabilities				
Common stock warrant liabilities[2]	$ 0	0	24,915	$ 24,915
Embedded derivative liabilities[3]	$ 0	0	679	$ 679
At December 31, 2011				
Assets				
Money market fund shares[1]	$ 49,752	0	0	$ 49,752
Liabilities				
Common stock warrant liability[4]	$ 0	0	345	$ 345
Embedded derivative liabilities[3]	$ 0	0	845	$ 845

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(1) Money market fund shares are included as a component of cash and cash equivalents on the consolidated balance sheets.

(2) Common stock warrants are measured at fair value using the Black-Scholes option pricing valuation model and the assumptions identified in (4) below. The following additional assumptions were used in the Black-Scholes option pricing valuation model to measure the fair value of the warrants sold in the July 2012 Offering: (a) management s projections regarding the probability of the occurrence of an extraordinary event that would require cash settlement of the warrants; and for the valuation scenario in which an extraordinary event occurs, (b) a volatility rate of no more than 40%, as defined in the warrant agreement. Significant increases in the probability of an extraordinary event occurring would result in a significantly lower fair value measurement.

(3) Embedded derivative liabilities measured at fair value using various discounted cash flow valuation models are included as a component of other long-term liabilities on the consolidated balance sheets. The assumptions used in the discounted cash flow valuation models include: (a) management s revenue projections and a revenue sensitivity analysis based on possible future outcomes; (b) probability weighted net cash flows based on the likelihood of Healthcare Royalty receiving revenue interest payments over the term of the financing agreement; (c) probability of bankruptcy; (d) weighted average cost of capital that included the addition of a company specific risk premium to account for uncertainty associated with the Company achieving future cash flows; (e) the probability of a change in control occurring during the term of the Healthcare Royalty financing agreement; and (f) the probability of an exercise of the embedded derivative instruments. The significant unobservable inputs used in measuring the fair value of the embedded derivatives are management s revenue projections. Significant decreases in these significant inputs would result in a higher fair value measurement.

(4) Common stock warrants are measured at fair value using the Black-Scholes option pricing valuation model. The assumptions used in the Black-Scholes option pricing valuation model were: (a) a risk-free interest rate based on the rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the remaining contractual term of the warrants; (b) an assumed dividend yield of zero based on the Company s expectation that it will not pay dividends in the foreseeable future; (c) an expected term based on the remaining contractual term of the warrants; and (d) given the Company s lack of relevant historical data due to the Company s limited historical experience, an expected volatility based upon the historical volatility of comparable companies whose share prices have been publicly available for a sufficient period of time. The significant unobservable input used in measuring the fair value of the warrant liabilities is the expected volatility based upon the historical volatility of comparable companies. Significant increases in the volatility of comparable companies would result in a higher fair value measurement.

The following table provides a reconciliation of liabilities measured at fair value using significant observable inputs (Level 3) for the nine months ended September 30, 2012 (in thousands):

	Common Stock Warrant Liabilities	Embedded Derivative Liabilities
Balance at December 31, 2011	$ 345	$ 845
Issuance of common stock warrants	20,959	0
Changes in fair value	3,611	(166)
Balance at September 30, 2012	$ 24,915	$ 679

Changes in fair value of the liabilities shown in the table above are recorded through a change in fair value of warrant liabilities and change in fair value of embedded derivatives in other income (expense) in the consolidated statements of operations.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period reduced by weighted average shares subject to repurchase, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common share equivalents outstanding for the period determined using the treasury-stock method and as-if converted method, as applicable. For purposes of this calculation, stock options and warrants are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

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The following table presents the computation of basic and diluted net loss per share (in thousands, except per share amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2012	2011	2012	2011
Numerator				
Net loss	$ (19,282)	$ (22,038)	$ (46,743)	$ (60,199)
Denominator				
Weighted average common shares outstanding	90,370	37,320	73,790	35,132
Weighted average shares subject to repurchase	0	0	0	(5)
Weighted average shares outstanding, basic and diluted	90,370	37,320	73,790	35,127
Basic and diluted net loss per share	$ (0.21)	$ (0.59)	$ (0.63)	$ (1.71)

The following table presents potentially dilutive securities not included in the calculation of diluted net loss per share because to do so would be anti-dilutive (in thousands, of common equivalent shares):

	Three and Nine Months Ended September 30,	
	2012	2011
Common stock warrants	16,285	508
Common stock options and restricted stock units	9,476	3,441
	25,761	3,949

Segment Reporting

Management has determined that the Company operates in one business segment, which is the commercialization and development of pharmaceutical products.

Recent Accounting Pronouncements

In May 2011, the Financial Accounting Standards Board (FASB) issued accounting guidance related to fair value measurements and disclosures to achieve common fair value measurements and disclosures between GAAP and International Financial Reporting Standards. This guidance clarifies the application of certain existing fair value measurement guidance and expands the disclosures for fair value measurements that are estimated using significant unobservable (Level 3) inputs. This guidance is effective on a prospective basis for annual and interim reporting periods beginning on or after December 15, 2011. The Company adopted this guidance on January 1, 2012 and it did not have a material impact on the Company s results of operations.

In June 2011, the FASB issued an Accounting Standards Update which requires entities to present reclassification adjustments included in other comprehensive income on the face of the financial statements and allows entities to present the total of comprehensive income, the components of net income and the components of other comprehensive income either in a single continuous statement of comprehensive income or in two separate consecutive statements. It also eliminates the option for entities to present components of other comprehensive income as part of the statement of changes to stockholders equity. The updated guidance is effective for fiscal and interim periods beginning after December 15, 2011, with early adoption permitted. The Company adopted this guidance on January 1, 2012 and it did not have a material impact on the Company s results of operations.

3. Inventory, net (in thousands)

	September 30, 2012	December 31, 2011
Raw materials	$ 4,087	$ 5,260
Work in process	6,643	7,338
Finished goods	2,975	3,653
	$ 13,705	$ 16,251

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4. Collaboration and Financing Agreements

Mallinckrodt LLC Co-Promotion Agreement

On June 6, 2012, the Company and Mallinckrodt LLC (Mallinckrodt) entered into a co-promotion agreement (the Co-Promotion Agreement). Under the terms of the Co-Promotion Agreement, Mallinckrodt was granted a co-exclusive right (with the Company) to promote Sumavel DosePro to a mutually agreed prescriber audience in the United States. Mallinckrodt s sales team began selling Sumavel DosePro to its customer base of prescribers in August 2012. Mallinckrodt has committed to a minimum number of sales representatives for the initial term of the Co-Promotion Agreement, which runs through June 30, 2014, and can be extended by mutual agreement of the parties in additional six month increments. The Company remains responsible for the manufacture, supply and distribution of commercial product for sale in the United States. In addition, the Company will supply product samples to Mallinckrodt at an agreed upon transfer price and Mallinckrodt will reimburse the Company for all other promotional materials used.

In partial consideration of Mallinckrodt s sales efforts, the Company will pay Mallinckrodt a service fee on a quarterly basis that represents a specified fixed percentage of net sales of prescriptions generated from Mallinckrodt s prescriber audience over a baseline amount of net sales to the same prescriber audience (the Baseline Net Sales). In addition, upon completion of the co-promotion term in June 30, 2014 (unless otherwise extended), and only if the Co-Promotion Agreement is not terminated as a result of certain circumstances, the Company will be required to pay Mallinckrodt an additional tail payment calculated as a fixed percentage of the Mallinckrodt net sales over the Baseline Net Sales during the first full 12 months following the last day of the term.

Mallinckrodt may terminate the Agreement with sixty days notice in the event a material change is made to the net sales price of Sumavel DosePro that would result in a material adverse effect to Mallinckrodt s financial return (as defined in the Co-Promotion Agreement). Mallinckrodt may also terminate the Co-Promotion Agreement if its request for the inclusion on its call list of a certain number of additional prescribers is not mutually agreed upon. Lastly, Mallinckrodt may terminate the Co-Promotion Agreement if a governmental authority takes action or raises an objection that prevents or would reasonably be expected to make it unlawful for Mallinckrodt to perform, or subject Mallinckrodt to any penalty or claim, investigation or similar action related to, its obligations under the Co-Promotion Agreement, in the event of Company s inability to meet trade demand for commercial product or where a third party files an action alleging that the making or selling of Sumavel DosePro infringes the intellectual property rights of such third party.

The Company may terminate the Co-Promotion Agreement with sixty days notice if Mallinckrodt does not achieve an agreed-upon minimum sales effort. Either party may terminate the agreement if certain minimum net sales thresholds are not met for any quarter ending after December 31, 2012 or certain levels of prescriptions are not met in a specified period. In addition, either party may terminate the Co-Promotion Agreement related to safety concerns, in the event of a change of control of itself or the other party (excluding with respect to Mallinckrodt, any public spin-off of Mallinckrodt from its corporate parent Covidien plc), upon the introduction of a generic product, in connection with the material breach of the other party s obligations or if a bankruptcy event occurs under certain circumstances.

For the three and nine months ended September 30, 2012 and 2011, the Company incurred $92,000 in service fee expenses under the Co-Promotion Agreement.

Astellas Pharma US, Inc. Co-Promotion Agreement

In July 2009, the Company entered into the co-promotion agreement with Astellas (Astellas Co-Promotion Agreement). Under the terms of the agreement, the Company granted Astellas the co-exclusive right (with the Company) to market and sell Sumavel DosePro in the United States until June 30, 2013. Under the Astellas Co-Promotion Agreement, both Astellas and the Company were obligated to collaborate and fund the marketing of Sumavel DosePro and to provide annual minimum levels of sales effort directed at Sumavel DosePro during the term. On December 20, 2011, the Company entered into an amendment to the Astellas Co-Promotion Agreement, or the amended Astellas Co-Promotion Agreement, whereby the agreement terminated on March 31, 2012.

In connection with the execution of the Astellas Co-Promotion Agreement, Astellas made a non-refundable up-front payment of $2,000,000 and made an additional $18,000,000 of payments to the Company upon the achievement of a series of milestones. In consideration for Astellas performance of its commercial efforts, the Company paid Astellas a service fee on a quarterly basis that represents a fixed percentage of between 45% and 55% of Sumavel DosePro net sales to primary care physicians, OB/GYNs, emergency medicine physicians, and urologists in the United States (Astellas Segment).

In accordance with accounting guidance for revenue arrangements with multiple deliverables, the Company initially recorded the $20,000,000 in upfront and milestone payments received from Astellas as deferred revenue. Beginning with the launch of Sumavel DosePro in January 2010, the Company began amortizing the upfront and milestone payments as contract

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revenue in the consolidated statement of operations over the term of the Astellas Co-Promotion Agreement. Upon termination of the Astellas Co-Promotion Agreement, the Company concluded that the remaining deferred revenue balance should be recognized ratably through the amended term of the agreement, and consequently, the remaining $8,462,000 of these deferred contract revenues as of December 31, 2011 was recognized during the three months ended March 31, 2012. For the three months ended September 30, 2012 and 2011, the Company recognized $0 and $1,563,000, respectively, of contract revenue. For the nine months ended September 30 2012 and 2011, the Company recognized $8,462,000 and $4,688,000, respectively, of contract revenue.

The Company is required to make two annual tail payments to Astellas, calculated as decreasing fixed percentages (ranging from mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion**.** The value of such tail payments was estimated at a total of $5,291,000 based upon the agreement termination date of March 31, 2012, and recorded as a long-term liability on the amendment date of December 20, 2011. The fair value of the tail payments will be accreted through interest expense through the dates of payment in July 2013 and July 2014. As of September 30, 2012, the tail payment liability is **$**2,659,000 (including the service fee reduction discussed below), and $93,000 and $414,000 of related interest expense was recognized during the three and nine months ended September 30, 2012, respectively.

Further, under the terms of the amended Astellas Co-Promotion Agreement, Astellas contributed its agreed upon portion of marketing expenses through March 31, 2012, and continued to earn a service fee based on product sales to the Astellas Segment during that period. As of April 1, 2012, the Company was no longer required to pay service fees to Astellas for sales of Sumavel DosePro. Additionally, beginning in the second quarter of 2012, the Company s sales force assumed full responsibility for the commercialization and the continued marketing of Sumavel DosePro, expanding their focus to include headache specialists, neurologists and primary care physicians in the United States. Amounts received from Astellas for shared marketing costs and sample product are reflected as a reduction of selling, general and administrative expenses, and amounts payable to Astellas for shared marketing expenses and service fees are reflected as selling, general and administrative expenses, inclusive of the estimated cost of the tail payments owed upon the termination of the agreement.

In August 2012, the Company and Astellas completed a final reconciliation under the terms of the agreement and agreed to adjust the service fees paid to Astellas over the term of the Astellas Co-Promotion Agreement, resulting in a service fee reduction of $1,500,000, which will offset the two annual tail payments, and a reduction to the annual tail payment liability of $742,000. The present value of the service fee receivable and tail payment reduction of $1,924,000 was recorded as a reduction in selling, general and administrative expenses during the three and nine months ended September 30, 2012, and an offset to the tail payment liability. The fair value of the service fee receivable and tail payment reduction will be accreted through interest income through the dates of the two tail payments in July 2013 and July 2014.

For the three months ended September 30, 2012 and 2011, the Company recognized shared marketing expense of $0 and $400,000, respectively, under the Astellas Co-Promotion Agreement. For the nine months ended September 30, 2012 and 2011, the Company recognized shared marketing expense of $253,000 and $1,500,000, respectively. For the three months ended September 30, 2012 and 2011, and prior to the final reconciliation of service fees, the Company incurred $0 and $1,700,000 in service fee expenses, respectively. For the nine months ended September 30, 2012 and 2011, and prior to the final reconciliation of service fees, the Company incurred $1,757,000 and $4,900,000 in service fee expenses, respectively.

Healthcare Royalty Financing Agreement

On July 18, 2011, the Company closed the royalty financing agreement (the Financing Agreement) with Healthcare Royalty. Under the terms of the Financing Agreement, the Company borrowed $30,000,000 from Healthcare Royalty (the Borrowed Amount) and the Company agreed to repay such Borrowed Amount together with a return to Healthcare Royalty, as described below, out of the Company s direct product sales, co-promotion revenues and out-license revenues (collectively, Revenue Interest) that the Company may record or receive as a result of worldwide commercialization of the Company s products including Sumavel DosePro, Zohydro ER and other future products.

In addition, upon the closing of and in connection with the Financing Agreement, the Company issued and sold to Healthcare Royalty $1,500,000 of the Company s common stock, or 388,601 shares, at a price of $3.86 per share. The Company also issued to Healthcare Royalty a warrant exercisable for up to 225,000 shares of the Company s common stock. The warrant is exercisable at $9.00 per share and has a term of 10 years. As the warrant contains covenants where compliance with such covenants may be outside the control of the Company, the warrant was recorded as a current liability and marked to market at each reporting date using the Black-Scholes option pricing valuation model (see Note 2).

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Under the Financing Agreement, the Company is obligated to pay to Healthcare Royalty:

- 5% to 5.75% of the first $75,000,000 of Revenue Interest recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year (initially 5% and then 5.75% after the co-promotion agreement with Astellas terminated on March 31, 2012, with a reversion back to 5% if certain net sales of Sumavel DosePro are achieved or if Zohydro ER is commercialized in the four calendar quarters immediately following the effective date of termination);

- 2.5% of the next $75,000,000 of Revenue Interest recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year; and

- 0.5% of Revenue Interest over and above $150,000,000 recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year.

Net sales of Sumavel DosePro outside the United States are only included in the Revenue Interest if such net sales exceed $10,000,000. Once the aggregate payments, including the fixed payments described below, made by the Company to Healthcare Royalty equal $75,000,000, the percentage of Revenue Interest owed to Healthcare Royalty is reduced to 0.5% for the remainder of the term of the Financing Agreement, with only Sumavel DosePro and Zohydro ER subject to the Revenue Interest payments thereafter. The Company is also obligated to make three fixed payments of $10,000,000 on (or before at the option of the Company) each of January 31, 2015, January 31, 2016 and January 31, 2017. Unless terminated as discussed below, the Financing Agreement terminates on March 31, 2018.

The obligation of the Company to make the Revenue Interest payments during the term of the Financing Agreement are secured under a security agreement by a security interest in all assets of the Company, including intellectual property and other rights of the Company to the extent necessary or used to commercialize the Company products. Healthcare Royalty entered into an intercreditor agreement under which its security interest was junior to the security interest of the lenders under the Company s $25.0 million loan and security agreement. The intercreditor agreement terminated on July 30, 2012 when the Company terminated its $25.0 million loan and security agreement. Healthcare Royalty s security interest will be extinguished at the end of the term or once the aggregate payments made by the Company to Healthcare Royalty equal to $75,000,000, whichever is sooner. The Company has agreed to specified positive and negative covenants in connection with the Financing Agreement.

The Company has the option to terminate the Financing Agreement at the Company s election in connection with a change of control of the Company, upon the payment of a base amount of $52,500,000, or, if higher, an amount that generates a 19% internal rate of return on the Borrowed Amount as of the date of prepayment, in each case reduced by the Revenue Interest and principal payments received by Healthcare Royalty up to the date of prepayment.

Healthcare Royalty has the option to terminate the Financing Agreement at its election in connection with a change of control of the Company (which includes the sale, transfer, assignment or licensing of the Company s rights in the United States to either Sumavel DosePro or Zohydro ER), or an event of default (which includes the occurrence of a bankruptcy event or other material adverse change in the Company s business), as defined in the Financing Agreement. Upon such a termination by Healthcare Royalty, the Company is obligated to make a payment of a base amount of $45,000,000, or, if higher, an amount that generates a 17% internal rate of return on the Borrowed Amount as of the date of prepayment, in each case reduced by the Revenue Interest and principal payments received by Healthcare Royalty up to the date of prepayment.

The rights of the Company and Healthcare Royalty to terminate the Financing Agreement early meet the definition of an embedded derivative. As a result, the Company carved out these embedded derivatives from the Financing Agreement and determined the fair value of each derivative using various discounted cash flow valuation models taking into account the probability of these events occurring and various scenarios surrounding the potential Revenue Interest payments that would be made if these events occurred (see Note 2). The aggregate fair value of the embedded derivatives as of September 30, 2012 is $679,000 and is included in other long-term liabilities.

The Company received aggregate net proceeds of $29,485,000 from the Financing Agreement (including the purchase of common stock). The discounts, which are being amortized using the effective interest method over the term of the arrangement within interest expense, include the fair value of the common stock warrants issued to Healthcare Royalty of $790,000 upon the closing of the Financing Agreement, fees payable to Healthcare Royalty in connection with the execution of the arrangement of $476,000 and the fair value of embedded derivatives of $605,000 upon the closing of the Financing Agreement. The Company has recognized other income (expense) in relation to the change in the fair value of the Healthcare Royalty common stock warrant of $(23,000) and $546,000, respectively, for the three months ended September 30, 2012 and

2011, and $(65,000) and $546,000, respectively, for the nine months ended September 30, 2012 and 2011 in the statement of operations. The Company has recognized other income (expense) in relation to the change in the fair value of the embedded derivatives of $(202,000) and $137,000, respectively, for the three months ended September 30, 2012 and 2011, and $166,000 and $137,000, respectively, for the nine months ended September 30, 2012 and 2011 in the statement of operations.

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Term Debt

In June 2008, the Company entered into and borrowed $18,000,000 under the Loan and Security Agreement with Oxford and CIT Healthcare LLC (the Oxford Agreement). The obligations under the Oxford Agreement were collateralized by personal property excluding certain intellectual property and all equipment pledged to secure the equipment financing described below. In July and October 2010, the Company amended and restated the Oxford Agreement, and Oxford and Silicon Valley Bank (SVB) became party to the amended agreement. In June 2011, the Company again amended and restated the amended Oxford/SVB agreement (the Amended Oxford/SVB Agreement), which provided among other things, the addition of intellectual property to the collateral securing the Oxford/SVB loan and the deferral of principal repayment to commence on February 1, 2012.

On July 30, 2012, the Company exercised its right to terminate the Amended Oxford/SVB Agreement prior to the loan maturity date. The Amended Oxford/SVB Agreement consisted of a $25,000,000 term loan and a $10,000,000 revolving credit facility. The obligations under the Amended Oxford/SVB Agreement were collateralized by the Company s intellectual property (including among other things, copyrights, patents, patent applications, trademarks, service marks and trade secret rights) and personal property (including, among other things, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash). The $25,000,000 term loan bore an interest rate of 12.06% per annum. Under the terms of the revolving credit facility, $10,000,000 was available to be borrowed within a specified percentage of the Company s eligible accounts receivable and inventory balances (as defined in the agreement). Amounts outstanding under the revolving credit facility accrued interest payable monthly at a floating rate per annum equal to the greater of 3.29% above SVB s prime rate or 7.29%. In addition, the Company paid a monthly fee equal to 0.5% per annum of the average unused portion of the revolving credit facility. The outstanding balance of the term loan and the revolving credit facility as of December 31, 2011 was $25,000,000 and $5,100,000, respectively.

In connection with the termination of the Amended Oxford/SVB Agreement, the Company repaid $19,500,000 of outstanding principal and interest under the agreement. In addition to the repayment of all principal and interest outstanding, the Company was also required to make a final payment of $1,200,000 and a prepayment premium of $400,000, or 2% of the then outstanding principal. The Company also paid a $100,000 prepayment premium to terminate the revolving credit facility. As a result of the termination of the Amended Oxford/SVB Agreement, the lenders no longer have a security interest in the Company s intellectual property and personal property (including, among other things, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash).

5. Common Stock Warrants

In June 2011, and in connection with entering into the Amended Oxford/SVB Agreement, the Company issued to Oxford and SVB warrants exercisable into an aggregate of 26,455 shares of common stock. The warrants are exercisable at $3.78 per share of common stock and have a term of 7 years. The value of the warrants of approximately $76,000 was recorded as debt discount and additional paid in capital in the consolidated balance sheet as of December 31, 2011.

In July 2011, upon the closing of and in connection with the Financing Agreement, the Company issued to Cowen Royalty a warrant exercisable into 225,000 shares of common stock. The warrant is exercisable at $9.00 per share of common stock and has a term of 10 years. As the warrant contains covenants where compliance with such covenants may be outside of the Company s control, the warrant was recorded as a current liability and is marked to market at each reporting date. The fair value of the warrant was approximately $410,000 as of September 30, 2012 and $345,000 as of December 31, 2011.

In July 2012, and in connection with the Offering, the Company sold warrants to purchase 15,776,235 shares of common stock (including over-allotment purchase). The warrants will be exercisable beginning on July 27, 2013 at an exercise price of $2.50 per share and will expire on July 27, 2017, which is five years from the date of issuance. As the warrants contain a cash settlement feature upon the occurrence of certain events that may be outside of the Company s control, the warrants are recorded as a current liability and are marked to market at each reporting period. The fair value of the warrants was approximately $24,505,000 as of September 30, 2012.

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6. Stock-Based Compensation

The Company uses the Black-Scholes option-pricing model for determining the estimated fair value of stock-based compensation for stock-based awards to employees and the board of directors. The assumptions used in the Black-Scholes option-pricing model for the three and nine months ended September 30, 2012 and 2011 are as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2012	2011	2012	2011
Risk free interest rate	0.7% to 0.9%	1.6%	0.2% to 1.2%	1.6% to 2.6%
Expected term	5.0 to 6.1 years	6.1 years	5.0 to 6.1 years	5.0 to 6.1 years
Expected volatility	80.1% to 81.7%	80.9%	80.1% to 82.8%	72.3% to 89.7%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

The risk-free interest rate assumption was based on the rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the award being valued. The assumed dividend yield was based on the Company s expectation of not paying dividends in the foreseeable future. The weighted average expected term of options was calculated using the simplified method as prescribed by accounting guidance for stock-based compensation. This decision was based on the lack of relevant historical data due to the Company s limited historical experience. In addition, due to the Company s limited historical data, the estimated volatility was calculated based upon the historical volatility of comparable companies whose share prices have been publicly available for a sufficient period of time.

The Company recognized stock-based compensation expense as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2012	2011	2012	2011
Cost of sales	$ 53	$ 42	$ 130	$ 105
Research and development	256	209	687	540
Selling, general and administrative	1,433	1,066	3,721	2,857
Total	$ 1,742	$ 1,317	$ 4,538	$ 3,502

As of September 30, 2012, there was approximately $13,025,000 of total unrecognized compensation costs related to outstanding options, which is expected to be recognized over a weighted average period of 3.1 years.

7. Operating Lease

In April 2012, the Company entered into an operating lease for approximately 13,124 rentable square feet of office space located in San Diego, California. The Company uses the leased premises as its new corporate headquarters, and the new space replaces the Company s former San Diego office lease that expired in April 2012. The term of the lease commenced on April 23, 2012 and will expire on November 27, 2014. The initial base rent is $34,122 per month, with rent being abated for the second, third and fourth months of the lease term. The base rent will increase approximately 3% on an annual basis throughout the term. The lease also requires the Company to pay, following the first 12 lease months, additional rent consisting of a portion of common area and pass-through expenses in excess of base year amounts.

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

Forward-Looking Statements

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. These forward looking statements include, but are not limited to, statements about:

- our ability to maintain and increase market demand for, and sales of, Sumavel DosePro;
- our ability to successfully execute our sales and marketing strategy for the commercialization of Sumavel DosePro and our dependence on our collaboration with Mallinckrodt LLC to promote Sumavel DosePro to a prescriber audience in the Unites States;
- the target action date for the FDA to complete its review of the Zohydro ER NDA and the potential for, and timing of, regulatory approval of Zohydro ER by the FDA;
- the potential for delays associated with any additional data required to be submitted by us in support of our NDA for Zohydro ER;
- the progress and timing of clinical trials for Relday;
- the timing of submissions to, and decisions made by, the FDA and other regulatory agencies, including foreign regulatory agencies, and demonstrating the safety and efficacy of Zohydro ER or any other product candidates to the satisfaction of the FDA and such other agencies;
- adverse side effects or inadequate therapeutic efficacy of Sumavel DosePro that could result in product recalls, market withdrawals or product liability claims;
- the safety and efficacy of Zohydro ER and our other product candidates;
- the market potential for migraine treatments, and our ability to compete within that market;
- the goals of our development activities and estimates of the potential markets for our product candidates, and our ability to compete within those markets;
- estimates of the capacity of manufacturing and other facilities to support our product and product candidates;
- our ability to ensure adequate and continued supply of Sumavel DosePro to successfully meet anticipated market demand;
- our expected remaining third party research and development costs for Zohydro ER;

our and our licensors ability to obtain, maintain and successfully enforce adequate patent and other intellectual property protection of our products and product candidates and the ability to operate our business without infringing the intellectual property rights of others;

our ability to obtain and maintain adequate levels of coverage and reimbursement from third-party payors for Sumavel DosePro or any of our other product candidates that may be approved for sale, the extent of such coverage and reimbursement and the willingness of third-party payors to pay for our products versus less expensive therapies;

the impact of healthcare reform legislation; and

projected cash needs and our expected future revenues, operations and expenditures.

The forward-looking statements are contained principally in the sections entitled Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations. In some cases, you can identify forward-looking statements by the following words: may, will, could, would, should, expect, intend, plan, anticipate, believe, estimate, predict, project, potential, continue, ongoin terms or other comparable terminology, although not all forward-looking statements contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. We discuss many of these risks, uncertainties and other factors in this Quarterly Report on Form 10-Q in greater detail under the heading Item 1A Risk Factors.

Given these risks, uncertainties and other factors, we urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. 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 what we expect. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. We undertake no obligation to revise or update publicly any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

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DosePro®, Intraject®, Relday , Sumavel®, Zogenix and Zohydro ER are our trademarks. All other trademarks, trade names and service marks appearing in this Quarterly Report on Form 10-Q are the property of their respective owners. Use or display by us of other parties trademarks, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owner.

Unless the context requires otherwise, references in this Quarterly Report on Form 10-Q to Zogenix, we, us and our refer to Zogenix, Inc., including, as of June 7, 2010, its consolidated subsidiary.

The interim consolidated financial statements and this Management s Discussion and Analysis of Financial Condition and Results of Operations should be read in conjunction with the consolidated financial statements and notes thereto for the year ended December 31, 2011 and the related Management s Discussion and Analysis of Financial Condition and Results of Operations, both of which are contained in our Annual Report on Form 10-K for the year ended December 31, 2011.

Overview

Background

We are a pharmaceutical company commercializing and developing products for the treatment of central nervous system disorders and pain. Our first commercial product, Sumavel® DosePro® (*sumatriptan* injection) Needle-free Delivery System, was launched in January 2010. Sumavel DosePro offers fast-acting, easy-to-use, needle-free subcutaneous administration of *sumatriptan* for the acute treatment of migraine and cluster headache in a pre-filled, single-use delivery system. Sumavel DosePro is the first drug product approved by the U.S. Food and Drug Administration, or FDA, that allows for the needle-free, subcutaneous delivery of medication. In June 2012, we entered into a co-promotion agreement with Mallinckrodt pursuant to which we granted to Mallinckrodt a co-exclusive right, with us, to promote Sumavel DosePro to a mutually agreed prescriber audience in the United States, beginning in August 2012. Our lead product candidate, Zohydro ER (*hydrocodone* bitartrate, formerly ZX002) is a 12-hour extended-release formulation of *hydrocodone* without acetaminophen for the treatment of moderate to severe chronic pain requiring around-the-clock opioid therapy. We completed Phase 3 development of Zohydro ER in 2011, and we submitted the New Drug Application, or NDA, for Zohydro ER to the FDA in May 2012. In July 2012, the FDA accepted our NDA as being sufficiently complete for a full review and assigned a Prescription Drug User Fee Act (PDUFA) target date of March 1, 2013. The agency will convene an advisory committee for Zohydro ER on December 7, 2012. The advisory committee provides the FDA with independent expert advice and recommendations; however the final decision regarding approval is made by the FDA.

We are also developing Relday , a proprietary, long-acting injectable formulation of *risperidone* using Durect Corporation s SABER controlled-release formulation technology in combination with our DosePro needle-free, subcutaneous drug delivery system through a July 2011 development and license agreement with Durect. *Risperidone* is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. If successfully developed and approved, we believe Relday may be the first once-monthly, subcutaneous antipsychotic product available in a needle-free delivery system. In May 2012 we filed an investigational new drug, or IND, application with the FDA. In July 2012, we initiated our first IND clinical trial for Relday. This Phase 1 clinical trial is a single-center, open-label, safety and pharmacokinetic trial that will enroll 30 patients with chronic, stable schizophrenia or schizoaffective disorder. We expect this study to complete by the end of 2012.

In addition to Relday, we are also evaluating the market potential, formulation requirements and clinical development pathway of an additional central nervous system compound that could be paired with DosePro to enhance its commercial attractiveness. We are also seeking to capitalize on our DosePro drug delivery technology by out-licensing it to potential partners enabling them to enhance, differentiate or extend the life cycle of their proprietary injectable products. In March 2012, we entered into a Co-Marketing and Option Agreement with Battelle Memorial Institute, or Battelle, pursuant to which we granted to Battelle the exclusive right to co-market our DosePro drug delivery technology to a specified list of Battelle s pharmaceutical clients.

We have experienced net losses and negative cash flow from operating activities since inception, and as of September 30, 2012, had an accumulated deficit of $328.7 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next several years primarily as a result of the expenses incurred in connection with our efforts in seeking marketing approval for Zohydro ER, the initiation of clinical development for Relay, any additional required testing for Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro ER. As of September 30, 2012, we had cash and cash equivalents of $49.6 million.

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On July 27, 2012, we completed a public offering of common stock and warrants for net proceeds of approximately $65.4 million (including over-allotment purchase), after deducting underwriting discounts and commissions of $4.2 million and offering expenses of $0.5 million. We sold a total of 32,500,000 shares of our common stock and warrants to purchase 14,625,000 shares of common stock (excluding over-allotment purchase) in the offering, at a purchase price to the public of $1.99 per share of common stock and $0.01 per share underlying each warrant. The underwriters were granted a 30-day option to cover over-allotments, to purchase up to an additional 4,875,000 shares of common stock and warrants to purchase 2,193,750 shares of common stock, of which the underwriters exercised their option with respect to 2,558,300 shares of common stock and warrants for 1,151,235 shares of common stock. The warrants will be exercisable beginning on July 27, 2013 at an exercise price of $2.50 per share and will expire on July 27, 2017, which is five years from the date of issuance.

Although it is difficult to predict future liquidity requirements, we believe that with our cash and cash equivalents as of September 30, 2012, together with future proceeds from the sale of Sumavel DosePro, we will have sufficient resources to fund our operations for the next 12 months.

We may need to obtain additional capital to finance our operations beyond that point through debt or equity financings or through collaborations or partnerships with other companies. There can be no assurance that we will be able to obtain any source of financing on acceptable terms, or at all, if required. If we are not able to raise additional capital on terms acceptable to us, or at all, as and when needed, we may be required to reduce or curtail our operations and costs, and we may be unable to continue as a going concern. In its report on our consolidated financial statements for the year ended December 31, 2011, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern.

Mallinckrodt Co-Promotion Agreement

In June 2012, we and Mallinckrodt entered into a co-promotion agreement. Under the terms of the co-promotion agreement Mallinckrodt has committed to a minimum number of sales representatives for the initial term of the agreement, which runs through June 30, 2014, and can be extended by mutual agreement of the parties in additional six month increments. We remain responsible for the manufacture, supply and distribution of commercial product for sale in the United States. In addition, we will supply product samples to Mallinckrodt at an agreed upon transfer price and Mallinckrodt will reimburse us for all other promotional materials used.

In partial consideration of Mallinckrodt s sales efforts, we will pay Mallinckrodt a service fee on a quarterly basis that represents a specified fixed percentage of net sales of prescriptions generated from Mallinckrodt s prescriber audience over a baseline amount of net sales to the same prescriber audience, or baseline net sales. In addition, upon completion of the co-promotion term in June 30, 2014 (unless otherwise extended), and only if the co-promotion agreement is not terminated as a result of certain circumstances, we will be required to pay Mallinckrodt an additional tail payment calculated as a fixed percentage of the Mallinckrodt net sales over the baseline net sales during the first full twelve months following the last day of the term.

For the three and nine months ended September 30, 2012 and 2011, we incurred service fee expenses of $0.1 million under the co-promotion agreement.

Astellas Co-Promotion Agreement

We launched the commercial sale of Sumavel DosePro in the United States in January 2010 with our co-promotion partner, Astellas Pharma US, Inc., or Astellas. Under our co-promotion agreement with Astellas that we entered into in July 2009, or the Astellas co-promotion agreement, Astellas primarily promoted Sumavel DosePro to primary care physicians (including internal medicine, family practice and general practice), OB/GYNs, emergency medicine physicians and urologists, or collectively, the Astellas Segment, in the United States. Our sales force historically promoted Sumavel DosePro primarily to neurologists and other key prescribers of migraine medications, including headache clinics and headache specialists in the United States. We jointly shared in the cost of advertising, marketing and other promotional activities related to the Sumavel DosePro brand and were required to provide minimum levels of sales effort to promote Sumavel DosePro. In December 2011, we entered into an amendment to the Astellas co-promotion agreement, or the amended Astellas co-promotion agreement, whereby the agreement terminated on March 31, 2012.

At the inception of the Astellas co-promotion agreement and in exchange for the right to promote Sumavel DosePro, Astellas made a non-refundable up-front payment of $2.0 million to us and made aggregate additional payments of $18.0 million to us upon the achievement of a series of milestones. These proceeds are reflected as $8.5 million of deferred revenues on our consolidated balance sheet at December 31, 2011. Beginning with the launch of Sumavel DosePro in January 2010, we began recognizing these proceeds as contract revenues on a ratable basis over 42 months (the original term of the agreement). Upon amendment of the Astellas co-promotion agreement on December 20, 2011, the remaining deferred

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proceeds were recognized as contract revenues on a ratable basis over 3.4 months (the remaining term of the amended agreement). This acceleration in the recognition of the contract proceeds resulted in the recognition of $8.5 million of contract revenue during the three months ended March 31, 2012.

Under the terms of the amended Astellas co-promotion agreement, we are required to make two annual tail payments to Astellas, estimated as a total of $5.3 million, calculated as decreasing fixed percentages (ranging from a mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion. The present value of such tail payments was recorded as a long-term liability on the amendment date and is payable in July 2013 and July 2014. The fair value of the tail payments will be accreted through interest expense on a monthly basis through the date of payment. As of September 30, 2012, the long-term tail payment liability was $2.7 million (including the service fee reduction discussed below), and there was $0.1 million and $0.4 million of related interest expense recognized during the three and nine months ended September 30, 2012, respectively. Additionally, beginning in the second quarter of 2012, pursuant to a promotion transition plan, our field sales force of approximately 95 representatives assumed full responsibility from approximately 400 Astellas sales representatives for the continued marketing of Sumavel DosePro. This promotion transition expanded our focus to include a portion of the high-prescribing primary care physicians previously covered by Astellas under the Astellas co-promotion agreement.

In consideration for Astellas performance of its commercial efforts, we were required to pay Astellas a service fee on a quarterly basis that represents a fixed percentage of between 45% and 55% of Sumavel DosePro net sales to the Astellas Segment through the date of termination. Astellas paid us a fixed fee for all sample units they ordered for distribution to their sales force. Amounts received from Astellas for shared marketing costs and sample product are reflected as a reduction of selling, general and administrative expenses, and amounts payable to Astellas for shared marketing expenses and service fees are reflected as selling, general and administrative expenses.

In August 2012, we and Astellas completed a final reconciliation under the terms of the agreement and agreed to adjust the service fees paid to Astellas over the term of the co-promotion agreement, resulting in a service fee receivable of $1.5 million, which will offset the two annual tail payments, and a reduction to the annual tail payment liability of $0.7 million. The present value of the service fee receivable and tail payment reduction of $1.9 million was recorded as a reduction in selling, general and administrative expenses during the three and nine months ended September 30, 2012, and an offset to the tail payment liability. The fair value of the service fee receivable and tail payment reduction will be accreted through interest income through the dates of the two tail payments in July 2013 and July 2014.

For the three months ended September 30, 2012 and 2011, we recognized shared marketing expense of $0 and $0.4 million, respectively, and for the nine months ended September 30, 2012 and 2011, we recognized shared marketing expense of $0.3 million and $1.5 million, respectively. For the three months ended September 30, 2012 and 2011, and prior to the final reconciliation of service fees, the Company incurred $0 and $1.7 million in service fee expenses, respectively. For the nine months ended September 30, 2012 and 2011, and prior to the final reconciliation of service fees, the Company incurred $1.8 and $4.9 million in service fee expenses, respectively.

Revenues

For the three months ended September 30, 2012 and 2011, we recognized $8.5 million and $8.8 million, respectively, in net product revenues, and for the nine months ended September 30, 2012 and 2011 we recognized $26.4 million and $25.0 million, respectively, in net product revenues. For the three months ended September 30, 2012 and 2011 we recognized $0 and $1.6 million, respectively, in contract revenues, and for the nine months ended September 30, 2012 and 2011 we recognized $8.5 million and $4.7 million, respectively, in contract revenues in each case associated with license and milestone payments made to us by Astellas under the Astellas co-promotion agreement.

We sell Sumavel DosePro product in the United States to wholesale pharmaceutical distributors and retail pharmacies, or collectively, our customers, subject to rights of return. Prior to the third quarter of 2011, Sumavel DosePro had a limited sales history, and we could not reliably estimate expected returns of the product at the time of shipment. Accordingly, we deferred recognition of revenue on product shipments of Sumavel DosePro until the right of return no longer existed, which occurred at the earlier of the time Sumavel DosePro units were dispensed through patient prescriptions or expiration of the right of return. Units dispensed are generally not subject to return, except in the rare cases where the product malfunctions or the product is damaged in transit. We estimate patient prescriptions dispensed using an analysis of third-party information, including third-party market research data.

Beginning in the third quarter of 2011, we began recognizing Sumavel DosePro product sales at the time title transfers to our customer, and providing for an estimate of future product returns at that time. We believe that our estimated product return allowances for Sumavel DosePro require a high degree of judgment and are subject to change based on our experience and certain quantitative and qualitative factors. Sumavel DosePro s shelf life is determined by the shorter expiry date of its

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two subassemblies, which is currently approximately 30 months from the date of manufacture. We accept unused product from our customers that are within six months before and up to one year after its expiration date for a credit at the then-current whole acquisition cost, or WAC, reduced by a nominal fee for processing the return. Our initial product inventories reached expiration in 2011.

We have monitored actual return history on an individual product lot basis since product launch. Actual product return experience in 2011 and for the nine months ending September 30, 2012 included a disproportionately high amount of returns from a single retail chain. In addition, we have also experienced a high level of returned product from our initial launch stocking initiatives. We may experience higher levels of returns due to the termination of the Astellas co-promotion agreement on March 31, 2012 and the potential fall-off of prescription demand in territories that may no longer be supported with direct promotional efforts. We consider these factors as well as the dating of our product at the time of shipment into the distribution channel, prescription trends and changes in the estimated levels of inventory within the distribution channel to estimate our exposure for returned product. Because of the shelf life of Sumavel DosePro and our return policy of issuing credits on returned product that is within six months before and up to one year after its product expiration date, there may be a significant period of time between when the product is shipped and when we issue credits on returned product. Accordingly, we may have to adjust these estimates, which could have an effect on product sales and earnings in the period of adjustments. A 1% increase or decrease in our returns reserve as a percentage of product shipped in the three and nine months ended September 30, 2012 would have a cumulative financial statement impact of approximately $0.1 million and $0.4 million, respectively, for the three and nine months ended September 30, 2012. As our returns reserve also includes product shipped prior to 2012 that is within the product return period, our financial statements may be further affected if we experience higher levels of returns than estimated.

We permit certain wholesale pharmaceutical distributors to purchase limited quantities of product after the announcement of an increase to the WAC of our product and prior to the effectiveness of the increase. In turn, WAC price increases can result in accelerated purchases by wholesalers relative to anticipated retail and prescription demand. The timing of purchases made by wholesale distributors and retail pharmacies are subject to fluctuations for these reasons among others. Absent accelerated purchasing by wholesalers or other periodic changes in buying patterns, the wholesale channel has historically contained two to three weeks of product on hand. As of September 30, 2012, wholesale distributors reported approximately three weeks of our product on hand.

Cost of Sales

Cost of sales consist primarily of materials, third-party manufacturing costs, freight and indirect personnel and other overhead costs associated with sales of Sumavel DosePro based on units sold to wholesale pharmaceutical distributors and retail pharmacies, as well as reserves for excess, dated or obsolete commercial inventories and production manufacturing variances. For the three months ended September 30, 2012 and 2011, our cost of sales was $4.2 million and $5.5 million, respectively, and for the nine months ended September 30, 2012 and 2011 our cost of sales was $13.5 million and $14.3 million, respectively. Our product gross margin for the three months ended September 30, 2012 and 2011 was 50% and 38%, respectively, and our product gross margin for the nine months ended September 30, 2012 and 2011 was 49% and 43%, respectively.

Royalty Expense

Royalty expense consists of the amortization of the $4.0 million milestone payment paid by us to Aradigm Corporation upon the first commercial sale of Sumavel DosePro in the United States (which occurred in January 2010) and royalties payable to Aradigm based on net sales of Sumavel DosePro by us or one of our licensees. We are not required to make any further milestone payments to Aradigm. Our ongoing royalty obligation payable to Aradigm is set forth in the asset purchase agreement we entered into with Aradigm in August 2006 pursuant to which we acquired the rights to the DosePro technology. During each of the three months ended September 30, 2012 and 2011, we incurred $0.3 million in royalty expense to Aradigm, and during each of the nine months ended September 30, 2012 and 2011, we incurred $1.0 million in royalty expense to Aradigm.

Research and Development Expenses

Our research and development expenses consist of expenses incurred in developing, testing and seeking marketing approval of our product candidates, including:

- payments made to Durect for the license to and further development of Relday;

milestone payments made to Alkermes in connection with development and regulatory milestones of Zohdyro;

payments made to third-party contract research organizations, or CROs, and investigational sites, which conduct our trials on our behalf, and consultants;

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expenses associated with regulatory submissions, pre-clinical development and clinical trials;

payments to third-party manufacturers, which produce our active pharmaceutical ingredient and finished product;

payments made to third-party CROs, laboratories and consultants in connection with pre-clinical studies;

personnel related expenses, such as salaries, benefits, travel and other related expenses, including stock-based compensation; and

facility, maintenance, depreciation and other related expenses.

We expense all research and development costs as incurred.

In March 2010, we initiated our Phase 3 clinical development program for Zohydro ER. We utilize CROs, contract laboratories and independent contractors for the conduct of pre-clinical studies and clinical trials. We track third party costs by type of study being conducted. We recognize the expenses associated with the services provided by CROs based on the percentage of each study completed at the end of each reporting period. We coordinate clinical trials through a number of contracted investigational sites and recognize the associated expense based on a number of factors, including actual and estimated subject enrollment and visits, direct pass-through costs and other clinical site fees. For the three months ended September 30, 2012 and 2011, we incurred $1.3 million and $4.9 million in third party research and development costs related to Zohydro ER, respectively. For the nine months ended September 30, 2012 and 2011, we incurred $8.4 million and $17.8 million in third party research and development costs related to Zohydro ER, respectively. The third party research and development costs for the nine months ended September 30, 2012 included $1.8 million in fees related to the submission of the NDA for Zohydro ER to the FDA and $1.0 million for a milestone payment made to Alkermes in connection with the NDA submission.

In July 2012 we initiated our first IND clinical trial for Relday. Under the Relday license agreement, Durect is responsible for non-clinical, formulation, chemistry, and manufacturing and controls development for Relday. We paid a non-refundable upfront fee to Durect of $2.25 million in July 2011. In addition, we incurred $0.1 million and $1.7 million in research and development costs payable to Durect during the three and nine months ended September 30, 2012, respectively.

We use our employee and infrastructure resources across our product and product candidate development programs. Therefore, we have not tracked salaries, other personnel related expenses, facilities or other related costs to our product development activities on a program-by-program basis. The following table illustrates, for each period presented, our research and development costs broken down by our major development programs, as well as other expenses not tracked on a program-by-program basis, as described above, and expenses associated with all other product candidates:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2012	2011	2012	2011
	(In Thousands)		(In Thousands)	
Research and development expenses:				
Zohydro	$ 1,253	$ 4,926	$ 8,380	$ 17,820
Relday	700	3,051	2,779	4,257
Sumavel DosePro	236	146	581	349
Other[(1)]	1,471	2,011	4,265	5,114
Total	$ 3,660	$ 10,134	$ 16,005	$ 27,540

(1) Other research and development expenses include development costs incurred for the DosePro technology sound enhancement and other product candidate development, as well as employee and infrastructure resources that are not tracked on a program-by-program basis.

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We expect our research and development costs for 2012 to decrease over amounts incurred in 2011 as we completed the Phase 3 clinical trials for Zohydro ER in December 2011. We incurred the cost of a $1.0 million milestone payment to Alkermes in the second quarter of 2012 in connection with the submission of the NDA for Zohydro ER to the FDA. We may be obligated to pay Alkermes up to $2.8 million in total additional future milestone payments with respect to Zohydro ER depending upon the achievement of other various development and regulatory events. These future milestone payments include a payment of $0.8 million upon successful completion of an FDA pre-approval inspection of our manufacturing facility and a payment of $2.0 million upon the first NDA approval of Zohydro ER. If Zohydro ER is approved, we are also required to pay a mid single-digit percentage royalty on its net sales for a specified period of time and continue to pay royalties on net sales of the product thereafter at a reduced low single-digit percentage rate in accordance with the terms of the license agreement.

While we submitted an NDA for Zohydro ER with the FDA early in the second quarter of 2012, and the FDA accepted our NDA in July 2012 as being sufficiently complete for a full review, the successful development and commercialization of Zohydro ER is highly uncertain. We also expect to incur customary regulatory costs associated with the NDA, which will be significant. If Zohydro ER is approved, we also expect to incur significant expenses related to manufacturing and marketing activities. However, at this time, we cannot reasonably estimate or know the nature, specific timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of Zohydro ER after submission of our NDA filing, if or when Zohydro ER will receive regulatory approval and, if approved, if and when material net cash inflows may commence from Zohydro ER or the amount of any such inflows. This is due to the numerous risks and uncertainties associated with developing and commercializing drugs, including the uncertainty of:

- the costs, timing and outcome of regulatory review of Zohydro ER;
- the costs, timing and outcome of any additional pre-clinical studies and clinical trials for Zohydro ER, if required;
- the scope of the Risk Evaluation and Mitigation Strategy for Zohydro ER and the timing and costs associated therewith;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the potential for future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development and commercialization plans and capital requirements;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the emergence of competing technologies and products and other adverse marketing developments;
- the effect on our product development activities of actions taken by the FDA or other regulatory authorities; and
- our degree of success in commercializing Zohydro ER, if approved.

A change in the outcome of any of these variables with respect to the development of Zohydro ER could mean a significant change in the costs and timing associated with these efforts.

We also expect to incur costs associated with clinical studies for our early-stage product candidates. We expect to incur total research and development costs of approximately $0.5 million to $1.0 million in the last three months of 2012 for initial clinical studies for Relday.

Selling, General and Administrative Expenses

Our selling expenses, which include sales and marketing costs, consist primarily of salaries and benefits of sales and marketing management and sales representatives, shared marketing and advertising costs and service fees under our Astellas co-promotion agreement prior to its termination in March 2012, sample product costs, and consulting fees.

Our general and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, accounting, business development and internal support functions. In addition, general and administrative expenses include facility costs and professional fees for legal, consulting and accounting services. We do not expect a significant change in general and administrative expense in 2012 as compared to 2011 levels.

Interest Income

Interest income consists of interest earned on our cash and cash equivalents.

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Interest Expense

Interest expense consists of interest or revenue interest costs incurred in connection with our $30.0 million royalty financing agreement, or the Healthcare Royalty financing agreement, with Healthcare Royalty Partners (formerly Cowen Healthcare Royalty Partners II, LP), or Healthcare Royalty, our $10.0 million revolving credit facility with Oxford Finance Corporation, or Oxford, and Silicon Valley bank, or SVB, our $25.0 million loan and security agreement, or the amended Oxford/SVB loan agreement, the $4.5 million borrowed under our loan and security agreement with General Electric Capital Corporation, or GE Capital, and non-cash interest expense associated with amortization of debt discount and debt issuance costs, the estimated cost of revenue interest payments calculated under the effective interest method, and imputed interest from the two annual tail payments to Astellas. The outstanding principal balance of the GE Capital agreement was repaid in full on June 30, 2011. Further, the revolving credit facility and the amended Oxford/SVB loan agreement were repaid in full and terminated in July 2012.

We expect that interest expense will increase over 2011 levels due to a full year of borrowing under our $30.0 million Healthcare Royalty financing agreement that we entered into in July 2011, and the recognition of imputed interest from the two annual tail payments to Astellas related to the termination of our Astellas co-promotion agreement.

Change in Fair Value of Warrant Liabilities

Change in fair value of warrant liabilities represents non-cash expense associated with the changes in the fair value of the warrants to purchase common stock issued in connection with our July 2012 public offering and issued in connection with our Healthcare Royalty financing agreement.

Change in Fair Value of Embedded Derivatives

Change in fair value of embedded derivatives represents non-cash income from changes in the fair value of the embedded derivatives associated with the Healthcare Royalty financing agreement.

Other Income (Expense)

Other income (expense) consists of costs related to the issuance of warrants during our public offering in July 2012 and foreign currency transaction gains and losses. All of our revenues are currently generated in U.S. dollars while a majority of our manufacturing expenses are payable in foreign currencies, primarily U.K. pounds sterling and the Euro.

Provision for Income Taxes

Income tax expense primarily consists of costs related to the taxable income generated by our wholly-owned subsidiary, Zogenix Europe Limited.

Internal Control Over Financial Reporting

Assessing our staffing and training procedures to improve our internal control over financial reporting is an ongoing process. For the year ending December 31, 2012, pursuant to Section 404 of the Sarbanes-Oxley Act, management is required to deliver a report that assesses the effectiveness of our internal control over financial reporting. Pursuant to Section 404(c) of the Sarbanes-Oxley Act, our independent registered public accounting firm will be required to deliver an attestation report on the effectiveness of our internal control over financial reporting for the year ending December 31, 2012 as we will be an accelerated filer.

Critical Accounting Policies and Estimates

There have been no significant changes in critical accounting policies during the nine months ended September 30, 2012, as compared to the critical accounting policies described in *Item 7 Management s Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies and Significant Judgments and Estimates* in our Annual Report on Form 10-K for the year ended December 31, 2011.

Results of Operations

Comparison of the three months ended September 30, 2012 and 2011

Revenue. Revenue for the three months ended September 30, 2012 was $8.5 million and $10.4 million for the three months ended September 30, 2011. Product revenue for the three months ended September 30, 2012 and 2011 was $8.5 million and $8.8 million, respectively. During the third quarter of 2011, we began to recognize net product sales upon the shipment of product to wholesale pharmaceutical distributors and retail pharmacies because we had developed sufficient

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historical experience and data to reasonably estimate future returns of Sumavel DosePro. Prior to the third quarter of 2011, we recognized product revenue based on product dispensed to patients as estimated by independent third party data providers, which amounts were recorded net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs, as applicable. As a result, product revenue for the three months ending September 30, 2012 and 2011 consists of Sumavel DosePro shipped to wholesale distributors and retail pharmacies, net of product-related discounts, allowances and product returns. The aggregate $0.4 million, or 4%, decrease in net product revenue is primarily due to a decrease in unit volume of 12%, partially offset by an increase in our average selling price per unit of approximately 8%. This increase in our average selling price per unit was driven by a reduction of $1.0 million in net product sales for the three months ended September 30, 2011 in connection with the establishment of an estimate for returned product and the recognition of previously reported deferred product revenues as of June 30, 2011, offset by an increase of 9% in sales allowances as a percentage of gross product revenue through increased third-party payor contracting/rebates and patient incentives.

Contract revenue for the three months ended September 30, 2012 and 2011 was $0 and $1.6 million, respectively. Contract revenue represents amortization of license fee payments and milestone payments we received in connection with the Astellas co-promotion agreement we entered into in July 2009 and which we began recognizing upon the commencement of sales of Sumavel DosePro in January 2010. On December 20, 2011, we amended the Astellas co-promotion agreement whereby the agreement terminated on March 31, 2012, rather than the initial termination date of June 30, 2013. Based upon this revised termination date, all deferred contract revenue was recognized ratably on an accelerated basis, from the date of the amendment through March 31, 2012.

Cost of Sales. Cost of sales for the three months ended September 30, 2012 was $4.2 million and $5.5 million for the three months ended September 30, 2011. Product gross margin for the three months ended September 30, 2012 was 50% compared to 38% for the three months ended September 30, 2011. Cost of sales represents the cost of Sumavel DosePro units recognized as net product revenues in the period and the impact of underutilized production capacity (if any) and other manufacturing variances. The increase in product gross margin of 12% was primarily a result of a decrease in excess capacity charges of our contract manufacturing organizations and an increase in our average selling price per unit during the three months ended September 30, 2012 as compared to the three months ended September 30, 2011.

Royalty Expense. Royalty expense was $0.3 million for each of the three months ended September 30, 2012 and 2011. Royalty expense represents the amortization of a $4.0 million milestone payment we made in connection with the asset purchase agreement with Aradigm payable on the first commercial sale of Sumavel DosePro, which occurred in January 2010, as well as royalties payable to Aradigm from net sales of Sumavel DosePro during the period.

Research and Development Expenses. Research and development expenses decreased to $3.7 million for the three months ended September 30, 2012 compared to $10.1 million for the three months ended September 30, 2011. This decrease of $6.4 million was primarily due to:

- a decrease of $3.6 million in third party research and development costs related to the Phase 3 clinical trials for Zohydro ER which were initiated in March 2011 and completed in December 2011, including the $0.8 million milestone payment to Alkermes that was paid during the three months ended September 30, 2011 in connection with the completion of Study 801;
- a decrease of $2.3 million as a result of the onetime non-refundable upfront fee paid to Durect in July 2011 upon execution of the Relday license agreement; and
- a decrease of $0.5 million in other development expenses primarily related to the development of our other product candidates and costs related to our employee and infrastructure resources that are not tracked on a program-by-program basis.

Selling, General and Administrative Expenses. Selling, general and administrative expenses decreased to $10.9 million for the three months ended September 30, 2012 compared to $14.7 million for the three months ended September 30, 2011. Selling expenses were $7.3 million for the three months ended September 30, 2012 compared to $11.5 million for the three months ended September 30, 2011. General and administrative expenses were $3.6 million for the three months ended September 30, 2012 compared to $3.2 million for the three months ended September 30, 2011. The decrease of $3.8 million in selling, general and administrative expenses primarily was due to:

a decrease of $4.2 million in sales and marketing expense primarily as a result of a $3.7 million decrease in service fees to Astellas due to the termination of the co-promotion agreement on March 31, 2012 and resulting reduction of service fees paid over the life of the agreement, and a decrease of $1.9 million in other advertising and promotional activities, offset by $1.2 million increase in sampling efforts due to the new co-promotion agreement with Mallinckrodt and $0.2 million increase in sales force costs; offset by

an increase of $0.4 million of general and administrative expenses primarily as a result of $0.6 million increase in personnel related costs related to non-cash stock-based compensation charges and recruiting costs and $0.2 million increase in public relations efforts, offset by $0.4 million decrease in professional service related costs, such as legal and accounting and advisory services.

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Interest Income. Interest income increased to $11,000 for the three months ended September 30, 2012 compared to $2,000 for the three months ended September 30, 2011. This increase of $9,000 was due primarily to the increase in average cash and cash equivalent balances.

Interest Expense. Interest expense increased to $3.5 million for the three months ended September 30, 2012 compared to $2.5 million for the three months ended September 30, 2011. The increase of $1.0 million was due primarily to:

- an increase of $0.7 million in the amortization of Oxford/SVB debt discount and acquisition fees and an increase of $0.6 million in final payment and prepayment fees from the termination of our Oxford/SVB loan agreement in July 2012;
- an increase of $0.1 million in revenue interest payments related to the $30.0 million borrowed from Healthcare Royalty and $0.1 million in accrued non-cash interest expense based on our estimate of future revenue interest payments on this facility; and
- an increase of $0.1 million in non-cash interest expense related to imputed interest from the two annual tail payments payable to Astellas; offset by
- a decrease of $0.6 million in interest expense due to the termination of our Oxford/SVB loan agreement in July 2012.

Change in Fair Value of Warrant Liabilities. Change in fair value of warrant liabilities resulted in $3.6 million of non-cash expense during the three months ended September 30, 2012, which was due to the $3.6 million change in fair value of the warrant liability established in connection with the July 2012 public equity offering and $23,000 change in fair value of the warrant established in connection with the Healthcare Royalty financing agreement in July 2011, compared to $0.5 million of non-cash income during the three months ended September 30, 2011, which was due to the change in fair value of the warrant liability established in connection with the Healthcare Royalty financing agreement.

Change in Fair Value of Embedded Derivatives. Change in fair value of embedded derivatives resulted in $0.2 million of non-cash expense during the three months ended September 30, 2012, compared to $0.1 million of non-cash income during the three months ended September 30, 2011, which was due to the change in fair value of the embedded derivatives associated with the Healthcare Royalty financing agreement in July 2011.

Other Income (Expense). Other income (expense) was $1.4 million of expense for the three months ended September 30, 2012 compared to $16,000 of income for the three months ended September 30, 2011. Changes in other income (expense) were primarily due to $1.4 million of expense incurred in July 2012 from the issuance of warrants in our public offering, slightly offset by foreign currency transaction gains which primarily related to the settlement of our liabilities payable in Euro and U.K pound sterling.

Comparison of the nine months ended September 30, 2012 and 2011

Revenue. Revenue for the nine months ended September 30, 2012 was $34.8 million and $29.7 million for the nine months ended September 30, 2011. Product revenue for the nine months ended September 30, 2012 and 2011 was $26.4 million and $25.0 million, respectively. During the third quarter of 2011, we began to recognize net product sales upon the shipment of product to wholesale pharmaceutical distributors and retail pharmacies because we had developed sufficient historical experience and data to reasonably estimate future returns of Sumavel DosePro. Prior to the third quarter of 2011, we recognized product revenue based on product dispensed to patients as estimated by independent third party data providers, which amounts were recorded net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs, as applicable. As a result, product revenue for the six months ended June 30, 2011 represents product revenue based on product dispensed to patients net of product-related discounts and allowances, as applicable, with the three months ended September 30, 2011 consisting of Sumavel DosePro shipped to wholesaler distributors and retail pharmacies, net of product-related discounts, allowances and product returns, as applicable. Product revenue for the nine months ending September 30, 2012 consists of Sumavel DosePro shipped to wholesale distributors and retail pharmacies, net of product-related discounts, allowances and product returns, as applicable.

The aggregate $1.4 million, or 6%, increase in net product revenue is primarily due to an increase in unit volume of approximately 13%, partially offset by a decrease in our average selling price per unit of approximately 8%. This decrease in our average selling price per unit was driven by charges related to estimated product returns and an 18% increase in sales allowances as a percentage of gross product revenue through

increased third-party payor contracting/rebates and patient incentives.

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Contract revenue for the nine months ended September 30, 2012 and 2011 was $8.5 million and $4.7 million, respectively. Contract revenue represents amortization of license fee payments and milestone payments we received in connection with the Astellas co-promotion agreement we entered into in July 2009 and which we began recognizing upon the commencement of sales of Sumavel DosePro in January 2010. On December 20, 2011 we amended our Astellas co-promotion agreement whereby the agreement terminated on March 31, 2012, rather than the initial termination date of June 30, 2013. Based upon this revised termination date, all deferred contract revenue was recognized ratably on an accelerated basis, from the date of the amendment through March 31, 2012.

Cost of Sales. Cost of sales for the nine months ended September 30, 2012 was $13.5 million and $14.3 million for the nine months ended September 30, 2011. Product gross margin for the nine months ended September 30, 2012 was 49% compared to 43% for the nine months ended September 30, 2011. Cost of sales represents the cost of Sumavel DosePro units recognized as net product revenues in the period and the impact of underutilized production capacity (if any) and other manufacturing variances. The improvement in product gross margin of 6% was primarily a result of a decrease in excess capacity charges of our contract manufacturing organizations, partially offset by a decrease in our average selling price per unit during the nine months ended September 30, 2012 as compared to the nine months ended September 30, 2011.

Royalty Expense. Royalty expense was $1.0 million for each of the nine months ended September 30, 2012 and 2011. Royalty expense represents the amortization of a $4.0 million milestone payment we made in connection with the asset purchase agreement with Aradigm payable on the first commercial sale of Sumavel DosePro, which occurred in January 2010, as well as royalties payable to Aradigm from net sales of Sumavel DosePro during the period.

Research and Development Expenses. Research and development expenses decreased to $16.0 million for the nine months ended September 30, 2012 compared to $27.5 million for the nine months ended September 30, 2011. This decrease of $11.5 million primarily was due to:

- a decrease of $9.4 million in third party research and development costs related to the Phase 3 clinical trials for Zohydro ER, which were initiated in March 2010 and completed in December 2011, which included $1.8 million in fees related to the submission of the NDA for Zohydro ER to the FDA in May 2012, $1.0 million for a milestone payment to Alkermes in connection with the NDA submission in May 2012 and $0.8 million for a milestone payment to Alkermes in connection with the completion of Study 801 of the Zohydro ER Phase 3 clinical trials;

- a decrease of $2.3 million as a result of the onetime non-refundable upfront fee paid to Durect in July 2011 upon execution of the Relday license agreement; and

- a decrease of $0.9 million in other development expenses primarily related to the development of our other product candidates and costs related to our employee and infrastructure resources that are not tracked on a program-by-program basis; offset by

- an increase of $0.8 million in research and development costs related to the pre-clinical studies and formulation and stability testing for Relday; and

- an increase of $0.3 million in research and development expenses primarily related to Sumavel DosePro publications.

Selling, General and Administrative Expenses. Selling, general and administrative expenses decreased to $37.6 million for the nine months ended September 30, 2012 compared to $42.6 million for the nine months ended September 30, 2011. Selling expenses were $27.4 million for the nine months ended September 30, 2012 compared to $32.9 million for the nine months ended September 30, 2011. General and administrative expenses were $10.2 million for the nine months ended September 30, 2012 compared to $9.7 million for the nine months ended September 30, 2011. The decrease of $5.0 million in selling, general and administrative expenses primarily was due to:

- a decrease of $5.5 million in sales and marketing expense primarily as a result of $5.1 million decrease in service fees to Astellas due to the termination of the co-promotion agreement on March 31, 2012 and resulting reduction of service fees paid over the life of the agreement, and a decrease of $2.2 million in other advertising and promotional activities, offset by $1.8 million increase in sales

force costs due to an increase in the average number of sales representatives; and

an increase of $0.5 million of general and administrative expenses primarily as a result of a $1.1 million increase in personnel costs consisting of an increase of $0.5 million in non-cash stock-based compensation charges, an increase of $0.4 million in salary expenses and an increase of $0.2 million in recruiting costs, and a $0.3 million increase in public relation efforts, offset by a $0.9 million decrease in professional service related costs, such as legal and accounting and advisory services.

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Interest Income. Interest income increased to $40,000 for the nine months ended September 30, 2012 compared to $21,000 for the nine months ended September 30, 2011. This increase of $19,000 was due primarily to the increase in average cash and cash equivalent balances.

Interest Expense. Interest expense increased to $8.7 million for the nine months ended September 30, 2012 compared to $5.0 million for the nine months ended September 30, 2011. The increase of $3.7 million was due primarily to:

- an increase of $0.3 million in revenue interest payments related to the $30.0 million borrowed from Healthcare Royalty and $2.6 million in accrued non-cash interest expense based on our estimate of future revenue interest payments on this facility;
- an increase of $0.7 million in the amortization of Oxford/SVB debt discount and acquisition fees and an increase of $0.6 million in final payment and prepayment fees from the termination of our Oxford/SVB loan agreement in July 2012; and
- an increase of $0.4 million in non-cash interest expense related to imputed interest from the two annual tail payments payable to Astellas; offset by
- a decrease of $0.9 million in interest expense due to the termination of our Oxford/SVB loan agreement in July 2012.

Change in Fair Value of Warrant Liabilities. Change in fair value of warrant liabilities resulted in $3.6 million of non-cash expense during the nine months ended September 30, 2012, which was due to the $3.6 million change in fair value of the warrant liability established in connection with the July 2012 public equity offering and $65,000 change in fair value of the warrant established in connection with the Healthcare Royalty financing agreement in July 2011, compared to $0.5 million of non-cash income during the nine months ended September 30, 2011, which was due to the change in fair value of the warrant liability established in connection with the Healthcare Royalty financing agreement.

Change in Fair Value of Embedded Derivatives. Change in fair value of embedded derivatives resulted in $0.2 million and $0.1 million of non-cash income during the nine months ended September 30, 2012 and 2011, respectively, which was due to the change in fair value of the embedded derivatives associated with the Healthcare Royalty financing agreement in July 2011.

Other Income (Expense). Other income (expense) was $1.4 million of expense for the nine months ended September 30, 2012 compared to $86,000 of expense for the nine months ended September 30, 2011. The increase in other expense was primarily due to $1.4 million of expense incurred in July 2012 from the issuance of warrants in our public offering, slightly offset by foreign currency transaction gains during the nine months ended September 30, 2012 which primarily related to the settlement of our liabilities payable in Euro and U.K pound sterling.

Liquidity and Capital Resources

We have experienced net losses and negative cash flow from operating activities since inception, and as of September 30, 2012, had an accumulated deficit of $328.7 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next several years primarily as a result of the expenses incurred in connection with our efforts in seeking marketing approval for Zohydro ER, the clinical development for Relay, any additional required testing for Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro ER. As of September 30, 2012, we had cash and cash equivalents of $49.6 million.

On July 27, 2012, we completed a public offering of common stock and warrants for net proceeds of approximately $65.4 million (including over-allotment purchase), after deducting under writer discounts and commissions of $4.2 million and offering costs of $0.5 million.

Since inception, our operations have been financed primarily through equity and debt financings, the issuance of convertible notes and payments received from Astellas under our Astellas co-promotion agreement. Through September 30, 2012, we received aggregate net cash proceeds of approximately $340.6 million from the sale of shares of our preferred and common stock, including the following recent financing transactions:

in July 2011, we entered into the Healthcare Royalty financing agreement pursuant to which we sold 388,601 shares of our common stock, resulting in $1.4 million of net proceeds;

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- in September 2011 and October 2011, we issued and sold a total of 30,711,566 shares of common stock in a follow-on public offering, including shares issued upon the exercise of the underwriters option to purchase shares, for aggregate net proceeds of $57.9 million; and

- in July 2012, we issued and sold a total of 35,058,300 shares of common stock and warrants to purchase 15,776,235 shares of common stock in a public offering, including the underwriters over-allotment purchase, for aggregate net proceeds of $65.4 million.

On July 30, 2012, we terminated our amended Oxford/SVB loan agreement. The amended Oxford/SVB Agreement consisted of a $25.0 million term loan and a $10.0 million revolving credit facility. The obligations under the amended Oxford/SVB loan agreement were collateralized by our intellectual property (including among other things, copyrights, patents, patent applications, trademarks, service marks and trade secret rights) and personal property (including, among other things, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash). The $25.0 million term loan bore an interest rate of 12.06% per annum. Under the terms of the revolving credit facility, $10.0 million was available to be borrowed within a specified percentage of our eligible accounts receivable and inventory balances (as defined in the agreement). Amounts outstanding under the revolving credit facility accrued interest payable monthly at a floating rate per annum equal to the greater of 3.29% above SVB s prime rate or 7.29%. In addition, we paid a monthly fee equal to 0.5% per annum of the average unused portion of the revolving credit facility. As of December 31, 2011, the outstanding balance of the term loan was $25.0 million and the outstanding balance of the revolving credit facility was $5.1 million.

In connection with the repayment of the amended Oxford/SVB loan agreement, we repaid $19.5 million of outstanding principal and interest under the agreement. In addition to the repayment of all principal and interest outstanding, we were also required to make a final payment of $1.2 million and a prepayment premium of $0.4 million, or 2% of the then outstanding principal. We also paid a $0.1 million prepayment premium to terminate the revolving credit facility. As a result of the termination of the amended Oxford/SVB loan agreement, the lendors no longer have a security interest in our intellectual property and personal property (including, among other things, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash).

On July 18, 2011, we closed the Healthcare Royalty financing agreement. Under the terms of the Healthcare Royalty Financing agreement, we borrowed $30.0 million and we are obligated to repay such borrowed amount together with a specified return to Healthcare Royalty, through the payment of tiered royalties ranging from .5% to 5% of our direct product sales, co-promotion revenues and out-license revenues, or collectively, revenue interest, that we may record or receive as a result of worldwide commercialization of our products including Sumavel DosePro, Zohydro ER and other future products. Pursuant to the terms of the Healthcare Royalty financing agreement, our royalty rate increased to 5.75% in April 2012 in connection with the early termination of the Astellas co-promotion agreement, with a reversion back to 5% if certain net sales of Sumavel DosePro are achieved or if Zohydro ER is commercialized in the four calendar quarters immediately following the effective date of termination.

We are also obligated to make three fixed payments of $10.0 million on (or before at our option) each of January 31, 2015, January 31, 2016 and January 31, 2017. Prepayment requires the consent of the lenders under the amended Oxford/SVB loan agreement while balances remain outstanding under that facility.

We have the option to terminate the Healthcare Royalty financing agreement at our election in connection with a change of control of our company, upon the payment of a base amount of $52.5 million, or, if higher, an amount that generates a 19% internal rate of return on the borrowed amount as of the date of prepayment, in each case reduced by the revenue interest and principal payments received by Healthcare Royalty up to the date of prepayment.

Healthcare Royalty has the option to terminate the Healthcare Royalty financing agreement at its election in connection with a change of control of our company (which includes the sale, transfer, assignment or licensing of our rights in the United States to either Sumavel DosePro or Zohydro ER), or an event of default (which includes the occurrence of a bankruptcy event or other material adverse change in our business), as defined in the Healthcare Royalty financing agreement. Upon such a termination by Healthcare Royalty, we are obligated to make a payment of a base amount of $45.0 million, or, if higher, an amount that generates a 17% internal rate of return on the borrowed amount as of the date of prepayment, in each case reduced by the Revenue Interest and principal payments received by Healthcare Royalty up to the date of prepayment. Unless terminated earlier as discussed above, the Healthcare Royalty financing agreement terminates on March 31, 2018.

Any requirement that we repay the borrowed amount under the Healthcare Royalty financing agreement, whether as the result of our default under the applicable agreement or otherwise, could have a material adverse effect on our business, results of operations and financial condition.

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Cash and Cash Equivalents. Cash and cash equivalents totaled $49.6 million and $56.5 million at September 30, 2012 and December 31, 2011, respectively.

The following table summarizes our cash flows from (used in) operating, investing and financing activities for the nine months ended September 30, 2012 and 2011:

	Nine Months Ended September 30,	
	2012	2011
	(In Thousands)	
Statement of Cash Flows Data:		
Total cash provided by (used in):		
Operating activities	$ (43,708)	$ (64,235)
Investing activities	(255)	(426)
Financing activities	36,990	86,336
(Decrease) increase in cash and cash equivalents	$ (6,973)	$ 21,675

Operating Activities: Net cash used in operating activities was $43.7 million and $64.2 million for the nine months ended September 30, 2012 and 2011, respectively. Net cash used for the nine months ended September 30, 2012 and 2011 primarily reflects the use of $35.7 million and $54.9 million, respectively, for operations (excluding non-cash items), which includes personnel-related costs, research and development costs (primarily related to the development of Zohydro ER and Relday), sales and marketing expenses for Sumavel DosePro and other professional services. Net cash used for the nine months ended September 30, 2012 and 2011 also includes the use of $10.5 million and $10.4 million, respectively, for other working capital uses, offset by $2.5 million and $1.1 million, respectively, in the reduction of commercial inventory of Sumavel DosePro.

Investing Activities. Net cash used in investing activities was $0.3 million for the nine months ended September 30, 2012 and $0.4 million for the nine months ended September 30, 2011. These amounts are the result of the purchase of property and equipment primarily for use in manufacturing Sumavel DosePro.

We expect to incur capital expenditures of approximately $0.2 million to $0.7 million in the last three months of 2012. These planned capital expenditures primarily relate to further investments in our manufacturing operations in support of the sound enhancement version of the DosePro technology and toward enhancing our existing manufacturing technology and equipment.

Financing Activities. Net cash provided by financing activities was $37.0 million for the nine months ended September 30, 2012 and $86.3 million for the nine months ended September 30, 2011. Net cash provided by financing activities for the nine months ended September 30, 2012 relates to $67.1 million in net proceeds from the issuance of common stock and common stock warrants primarily during our July 2012 public offering, and $9.9 million of net proceeds provided by our revolving credit facility with Oxford/SVB, offset by payments of $40.0 million on our borrowed debt, including $21.1 million to terminate our $25.0 million term debt with Oxford/SVB and payments of $0.1 million to terminate our revolving credit facility with Oxford/SVB. Net cash provided by financing activities for the nine months ended September 30, 2011 relates to the net proceeds received from the issuance of common stock in our follow-on public offering in September 2011 of $56.6 million, net proceeds received in connection with the Healthcare Royalty financing agreement of $29.5 million, net proceeds received from our revolving credit facility with Oxford/SVB of $6.3 million, and proceeds from the exercise of options to purchase common stock of $0.1 million, offset by payments on borrowings of debt of $6.2 million.

Our sources of liquidity include our cash balances and cash receipts from the sale of Sumavel DosePro. Through September 30, 2012, we received aggregate net cash proceeds of approximately $340.6 million from the sale of shares of our preferred and common stock. As of September 30, 2012, we had $49.6 million in cash and cash equivalents. Other potential sources of near-term liquidity include entering into a commercialization agreement for Zohydro ER or a licensing arrangement for Relday.

Successful transition to profitability is dependent upon achieving a level of product revenues adequate to support our cost structure. We will continue to monitor and evaluate our sales progress, the level of our research, development, manufacturing, sales and marketing and general and administrative expenditures and may adjust such expenditures based upon a variety of factors, such as our available cash, our ability to obtain additional cash, the results and progress of our Sumavel DosePro commercialization efforts, results and progress in our clinical program, the

time and costs related to clinical trials and regulatory decisions, as well as the U.S. economic environment.

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As described above, we have agreed to specified positive and negative covenants under the Healthcare Royalty financing agreement and upon a termination by Healthcare Royalty, we are obligated to make a payment of a base amount of $45.0 million, or, if higher, an amount that generates a 17% internal rate of return on the borrowed amount as of the date of prepayment, in each case reduced by the payments received by Healthcare Royalty up to the date of prepayment. If we were required to accelerate the payment of these amounts upon a default, we would be required to find an alternate source of capital from which to draw funds and there can be no assurances that we would be able to do so on terms acceptable to us, or at all.

If we fail to pay amounts owing under the Healthcare Royalty financing agreement when due, if we breach our other covenants or obligations under the agreement, or if other events of default under the agreement occur, Healthcare Royalty would be entitled to demand immediate repayment of all borrowings and other obligations thereunder and to seize and sell the collateral pledged as security under the agreements to satisfy those obligations. If we were to breach our covenants and obligations and we were unable to obtain a waiver or amendment from the lender, we would be required to seek additional equity or debt financing to refinance our obligations under the agreement. Additional debt or equity financing may not be available to us in amounts or on terms we consider acceptable, or at all. In that regard, we have from time to time been required to obtain waivers and amendments under our debt instruments in order to avoid breaches or other defaults. For example, in each of 2010, 2011 and 2012 we were required to obtain amendments or waivers under our credit facilities.

We cannot be certain if, when and to what extent we will generate positive cash flow from operations from the commercialization of our product and, if approved, product candidates. We expect our expenses to be substantial and to increase over the next few years as we continue to grow the Sumavel DosePro brand and continue to advance our Zohydro ER product potentially through commercialization, and as we potentially advance Relday through clinical development.

Although it is difficult to predict future liquidity requirements, we believe that with our cash and cash equivalents as of September 30, 2012, together with future proceeds from the sale of Sumavel DosePro, we will have sufficient resources to fund our operations for the next 12 months.

We may need to obtain additional capital to finance our operations beyond that point through debt or equity financings or through collaborations or partnerships with other companies. There can be no assurance that we will be able to obtain any source of financing on acceptable terms, or at all, if required. If we are not able to raise additional capital on terms acceptable to us, or at all, as and when needed, we may be required to reduce or curtail our operations and costs, and we may be unable to continue as a going concern. In its report on our consolidated financial statements for the year ended December 31, 2011, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern. In addition, the fact that we have pledged substantially all of our assets to secure our existing loan facility will likely increase the cost, perhaps substantially, of any additional debt financing we may obtain or prevent us from obtaining additional debt financing altogether.

Recent Accounting Pronouncements

In May 2011, the Financial Accounting Standards Board, or FASB, issued accounting guidance related to fair value measurements and disclosures to achieve common fair value measurements and disclosures between GAAP and International Financial Reporting Standards. This guidance clarifies the application of certain existing fair value measurement guidance and expands the disclosures for fair value measurements that are estimated using significant unobservable (Level 3) inputs. This guidance is effective on a prospective basis for annual and interim reporting periods beginning on or after December 15, 2011. We adopted this guidance on January 1, 2012 and it did not have a material impact on our results of operations.

In June 2011, the FASB issued an Accounting Standards Update which requires entities to present reclassification adjustments included in other comprehensive income on the face of the financial statements and allows entities to present the total of comprehensive income, the components of net income and the components of other comprehensive income either in a single continuous statement of comprehensive income or in two separate consecutive statements. It also eliminates the option for entities to present components of other comprehensive income as part of the statement of changes to stockholders equity. The updated guidance is effective for fiscal and interim periods beginning after December 15, 2011, with early adoption permitted. We adopted this guidance on January 1, 2012 and it did not have a material impact on our results of operations.

Off-Balance Sheet Arrangements

We have not engaged in any off-balance sheet activities.

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Item 3. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

Our cash and cash equivalents as of September 30, 2012 consisted of cash and money market funds. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. The primary objective of our investment activities is to preserve principal. Instruments that meet this objective include commercial paper, money market funds and government and non-government debt securities. Some of the investment securities available-for-sale 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 securities available-for-sale to fluctuate. To minimize this risk, we intend to continue to maintain our portfolio of cash and money market funds. Due to the short-term nature of our investments and our ability to hold them to maturity, we believe that there is no material exposure to interest rate risk.

Foreign Exchange Risk

All of the revenues we have generated to date have been paid in U.S. dollars and we expect that our revenues will continue to be generated primarily in U.S. dollars for at least the next several years. Payments to our material suppliers and contract manufacturers are denominated in the Euro and U.K. pounds sterling, thereby increasing our exposure to exchange rate gains and losses on non-U.S. currency transactions. Foreign currency gains and losses associated with these expenditures have not been significant to date. However, fluctuations in the rate of exchange between the U.S. dollar and these or other foreign currencies could adversely affect our financial results in the future, particularly to the extent we increase production to support Sumavel DosePro sales demands. For the nine months ended September 30, 2012, approximately $12.5 million (based on exchange rates as of September 30, 2012) of our materials purchased and contract manufacturing costs were denominated in foreign currencies. We do not currently hedge our foreign currency exchange rate risk. As a result, we are exposed to gains and/or losses as the exchange rate of certain foreign currencies fluctuates. A 10% increase or decrease in the average rate of the Euro or the U.K. pound sterling during the nine months ended September 30, 2012 would have resulted in approximately $0.5 million or $0.8 million in gains or losses, respectively. In addition, we maintain funds in foreign bank accounts denominated in the Euro and U.K. pounds sterling, thereby further increasing our exposure to exchange rate gains and losses. We intend to evaluate various options to mitigate the risk of financial exposure from transacting in foreign currencies in the future.

Item 4. Controls and Procedures

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the timelines specified in the 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 timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Securities and Exchange Commission Rule 13a-15(b), 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 report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of September 30, 2012 at the reasonable assurance level.

Changes in Disclosure Controls and Procedures

There were no changes in our internal control over financial reporting during the fiscal quarter ended June 30, 2012 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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PART II OTHER INFORMATION

Item 1. Legal Proceedings

We are not currently a party to any legal proceedings.

Item 1A. Risk Factors

We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. Certain factors may have a material adverse effect on our business prospects, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this Quarterly Report on Form 10-Q and our other public filings with the Securities and Exchange Commission, or SEC. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

We have marked with an asterisk (*) those risk factors that reflect substantive changes from the risk factors included in our previously filed Annual Report on Form 10-K for the year ended December 31, 2011.

Risks Related to Our Business and Industry

We are at an early stage of commercialization and have a history of significant net losses and negative cash flow from operations. We cannot predict if or when we will become profitable and anticipate that our net losses and negative cash flow from operations will continue for at least the next several years.*

We were organized in 2006, have a limited operating history and there is little historical basis upon which to assess how we will respond to competitive, economic or technological challenges. Our business and prospects must be considered in light of the risks and uncertainties frequently encountered by pharmaceutical companies in the early stages of commercialization.

We have generated substantial net losses and negative cash flow from operations since our inception in 2006. For example, for the nine months ended September 30, 2012 and the years ended 2011 and 2010, we incurred net losses of $46.7 million, $83.9 million and $73.6 million, respectively, our net cash used in operating activities was $43.7 million, $80.5 million and $72.0 million, respectively, and, at September 30, 2012, our accumulated deficit was $328.7 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next several years primarily as a result of the expenses incurred in connection with our efforts in seeking marketing approval for Zohydro ER, the initiation of clinical development for Relay, any additional required testing for Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro ER. Our ability to generate revenues from Sumavel DosePro or any of our product candidates will depend on a number of factors, including, in the case of Sumavel DosePro, the factors described in the following two risk factors and, in the case of our product candidates, our ability to successfully complete clinical trials, obtain necessary regulatory approvals and negotiate arrangements with third parties to help finance the development of, and market and distribute, any product candidates that receive regulatory approval. In addition, we will be subject to the risk that the marketplace will not accept our products.

Because of the numerous risks and uncertainties associated with our product development and commercialization efforts, we are unable to predict the extent of our future losses or when or if we will become profitable and it is possible we will never become profitable. Our failure to increase sales of Sumavel DosePro or to successfully commercialize any of our product candidates that may receive regulatory approval would likely have a material adverse effect on our business, results of operations, financial condition and prospects and could result in our inability to continue operations.

We may require additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.*

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Our operations have consumed substantial amounts of cash since inception. To date, our operations have been primarily financed through the proceeds from the issuance of our common and preferred stock, including the proceeds from our initial public offering completed in November 2010, our follow-on public offerings completed in September 2011 and July 2012, and borrowings under our loan and financing agreements with Healthcare Royalty Partners, or Healthcare Royalty, Oxford Finance LLC, as successor in interest to Oxford Finance Corporation, or Oxford, and Silicon Valley Bank, or SVB. Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of September 30, 2012, together with future proceeds from the sale of Sumavel DosePro, will be sufficient resources to fund our operations for the next 12 months. We may need to obtain additional funds to finance our operations beyond that point in order to:

- maintain our sales and marketing activities for Sumavel DosePro;
- qualify secondary sources for the manufacturing of Sumavel DosePro;
- fund our operations, fund development of Zohydro ER, if required, Relday and any other product candidate to support potential regulatory approval of marketing applications; and
- commercialize Zohydro ER or any of our product candidates or any products or product candidates that we may develop, in-license or otherwise acquire, if any of these product candidates receive regulatory approval.

In addition, our estimates of the amount of cash necessary to fund our business and development and commercialization activities may prove to be wrong, and we could spend our available financial resources much faster than we currently expect. Our future funding requirements will depend on many factors, including, but not limited to:

- the commercial success of Sumavel DosePro;
- the timing of regulatory approval, if granted, of Zohydro ER or any other product candidates and the commercial success of any approved products;
- the rate of progress and cost of our clinical trials and other product development programs for Relday and our other product candidates and any other product candidates that we may develop, in-license or acquire;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with Sumavel DosePro, Zohydro ER, Relday and any of our other product candidates;
- the costs and timing of completion of outsourced commercial manufacturing supply arrangements for any product candidate;
- the costs of maintaining and expanding our sales and marketing infrastructure or establishing distribution capabilities;
- the effect of competing technological and market developments; and

the terms and timing of any additional collaborative, licensing, co-promotion or other arrangements that we may establish.

In its report on our consolidated financial statements for the year ended December 31, 2011, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern. A going concern opinion means, in general, that our independent registered public accounting firm has substantial doubt about our ability to continue our operations without continuing infusions of capital from external sources and this opinion could impair our ability to finance our operations through the sale of debt or equity securities or commercial bank loans.

Until we can generate a sufficient amount of product revenue and cash flow from operations and achieve profitability, we expect to finance future cash needs through public or private equity offerings, debt financings, receivables financings or corporate collaboration and licensing arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unsuccessful in raising additional required funds, we may be required to significantly delay, reduce the scope of or eliminate one or more of our development programs or our commercialization efforts, or cease operating as a going concern. We also may be required to relinquish, license or otherwise dispose of rights to product candidates or products that we would otherwise seek to develop or commercialize ourselves on terms that are less favorable than might otherwise be available. If we raise additional funds by issuing equity securities, substantial dilution to existing stockholders would result. If we raise additional funds by incurring debt financing, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to operate our business. If we are unable to maintain sufficient financial resources, including by raising additional funds when needed, our business, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern.

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We are largely dependent on the commercial success of Sumavel DosePro and although we have generated revenue from sales of Sumavel DosePro, we may never significantly increase these sales or become profitable.*

We anticipate that, for at least the next several years, or until we receive regulatory approval and commercialize Zohydro ER, if at all, our ability to generate revenues and become profitable will depend in large part on the commercial success of our only marketed product, Sumavel DosePro, which in turn, will depend on several factors, including our ability to:

- successfully maintain and increase market demand for, and sales of, Sumavel DosePro through our sales and marketing efforts and those of Mallinckrodt, our new collaboration partner;
- obtain greater acceptance of Sumavel DosePro by physicians and patients;
- maintain adequate levels of coverage and reimbursement for Sumavel DosePro from commercial health plans and government health programs, which we refer to collectively as third-party payors, particularly in light of the availability of other branded and generic competitive products;
- maintain compliance with regulatory requirements;
- establish and maintain agreements with wholesalers and distributors on commercially reasonable terms;
- maintain commercial manufacturing arrangements with third-party manufacturers as necessary to meet commercial demand for Sumavel DosePro and continue to manufacture commercial quantities at acceptable cost levels; and
- successfully maintain intellectual property protection for Sumavel DosePro.

We cannot be certain that our continued marketing of Sumavel DosePro will result in increased demand for, and sales of, the product. For example, while we have generally experienced annual growth in total prescriptions from the launch of Sumavel DosePro in January 2010 through December 31, 2011, we have at certain times experienced a reduction in total and new prescriptions month over month. If we and Mallinckrodt fail to successfully maintain and increase sales of Sumavel DosePro, we may be unable to generate sufficient revenues to grow or sustain our business and we may never become profitable, and our business, financial condition and results of operations will be materially adversely affected.

We may not be successful in executing our sales and marketing strategy for the commercialization of Sumavel DosePro, including as a result of the termination of our collaboration with Astellas in March 2012. As part of this strategy, we will be dependent on our collaboration with Mallinckrodt to promote Sumavel DosePro primarily to primary care physicians and physicians specializing in internal medicine. If we are unable to successfully execute such strategy, we may not be able to generate significant revenue.*

Prior to the launch of Sumavel DosePro in January 2010, we built a commercial sales and marketing organization including sales, marketing, communications, managed markets, trade and distribution functions, which is now focused exclusively on marketing and selling Sumavel DosePro primarily to physicians, nurses and other healthcare professionals in the United States. Our field sales force includes approximately 95 sales representatives who have historically promoted Sumavel DosePro primarily to neurologists and other prescribers of migraine medications, including headache clinics and headache specialists in the United States.

To complement our sales force, we entered into an exclusive co-promotion agreement with Astellas in July 2009 under which Sumavel DosePro was promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists, or collectively the Astellas Segment, in the United States by approximately 400 Astellas sales representatives. This agreement terminated on March 31, 2012, and beginning in the second quarter of 2012 our sales force assumed full responsibility for the continued promotion of Sumavel DosePro. We have expanded

the focus of our existing sales force to include targeting a portion of the high-prescribing primary care physicians previously part of the Astellas Segment. We also entered into a new co-exclusive (with us) co-promotion agreement with Mallinckrodt in June 2012, or the Mallinckrodt co-promotion agreement, under which in August 2012 Mallinckrodt began promoting Sumavel DosePro to a mutually agreed prescriber audience in the United States. Mallinckrodt has committed to a minimum number of sales representatives for the initial term of the co-promotion agreement. Although we believe we have adequately sized our sales force in order to reach our historically targeted audience, our existing sales force, along with the collaboration of Mallinckrodt s sales force, may be unable to effectively target these additional primary care physicians.

Although the Mallinckrodt co-promotion agreement stipulates minimum levels of sales effort, we have limited control over the amount and timing of resources that Mallinckrodt dedicates to the promotion of Sumavel DosePro, and we do not hire or manage such resources. The ability to generate revenue from our arrangement with Mallinckrodt depends on Mallinckrodt s efforts in promoting Sumavel DosePro and its ability to achieve broad market acceptance and prescribing of Sumavel DosePro in its targeted physician segment.

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We are subject to a number of additional risks associated with our dependence on our co-promotion arrangement with Mallinckrodt, including:

- Mallinckrodt could fail to devote sufficient resources to the promotion of Sumavel DosePro, including by failing to develop, deploy or expand its sales force as necessary;
- Mallinckrodt could fail to comply with applicable regulatory guidelines with respect to the promotion of Sumavel DosePro, which could result in administrative or judicially imposed sanctions, including warning letters, civil and criminal penalties, and injunctions; and
- disputes regarding the co-promotion agreement that negatively impact or terminate the commercialization efforts of Mallinckrodt may negatively impact or prevent the generation of sufficient revenue or result in significant litigation or arbitration.

Under the terms of the Mallinckrodt co-promotion agreement, Mallinckrodt may terminate the agreement with 60 days notice in the event a material change is made to the net sales price of Sumavel DosePro that would result in a material adverse effect to Mallinckrodt s financial return, as defined in the co-promotion agreement. Mallinckrodt may also terminate the co-promotion agreement if its request for the inclusion on its call list of a certain number of additional prescribers is not mutually agreed upon. Lastly, Mallinckrodt may terminate the co-promotion agreement if a governmental authority takes action or raises an objection that prevents or would reasonably be expected to make it unlawful for Mallinckrodt to perform, or subject Mallinckrodt to any penalty or claim, investigation or similar action related to, its obligations under the co-promotion agreement, in the event of our inability to meet trade demand for commercial product or where a third party files an action alleging that the making or selling of Sumavel DosePro infringes the intellectual property rights of such third party.

In addition, the initial term of our co-promotion agreement with Mallinckrodt expires on June 30, 2014, subject to extension of additional six month increments by mutual agreement of both parties. We cannot assure you that Mallinckrodt will enter into any extension of the co-promotion agreement or, if it does so, that it will not condition any such extension upon changes in the co-promotion agreement that could have a material adverse effect on us. If Mallinckrodt were to terminate the co-promotion agreement or elect not to extend the agreement upon its expiration, we would lose the efforts of their sales force, and we may be required to make arrangements with another third party to replace Mallinckrodt s sales force, or expand our sales and marketing organization. We may not be able to enter into such arrangements with third parties in a timely manner, on acceptable terms or at all. To the extent that we enter into another co-promotion or other licensing arrangement, our portion of retained product revenues is likely to be lower than if we directly marketed and sold Sumavel DosePro solely on our own, and a portion of those revenues generated will depend upon the efforts of such third parties similar to our dependence on Mallinckrodt, and these efforts may not be successful. If our co-promotion agreement with Mallinckrodt is terminated and we are unable to find another partner for the promotion of Sumavel DosePro in the primary care segment in the United States, we may not be able to expand our own sales and marketing capabilities or utilize our existing sales force effectively, to cover this segment and any such expansion could, in any event, substantially increase our expenses and capital requirements that we might not be able to fund.

If we are unable to successfully implement our commercialization plans and drive adoption by patients and physicians of Sumavel DosePro through our sales, marketing and commercialization efforts and the efforts of Mallinckrodt, then we will not be able to generate significant revenue which will have a material adverse effect on our business, results of operations, financial condition and prospects.

If Sumavel DosePro, and, if approved, Zohydro ER and Relday, or any other product candidate for which we receive regulatory approval does not achieve broad market acceptance or coverage by third-party payors, the revenues that we generate will be limited.

The commercial success of Sumavel DosePro, and, if approved, Zohydro ER and Relday, or any other product candidates for which we obtain marketing approval from the FDA or other regulatory authorities will depend upon the acceptance of these products by physicians, patients, healthcare payors and the medical community. Coverage and reimbursement of our approved product by third-party payors is also necessary for commercial success. The degree of market acceptance of Sumavel DosePro and any other product candidates for which we may receive regulatory approval will depend on a number of factors, including:

- our ability to provide acceptable evidence of safety and efficacy;

acceptance by physicians and patients of the product as a safe and effective treatment;

the relative convenience and ease of administration;

the prevalence and severity of adverse side effects;

limitations or warnings contained in a product s FDA-approved labeling;

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- the clinical indications for which the product is approved;
- in the case of product candidates that are controlled substances, the U.S. Drug Enforcement Agency, or DEA, scheduling classification;
- availability and perceived advantages of alternative treatments;
- any negative publicity related to our or our competitors products;
- the effectiveness of our or any current or future collaborators sales, marketing and distribution strategies;
- pricing and cost effectiveness;
- our ability to obtain sufficient third-party payor coverage or reimbursement; and
- the willingness of patients to pay out of pocket in the absence of third-party payor coverage.

For example, while we believe the needle-free nature of our DosePro technology will appeal to patients, some patients may not react favorably to the subcutaneous delivery of drug products by DosePro. Our experience indicates that some patients will experience pain upon injection with the DosePro technology and/or reactions at the site of injection. Any undesirable side effects have the potential to limit market acceptance of our product candidates.

In addition, products used to treat and manage pain, especially in the case of opioids, are from time to time subject to negative publicity, including political influences, illegal use, overdoses, abuse, diversion, serious injury and death. These events have led to heightened regulatory scrutiny. Controlled substances are classified by the DEA as Schedule I through V substances, with Schedule I substances being prohibited for sale in the United States, Schedule II substances considered to present the highest risk of abuse and Schedule V substances being considered to present the lowest relative risk of abuse. Zohydro ER contains *hydrocodone*, and we anticipate it will be regulated as a Schedule II controlled substance, and despite the strict regulations on the marketing, prescribing and dispensing of such substances, illicit use and abuse of *hydrocodone* is well-documented. Thus, the regulatory approval process and the marketing of Zohydro ER may generate public controversy that may adversely affect regulatory approval and market acceptance of Zohydro ER.

Our efforts to educate the medical community and third-party payors on the benefits of Sumavel DosePro, and, if approved, Zohydro ER and Relday or any of our other product candidates for which we obtain marketing approval from the FDA or other regulatory authorities and gain broad market acceptance may require significant resources and may never be successful. If our products do not achieve an adequate level of acceptance by physicians, third-party payors and patients, we may not generate sufficient revenue from these products to become or remain profitable.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our current and any future partners, contractors and consultants are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. For example, we have experienced failures in our information systems and computer servers in the past, which may have been the result of a cyber-attack. These failures resulted in an interruption of our normal business operations and required substantial expenditure of financial and administrative resources to remedy. We cannot be sure that similar failures will not occur in the future. System failures, accidents or security breaches can cause interruptions in our operations, and can result in a material disruption of our commercialization activities, drug development programs and our business operations. The loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Similarly, we rely on a large number of third parties to supply components for and manufacture our product and product candidates, warehouse

and distribute Sumavel DosePro and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the commercialization of Sumavel DosePro and development of Zohydro ER, Relday or any of our other product candidates could be delayed.

Our short operating history makes it difficult to evaluate our business and prospects.

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We commenced our operations on August 25, 2006. Our operations to date have been limited to organizing and staffing our company, scaling up manufacturing operations with our third-party contract manufacturers, building a sales and marketing organization, conducting product development activities for our product and product candidates, in-licensing rights to Zohydro ER and Relday, and commercializing Sumavel DosePro. Moreover, Sumavel DosePro is our only product that is approved for sale. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

We depend on wholesale pharmaceutical distributors for retail distribution of Sumavel DosePro, and if we lose any of our significant wholesale pharmaceutical distributors, our business could be harmed.*

The majority of our sales of Sumavel DosePro are to wholesale pharmaceutical distributors who, in turn, sell the products to pharmacies, hospitals and other customers. Two wholesale pharmaceutical distributors, McKesson Corporation and Cardinal Health, Inc., individually comprised 37% and 36%, respectively, of our total gross sales of Sumavel DosePro for the nine months ended September 30, 2012, which may result in substantial fluctuations in our results of operations from period to period. The loss of any of these wholesale pharmaceutical distributors accounts or a material reduction in their purchases could have a material adverse effect on our business, results of operations, financial condition and prospects.

In addition, these wholesale customers comprise a significant part of the distribution network for pharmaceutical products in the United States. This distribution network has undergone, and may continue to undergo, significant consolidation marked by mergers and acquisitions. As a result, a small number of large wholesale distributors control a significant share of the market. Consolidation of drug wholesalers has increased, and may continue to increase, competitive and pricing pressures on pharmaceutical products. In addition, at times, wholesaler purchases may exceed customer demand, resulting in reduced wholesaler purchases in later quarters, which may result in substantial fluctuations in our results of operations from period to period. We cannot ensure that we can manage these pricing pressures or that wholesaler purchases will not decrease as a result of this potential excess buying.

Our sales can be greatly affected by the inventory levels our wholesalers carry. We monitor wholesaler inventory of Sumavel DosePro using a combination of methods. Pursuant to distribution service agreements with our three largest wholesale customers, we receive inventory level reports. For most other wholesalers where we do not receive inventory level reports, however, our estimates of wholesaler inventories may differ significantly from actual inventory levels. Significant differences between actual and estimated inventory levels may result in excessive production (requiring us to hold substantial quantities of unsold inventory), inadequate supplies of products in distribution channels, insufficient product available at the retail level, and unexpected increases or decreases in orders from our wholesalers. These changes may cause our revenues to fluctuate significantly from quarter to quarter, and in some cases may cause our operating results for a particular quarter to be below our expectations or the expectations of securities analysts or investors. If our financial results are below expectations for a particular period, the market price of our common stock may drop significantly.

We face intense competition, including from generic products, and if our competitors market and/or develop treatments for migraine, pain or psychotic disorders that are marketed more effectively, approved more quickly than our product candidates or demonstrated to be safer or more effective than our products, our commercial opportunities will be reduced or eliminated.

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary therapeutics. We face competition from a number of sources, some of which may target the same indications as our product or product candidates, including large pharmaceutical companies, smaller pharmaceutical companies, biotechnology companies, academic institutions, government agencies and private and public research institutions, many of which have greater financial resources, sales and marketing capabilities, including larger, well-established sales forces, manufacturing capabilities, experience in obtaining regulatory approvals for product candidates and other resources than us. Many large, well-capitalized companies offer products in the United States that compete with Sumavel DosePro. Sumavel DosePro currently competes with branded products in the triptan class such as Imitrex and Treximet marketed by GlaxoSmithKline, or GSK, as well as six other branded triptan therapies being sold by AstraZeneca plc, Endo Pharmaceuticals Holdings Inc., Johnson & Johnson, Merck & Co., Inc., and Pfizer Inc. In addition to those migraine therapeutics, there are other marketed non-triptan migraine therapeutics such as Cambia sold by Nautilus Neurosciences, Inc. and Migranal sold by Valeant Pharmaceutical International. We also face competition from generic *sumatriptan* oral tablets and *sumatriptan* injection, now marketed in the United States as an authorized generic of the Imitrex STATdose System, or Imitrex STATdose, by Par Pharmaceutical Companies, Inc. and Sandoz Inc. (a Novartis AG company). In addition, in June 2010 the FDA approved Alsuma (*sumatriptan* injection), a needle-based autoinjector which was developed and is manufactured and marketed by Pfizer and its subsidiary, Meridian Medical Technologies. Finally, generic injectable *sumatriptan* in the form of vials and prefilled syringes is available from a number of pharmaceutical companies, and most recently, the FDA granted approval for a needle-based generic *sumatriptan* auto-injector from Sun

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Pharmaceutical Industries Limited in June 2011. Although these products may not be directly substituted for Sumavel DosePro, generic versions of *sumatriptan* injection and alternative autoinjector forms of *sumatriptan* injection may reduce the future adoption of Sumavel DosePro by third-party payors and consumers, as financial pressure to use generic products may encourage the use of a generic product over Sumavel DosePro. Sumavel DosePro is currently more expensive on a per dose basis than most of the competing branded and all of the generic triptan products for migraine, which may also limit the coverage and reimbursement by third-party payors, which could adversely affect adoption by physicians and patients.

If approved for the treatment of moderate to severe chronic pain, we anticipate that Zohydro ER would compete against other marketed branded and generic pain therapeutics. Opioid therapeutics generally fall into two classes: *codeines*, which include *oxycodones* and *hydrocodones,* and *morphines*. Zohydro ER is a *hydrocodone*, the most commonly prescribed opioid in the United States, and we expect Zohydro ER will compete with therapeutics within both the *codeine* and *morphine* classes. These therapeutics include both Schedule II and Schedule III products (meaning that they are considered controlled substances by the DEA) being marketed by companies such as Endo Pharmaceuticals Holdings Inc., Johnson & Johnson, Mallinckrodt Inc., Pfizer, Purdue Pharma L.P., Teva Pharmaceutical Industries Limited and Watson Pharmaceuticals, Inc.

In addition to already marketed therapeutics, we also face competition from product candidates that are or could be under development by many of the above-mentioned entities and others. For example, there are several products for the treatment of migraine under development by large pharmaceutical companies such as GSK and Merck & Co., and other smaller companies such as NuPathe, Inc. and MAP Pharmaceuticals, Inc. If approved, Zohydro ER may also compete with a significant number of opioid product candidates under development, including abuse and tamper resistant formulations of currently available opioids, novel opioids and alternative delivery forms of various opioids under development at other pharmaceutical companies, including single-entity extended-release *hydrocodone* product candidates being developed by Egalet A/S, Pfizer, Purdue Pharma L.P. and Teva Pharmaceutical Industries Limited. Zohydro ER may also face competition from non-opioid product candidates including new chemical entities, as well as alternative delivery forms of non-steroidal anti-inflammatory drugs. These new opioid and non-opioid product candidates are being developed by companies such as Acura Pharmaceuticals, Inc., Altea Therapeutics Corporation, Collegium Pharmaceutical, Inc., Eli Lilly and Company, Elite Pharmaceuticals, Inc., Hospira Inc., Inspirion Delivery Technologies, Inc, LLC, Intellipharmaceuticals International, Inc., Nektar Therapeutics, Pfizer and QRxPharma Ltd.

If approved for the treatment of schizophrenia, we anticipate that Relday will compete against other marketed, branded and generic, typical and atypical antipsychotics, including both long-acting injectable and oral products. Currently marketed long-acting injectable atypical antipsychotic products include Risperdal Consta, and Invega Sustenna marketed by Johnson & Johnson, and Zyprexa Relprevv marketed by Eli Lilly & Company. Currently approved and marketed oral atypical antipsychotics include Risperdal (*risperidone*) and Invega (*paliperidone*) marketed by Johnson & Johnson, generic *risperidone*, Zyprexa (*olanzapine*) marketed by Eli Lilly and Company, Seroquel (*quetiapine*) marketed by AstraZeneca plc, Abilify (*aripiprazole*) marketed by BMS/Otsuka Pharmaceutical Co., Ltd., Geodon (*ziprasidone*) marketed by Pfizer, Fanapt (*iloperidone*) marketed by Novartis AG, Saphris (*asenapine*) marketed by Merck & Co., Latuda (*lurasidone*) marketed by Dainippon Sumitomo Pharma, and generic *clozapine*. Finally, in addition to these currently marketed products, we may also face competition from additional long-acting injectable product candidates that could be developed by the large companies listed above, as well and by other pharmaceutical companies such as Alkermes plc, NuPathe, Inc., Novartis AG, H. Lundbeck A/S and Otsuka Pharmaceutical Co. Ltd., each of which has announced they are developing long-acting antipsychotic product candidates.

We expect Sumavel DosePro and, if approved, Zohydro ER, Relday and any of our other product candidates to compete on the basis of, among other things, product efficacy and safety, time to market, price, patient reimbursement by third-party payors, extent of adverse side effects and convenience of treatment procedures. One or more of our competitors may develop needle-free injectable products, products to address chronic pain or other products that compete with ours, obtain necessary approvals for such products from the FDA, or other agencies, if required, more rapidly than us or develop alternative products or therapies that are safer, more effective and/or more cost effective than any products developed by us. If any of our product candidates receive the requisite regulatory approval and classification and are marketed, the competition which we will encounter will have, and the competition we are currently encountering with our Sumavel DosePro product has had and will continue to have, an effect on our product prices, market share and results of operations. We may not be able to differentiate any products that we are able to market from those of our competitors, successfully develop or introduce new products that are less costly or offer better results than those of our competitors, or offer purchasers of our products payment and other commercial terms as favorable as those offered by our competitors.

In addition, competitors may seek to develop alternative formulations of our product candidates and/or alternative drug delivery technologies that address our targeted indications. The commercial opportunity for Sumavel DosePro and our product candidates could be significantly harmed if competitors are able to develop alternative formulations and/or drug delivery technologies outside the scope of our products. Compared to us, many of our potential competitors have substantially greater:

capital resources;

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research and development resources and experience, including personnel and technology;

drug development, clinical trial and regulatory resources and experience;

sales and marketing resources and experience;

manufacturing and distribution resources and experience;

name recognition; and

resources, experience and expertise in prosecution and enforcement of intellectual property rights.

As a result of these factors, our competitors may obtain regulatory approval of their products more rapidly than we are able to or may obtain patent protection or other intellectual property rights that limit or block us from developing or commercializing our product candidates. Our competitors may also develop drugs that are more effective, more useful, better tolerated, subject to fewer or less severe side effects, more widely prescribed or accepted or less costly than ours and may also be more successful than us in manufacturing and marketing their products. If we are unable to compete effectively with the marketed therapeutics of our competitors or if such competitors are successful in developing products that compete with Sumavel DosePro or any of our product candidates that are approved, our business, results of operations, financial condition and prospects may be materially adversely affected.

We are dependent on numerous third parties in our supply chain, all of which are currently single source suppliers, for the commercial supply of Sumavel DosePro and for the clinical supply of Zohydro ER and Relday, and if we experience problems with any of these suppliers, the manufacturing of Sumavel DosePro, Zohydro ER and Relday could be delayed.*

While we own most of the specialized equipment used to manufacture critical components of Sumavel DosePro, we do not own or operate manufacturing facilities and currently lack the in-house capability to manufacture Sumavel DosePro, Zohydro ER, Relday or any other product candidates. Our DosePro device and Sumavel DosePro are manufactured by contract manufacturers, component fabricators and secondary service providers. Aseptic fill, finish, assembly and packaging of Sumavel DosePro are performed at Patheon UK Limited, Swindon, United Kingdom, a specialist in the aseptic fill/finish of injectables and other sterile pharmaceutical products. In May 2012, Patheon announced plans to wind down or transfer its commercial production capacity for a number of products at this facility over a period of 24 to 36 months. While we cannot be sure of the impact of these plans on the continued fill, finish, assembly and packaging of Sumavel DosePro, we believe that we will have sufficient time to identify alternative suppliers for these services or negotiate alternative arrangements with Patheon for continued services at this or another facility. In addition, Nypro Limited, located in Bray, Ireland, manufactures the actuator assemblies and injection molded components for our DosePro device and MGlas AG, located in Münnerstadt, Germany, manufactures the specialized glass capsule (cartridge) that houses the *sumatriptan* active pharmaceutical ingredient, or API, in our DosePro device. Each of these manufacturers and each other company that supplies, fabricates or manufactures any component used in our DosePro device is currently the only qualified source of their respective components. We currently rely on Dr. Reddy s Laboratories as the only supplier of *sumatriptan* API for use in Sumavel DosePro. We also outsource all manufacturing and packaging of the clinical trial materials for Zohydro ER and Relday to third parties. Although we plan to qualify additional manufacturers and suppliers of some of the components used in Sumavel DosePro, there can be no assurance that we will be able to do so and the current manufacturers and suppliers of these components will likely be single source suppliers to us for a significant period of time. Similarly, under our license agreements, an affiliate of Alkermes plc is the exclusive manufacturer of Zohydro ER and Durect is the exclusive manufacturer of the *risperidone* formulation using Durect s SABER controlled-release technology for all Relday clinical trials through Phase 2 and has the option to supply the same formulation for Phase 3 and, if approved, commercial production. We have restrictions on establishing a second source of supply under our agreement with Alkermes, and we may never be able to establish additional sources of supply for Zohydro ER or Relday s *risperidone* formulation.

Manufacturers and suppliers are subject to regulatory requirements covering, among other things, manufacturing, testing, quality control and record keeping relating to our product and product candidates, and are subject to ongoing inspections by regulatory agencies. Failure by any of our manufacturers or suppliers to comply with applicable regulations may result in long delays and interruptions to our manufacturing supply, and increase our costs, while we seek to secure another supplier who meets all regulatory requirements. Accordingly, the loss of any of our current third-party manufacturers or suppliers could have a material adverse effect on our business, results of operations, financial condition and prospects.

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Reliance on third-party manufacturers and suppliers entails risks to which we would not be subject if we manufactured Sumavel DosePro or our product candidates ourselves, including:

- reliance on the third parties for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreements by the third parties because of factors beyond our control or the insolvency of any of these third parties or other financial difficulties, labor unrest, natural disasters or other factors adversely affecting their ability to conduct their business; and
- the possibility of termination or non-renewal of the agreements by the third parties, at a time that is costly or inconvenient for us, because of our breach of the manufacturing agreement or based on their own business priorities.

If our contract manufacturers or suppliers fail to deliver the required commercial quantities of Sumavel DosePro and its various components, the quantities of Zohydro ER, Relday or any of our other product candidates required for our clinical trials and, if approved, for commercial sale, on a timely basis and at commercially reasonable prices, and we are unable to find one or more replacement manufacturers or suppliers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality, and on a timely basis, we would likely be unable to meet demand for our products and would have to delay or terminate our pre-clinical or clinical trials, and we would lose potential revenue. It may also take a significant period of time to establish an alternative source of supply for our product, product candidates and components and to have any such new source approved by the FDA or any applicable foreign regulatory authorities. Furthermore, any of the above factors could cause the delay or suspension of initiation or completion of clinical trials, regulatory submissions or required approvals of our product candidates, cause us to incur higher costs and could prevent us from commercializing our product candidates successfully.

We may encounter delays in the manufacturing of Sumavel DosePro or fail to generate revenue if our supply of the components of our DosePro drug delivery system is interrupted.

Our DosePro drug delivery system is sourced, manufactured and assembled by multiple third parties across different geographic locations in Europe, including the United Kingdom, Germany and Ireland. All contract manufacturers and component suppliers have been selected for their specific competencies in the manufacturing processes and materials that make up the DosePro system. The components of DosePro include the actuator subassembly, capsule subassembly, and the setting mechanism. The actuator subassembly is comprised of nine individual components which are collectively supplied by six different third-party manufacturers. The capsule subassembly that houses the sterile drug formulation *sumatriptan* is comprised of five different components also supplied by four third-party manufacturers. Each of these third-party manufacturers is currently the single source of their respective components. If any of these manufacturers is unable to supply its respective component for any reason, including due to violations of the FDA s Quality System Regulation, or QSR, requirements, our ability to manufacture the finished DosePro device will be adversely affected and our ability to meet the distribution requirements for any product sales of Sumavel DosePro and the resulting revenue therefrom will be negatively affected. Accordingly, there can be no assurance that any failure in any part of our supply chain will not have a material adverse effect on our ability to generate revenue from Sumavel DosePro, which in turn could have a material adverse effect on our business, results of operations, financial condition and prospects.

We rely on third parties to perform many necessary services for our commercial products, including services related to the distribution, invoicing, storage and transportation of our products.

We have retained third-party service providers to perform a variety of functions related to the sale and distribution of our products, key aspects of which are out of our direct control. For example, we rely on Cardinal Health 105, Inc. (a/k/a Specialty Pharmaceutical Services) to provide key services related to logistics, warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management and call center management, and, as a result, most of our inventory is stored at a single warehouse maintained by the service provider. We place substantial reliance on this provider as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical damage or natural disaster at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired. In addition, we utilize third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services. If the quality or accuracy of the data maintained by these service providers is insufficient, our ability to continue to market our products could be jeopardized or we could be subject to regulatory sanctions. We do not currently have the internal capacity to perform these important commercial functions, and we may not be able to maintain commercial

arrangements for these services on reasonable terms.

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The perception that our DosePro needle-free drug delivery system should be pain free may limit patient adoption.

We believe that there is a perception among some patients, physicians and other customers that a needle-free delivery system should be pain free. While our experience indicates that some patients will experience pain upon injection with the DosePro technology, this pain sensation is consistent with the pain sensation associated with injection with a fine gauge needle and can be generally characterized as transient mild discomfort. In addition, some patients will experience local injection site signs and reactions following injection with DosePro. The fact that the use of our DosePro system may be accompanied by a certain amount of pain upon injection and local injection site signs and reactions may limit its adoption by patients, physicians and other customers.

Zohydro ER and Relday are subject to extensive regulation, and we cannot give any assurance that they or any of our other product candidates will receive regulatory approval or be successfully commercialized.*

We currently are developing Zohydro ER for the treatment of moderate to severe chronic pain and Relday for the treatment of the symptoms of schizophrenia. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products, among other things, are subject to extensive regulation by the FDA, the DEA (in the case of Zohydro ER) and other regulatory authorities in the United States. We are not permitted to market Zohydro ER, Relday or any of our other product candidates in the United States unless and until we receive regulatory approval from the FDA. We cannot provide any assurance that we will obtain regulatory approval for Zohydro ER, Relday or any of our other product candidates, or that any such product candidates will be successfully commercialized.

Under the policies agreed to by the FDA under The Prescription Drug User Fee Act, or PDUFA, the FDA is subject to a two-tiered system of review times Standard Review and Priority Review. For drugs subject to standard review, such as Zohydro ER, the FDA has a goal to complete its review of the NDA and respond to the applicant within ten months from the date of receipt of an NDA. The FDA has assigned a target action date of March 1, 2013 for the Zohydro ER NDA. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the three months prior to the PDUFA target action date. The FDA s review goals are subject to change, and it is unknown whether the review of our NDA for Zohydro ER, or an NDA filing for any of our other product candidates, will be completed within the FDA s review goals or will be delayed. Moreover, the duration of the FDA s review may depend on the number and type of other NDAs that are submitted with the FDA around the same time period.

The FDA may also refer applications for novel products or products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. In connection with the acceptance of our NDA for Zohydro, the FDA will convene an advisory committee for Zohydro ER on December 7, 2012. The FDA is not bound by the recommendation of an advisory committee. However, if our advisory committee were to recommend against the approval of our NDA due to adverse publicity concerning opioids or other concerns, we may not be able to succeed in securing approval for Zohydro. For example, products used to treat and manage pain, especially opioids, are from time to time subject to negative publicity, including illegal use, overdoses, abuse, diversion, serious injury and death. The FDA has announced plans to convene a separate advisory committee that was initially scheduled on October 29 and 30, 2012 concerning *hydrocodone* either combined with other analgesics or as an antitussive (cough suppressant), and to discuss the public health benefits and risks, including the potential for abuse, of these drugs. This advisory committee meeting was cancelled due to weather and is currently being rescheduled. We believe Zohydro ER is particularly appealing compared to existing *hydrocodone* products such as Vicodin, Norco, Lorcet, Lortab and their generic equivalents, which unlike Zohydro ER contain the analgesic combination ingredient acetaminophen. Acetaminophen, if taken in high quantities over time, can lead to serious side effects such as liver toxicity. However, we may not succeed in differentiating Zohydro ER from these other hydrocodone products and may suffer from heightened regulatory scrutiny and negative publicity. In addition, in advance of our advisory committee meeting, we and the FDA will submit briefing documents for the committee s review, and these briefing documents will be made available to the public. Press coverage and public scrutiny of hydrocodone products in general, the materials that will be discussed at the general hydrocodone advisory committee and our Zohydro ER advisory committee meeting may negatively affect the potential for our NDA for Zohydro ER to receive approval. Even if we obtain regulatory approval for Zohydro ER, the matters discussed at the advisory committee meetings, and in particular any concerns regarding safety and abuse potential, could limit our ability to successfully commercialize the product candidate.

As part of its review of the NDA, the FDA may inspect the facility or the facilities where the drug is manufactured. If the FDA s evaluations of the NDA and the clinical and manufacturing procedures and facilities are favorable, the FDA will issue an action letter, which will be either an approval letter, authorizing commercial marketing of the drug for a specified indication, or a complete response letter containing the conditions that must be met in order to secure approval of the NDA. These conditions may include deficiencies identified in connection with the FDA s evaluation of the NDA submission or the

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clinical and manufacturing procedures and facilities. Until any such conditions or deficiencies have been resolved, the FDA may refuse to approve the NDA. If and when those conditions have been met to the FDA s satisfaction, the FDA will issue an approval letter. The FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. For example:

- the FDA may not deem a product candidate safe and effective;
- the FDA may not find the data from pre-clinical studies and clinical trials sufficient to support approval;
- the FDA may require additional pre-clinical studies or clinical trials;
- the FDA may not approve of our third-party manufacturers processes and facilities; or
- the FDA may change its approval policies or adopt new regulations.

Zohydro ER has undergone Phase 1 pharmacokinetics studies, Phase 2 clinical trials, and a Phase 3 clinical development program. However, some of these studies and trials were conducted by a third party and, accordingly, we did not directly participate in their design or execution. We initiated the Phase 3 clinical development program for Zohydro ER in March 2010 and reported positive results from our pivotal Phase 3 efficacy trial, Study 801, in August 2011 and completed our Phase 3 safety trial, Study 802, in December 2011, which showed Zohydro ER to be safe and generally well tolerated. However, product candidates such as Zohydro ER may not be approved even if they achieve their specified endpoints in clinical trials. The FDA may disagree with our trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials. The FDA may also approve a product candidate for fewer or more limited indications than we request, or may grant approval contingent on the performance of costly post-approval clinical trials. In addition, the FDA may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates. Approval may be contingent on a Risk Evaluation and Mitigation Strategy, or REMS, which limits the labeling, distribution or promotion of a drug product.

Relday and any of our other product candidates may fail to achieve their specified endpoints in clinical trials. We initiated a Phase 1 safety and pharmacokinetic clinical trial for Relday in July 2012 and the outcome of this study and the subsequent development of Relday will be subject to most of the risks described above.

We believe that we have planned, designed and completed an adequate Phase 3 clinical trial program for Zohydro ER, and we presented the trial design for our Phase 3 trials to the FDA at our End of Phase 2 meeting in June 2008. Although we believe the FDA has generally agreed with the design of our Phase 3 clinical trial program, the FDA could still determine that it is not satisfied with our plan, the details of our pivotal clinical trial protocols and designs or the results of our studies. In addition, we concluded our pre-NDA meetings with the FDA in December 2011 during which we discussed the non-clinical, clinical and chemistry, manufacturing and controls, or CMC, development of Zohydro ER, and agreed on the submission requirements for the NDA under 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, or FFDCA. While the FDA has provided us with a written record of our discussions and responses to our questions at our End of Phase 2 meeting and our pre-NDA meetings, such records and responses do not guarantee that the FDA will deem our trial design to be sufficient for the purpose of obtaining marketing approval for Zohydro ER. We did not seek a Special Protocol Assessment from the FDA for our pivotal Phase 3 efficacy study for Zohydro ER (Study 801).

If we are unable to obtain regulatory approval for Zohydro ER, Relday or any other product candidates on the timeline we anticipate, we will not be able to execute our business strategy effectively and our ability to generate additional revenues beyond Sumavel DosePro will be limited, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

Our clinical trials may fail to demonstrate acceptable levels of safety and efficacy for Zohydro ER, Relday or any of our other product candidates, which could prevent or significantly delay their regulatory approval.*

Our Zohydro ER, Relday and any other product candidates are prone to the risks of failure inherent in drug development. Before obtaining U.S. regulatory approval for the commercial sale of Zohydro ER, Relday or any other product candidate, we must gather substantial evidence from well-controlled clinical trials that demonstrate to the satisfaction of the FDA that the product candidate is safe and effective, and similar regulatory approvals would be necessary to commercialize the product candidate in other countries.

In light of widely publicized events concerning the safety risk of certain drug products, particularly opioid drug products, regulatory authorities, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products after approval. In addition, the FFDCA, as amended by

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the Food and Drug Administration Amendments Act of 2007, grants significant expanded authority to the FDA, much of which is aimed at improving the safety of drug products before and after approval. In particular, the FFDCA authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information and require a REMS, for certain drugs, including certain currently approved drugs. It also significantly expands the federal government s clinical trial registry and results databank, which we expect will result in significantly increased government oversight of clinical trials. Under the FFDCA, companies that violate these and other provisions of the law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties.

The increased attention to drug safety issues may result in a more cautious approach by the FDA in its review of our clinical trials. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

With regard to Zohydro ER, results from our pivotal Phase 3 efficacy clinical trial in patients with chronic lower back pain has shown what we believe is a clinically acceptable efficacy and safety profile which supported submission of an NDA for the treatment of moderate to severe pain in patients requiring around-the-clock opioid therapy. The trial successfully met the primary efficacy endpoint of the study in demonstrating a significant difference (p=0.008) between the mean changes in daily pain intensity Numeric Rating Scale (NRS) scores between Zohydro ER and placebo groups. The two key secondary endpoints were also met, specifically, the proportion of patients with at least 30% improvement in pain intensity and the improvement of overall satisfaction of medication. In the pivotal Phase 3 efficacy trial, the observed adverse events were similar to the side effects we observed in prior Phase 2 trials of Zohydro ER and consistent with the reported side effects of opioids currently prescribed for chronic pain. The incidence of adverse events was 33.7% and 28.8% in the open-label titration and double blind treatment periods, respectively. Overall, the most commonly reported adverse events (2%) were constipation, nausea, somnolence, vomiting, diarrhea, insomnia, fatigue, headache, dizziness and dry mouth. We also completed a 48-week open-label safety study to support the safety profile of Zohydro ER and have reported top-line results. While the overall incidence of adverse events in this study was higher than in the controlled efficacy study, which we believe reflects the longer duration of the study, the results were consistent with results from similar studies with other extended-release and long-acting opioid products and we believe support an overall conclusion that Zohydro ER is safe and generally well tolerated. In addition, the data we have reported and may continue to report from our Zohydro ER clinical trials may change in connection with the FDA s review of our NDA. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. If Zohydro ER, Relday, or any of our other product candidates are not shown to be safe and effective in clinical trials, the program could be delayed or terminated, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Delays in the commencement or completion of any additional testing for Zohydro ER, if required, or clinical testing for Relday, or pre-clinical or clinical testing for or any of our other product candidates, could result in increased costs to us and delay or limit our ability to pursue regulatory approval for, or generate revenues from, such product candidates.*

Clinical trials are very expensive, time consuming and difficult to design and implement. Delays in the commencement or completion of any additional testing for Zohydro ER, if required, or clinical testing for Relday, or pre-clinical or clinical testing for any of our other product candidates, could significantly affect our product development costs and business plan. We initiated clinical testing for Relday in patients with schizophrenia in July 2012. We do not know whether this trial will be completed on schedule, or whether any of our other pre-clinical or clinical trials will begin on time or be completed on schedule. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- obtaining regulatory authorization to commence a clinical trial;
- reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, clinical investigators and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs, clinical investigators and trial sites;
- manufacturing or obtaining sufficient quantities of a product candidate for use in clinical trials;

obtaining institutional review board, or IRB, approval to initiate and conduct a clinical trial at a prospective site;

identifying, recruiting and training suitable clinical investigators;

identifying, recruiting and enrolling subjects to participate in clinical trials for a variety of reasons, including competition from other clinical trial programs for the treatment of pain, migraine or similar indications;

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retaining patients who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy, personal issues, or for any other reason they choose, or who are lost to further follow-up;

uncertainty regarding proper dosing; and

scheduling conflicts with participating clinicians and clinical institutions.

In addition, if a significant number of patients fail to stay enrolled in any of our current or future clinical trials of Relday or any of our other product candidates and such failure is not adequately accounted for in our trial design and enrollment assumptions, our clinical development program could be delayed. Clinical trials may also be delayed or repeated as a result of ambiguous or negative interim results or unforeseen complications in testing. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or other regulatory authorities due to a number of factors, including:

failure to design appropriate clinical trial protocols;

failure by us, our employees, our CROs or their employees to conduct the clinical trial in accordance with all applicable FDA, DEA or other regulatory requirements or our clinical protocols;

inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;

discovery of serious or unexpected toxicities or side effects experienced by study participants or other unforeseen safety issues;

lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties;

lack of effectiveness of any product candidate during clinical trials;

slower than expected rates of subject recruitment and enrollment rates in clinical trials;

failure of our CROs or other third-party contractors to comply with all contractual requirements or to perform their services in a timely or acceptable manner;

inability or unwillingness of medical investigators to follow our clinical protocols; and

unfavorable results from on-going clinical trials and pre-clinical studies.

Additionally, changes in applicable regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. All of the above risks will be applicable to Zohydro ER to the extent we are required by the FDA to conduct any additional clinical trials. If we experience delays in completion of, or if we terminate, any of our clinical trials, the

commercial prospects for Zohydro ER, Relday and our other product candidates may be harmed, which may have a material adverse effect on our business, results of operations, financial condition and prospects.

Our competitors could receive FDA approval for an extended-release hydrocodone product before we receive FDA approval for Zohydro ER, and thus could be granted regulatory exclusivity that could significantly delay our ability to receive approval for and commercialize Zohydro ER and therefore dramatically reduce its market potential. Our competitors could also pursue regulatory and other strategies to combat competition from 505(b)(2) products, which also may negatively affect the approval and commercialization of Zohydro ER and any of our other product candidates.

The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the FFDCA, or Section 505(b)(2). Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. For example, we obtained FDA marketing approval of Sumavel DosePro under Section 505(b)(2), and we submitted the NDA for Zohydro ER under Section 505(b)(2), and as such the NDA will rely, in part, on the FDA s previous findings of safety and effectiveness for *hydrocodone*.

Certain of our competitors may file a 505(b)(2) application for extended-release *hydrocodone* prior to the approval of our own NDA for Zohydro ER. The first approved 505(b)(2) applicant for a particular condition of use, or change to a marketed product, such as a new extended-release formulation for a previously approved product, may be granted three-year Hatch-Waxman exclusivity if one or more clinical studies, other than bioavailability or bioequivalence studies, was essential to the approval of the application and was conducted/sponsored by the applicant. Three-year Hatch-Waxman exclusivity

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delays the FDA s approval of other 505(b)(2) applicants for the same condition of use or change to the drug product that was granted exclusivity, regardless of the date of submission of each NDA. We believe that several competitors are developing extended-release *hydrocodone* products, and if the FDA approves a competitor s 505(b)(2) application for its extended-release *hydrocodone* product before our application, and granted the competitor three-year exclusivity, the FDA would be precluded from making effective our NDA for Zohydro ER until after that three-year exclusivity period has expired, and such delay would dramatically reduce our expected market potential for Zohydro ER. Additionally, even if our 505(b)(2) application for extended-release *hydrocodone* is approved first, we may still be subject to competition by other *hydrocodone* products, including approved products or other 505(b)(2) applications for different conditions of use that would not be restricted by the three-year exclusivity.

In addition, approval under Section 505(b)(2) generally requires the absence of any other patents covering the product candidate in question and competitors and others have the ability to take numerous steps to block or delay approval of product candidates under Section 505(b)(2), including:

- extending patent protection for existing products that would block Section 505(b)(2) approval of the product candidate by pursuing new patents for existing products that may be granted just before the expiration of one patent, which could extend patent protection for a number of years or otherwise delay the launch of generic, 505(b)(2) or other competing products;
- submitting Citizen Petitions to request the FDA to take adverse administrative action with respect to approval of a generic, 505(b)(2) or other competing product;
- filing patent infringement lawsuits, whether or not meritorious, to trigger up to a 30-month stay in the approval of a generic, 505(b)(2) or other competing product; and
- engaging in state-by-state initiatives to enact legislation or regulatory policies that restrict the substitution of some generic, 505(b)(2) or other competing drugs for brand-name drugs.

If any of these strategies are successful, our ability to obtain approval of and commercialize Zohydro ER and any of our other product candidates for which we rely on Section 505(b)(2) will be adversely affected.

We rely on third parties to conduct our pre-clinical and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.*

We conducted our Phase 3 trials for Zohydro ER under agreements with third-party CROs. We are also conducting our Phase 1 clinical trial for Relday under an agreement with a third-party CRO, and we anticipate that we may enter into agreements with third-party CROs in the future regarding Zohydro ER, Relday or any of our other product candidates. We rely heavily on these parties for the execution of our clinical and pre-clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol. We and our CROs are required to comply with current good clinical practices, or GCPs. The FDA enforces these GCP regulations through periodic inspections of trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCP regulations, the 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. We cannot assure you that, upon inspection, the FDA and similar foreign regulators will determine that any of our clinical trials comply or complied with GCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices, or cGMPs, regulations, and require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs on commercially reasonable terms, or at all. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced 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 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 our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate additional revenues could be delayed.

Switching or adding additional CROs can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, results of operations, financial condition and prospects.

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The development and implementation of a REMS for Zohydro ER could cause significant delays in the approval process for Zohydro ER and will add additional layers of regulatory requirements, including the requirement for a Medication Guide and educational requirements for prescribers and patients, which could significantly impact our ability to commercialize Zohydro ER and dramatically reduce its market potential.

The Food and Drug Administration Amendments Act, or FDAAA, added Section 505-1 to the FFDCA. Section 505-1 permits FDA to require a REMS for a drug product to ensure the safe use of the drug. A REMS is a strategic safety program that the FDA requires to ensure that the benefits of a drug outweigh its risks. In determining whether a REMS is necessary, the FDA will consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, and the seriousness of known or potential adverse events. If the FDA determines a REMS is necessary, the drug sponsor must agree to the REMS plan at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the drug s risks, limitations on who may prescribe or dispense the drug, requirements that patients enroll in a registry or undergo certain health evaluations or other measures that the FDA deems necessary to assure the safe use of the drug. In addition, the REMS must include a timetable to assess the strategy minimally at 18 months, three years and seven years after the strategy s approval.

In February 2009, the FDA informed opioid analgesic drug manufacturers that it will require a class-wide REMS for all long-acting and sustained-release opioid drug products. The FDA has since initiated efforts to develop a new standardized REMS for these opioid medications to ensure their safe use. In April 2011, the FDA announced that it had finalized the elements of a class-wide REMS for these products. The central component of the opioid REMS program is an education program for prescribers and patients. Specifically, the REMS for these products must include a Medication Guide available for distribution to patients who are dispensed the drug, as well as a number of elements to assure safe use. These elements include training for prescribers who prescribe the drug; information provided to prescribers that prescribers can use to educate patients in the safe use, storage, and disposal of opioids; and information provided to prescribers of the existence of the REMS and the need to successfully complete the necessary training. The FDA expects that the prescriber training required as part of the REMS is to be conducted by accredited, independent continuing education providers, without cost to the healthcare professionals, under unrestricted grants to accredited continuing education providers funded by the opioid analgesic sponsor. In November 2011, the FDA issued a draft blueprint for this prescriber education that outlines the core messages that the FDA believes should be conveyed to prescribers in a basic two to three hour educational module. This finalized and approved blueprint will be available for use by continuing education providers in developing continuing education courses. Moreover, the extended-release/long-acting opioid analgesic REMS must include a timetable for submission of assessments that shall be no less frequent than 6 months, 12 months, and annually after the REMS is approved to assess the extent to which the elements to assure safe use are meeting the goals of the REMS and whether the goals or elements should be modified. The FDA expects that manufacturers of long-acting and extended-release opioids work together to provide educational materials as part of a class-wide single shared system to reduce the burden of the REMS on the healthcare system.

An extended-release formulation of *hydrocodone*, such as Zohydro ER, will be required to have a REMS that contains the elements of the recently-issued class-wide REMS for long-acting and sustained-release opioids. We submitted a REMS at the time of the NDA submission for Zohydro ER. The REMS submission could cause significant delays in the approval process for the Zohydro ER NDA, and the educational requirements and requirements for a Medication Guide for patients could significantly impact our ability to commercialize Zohydro ER and dramatically reduce its market potential.

Our commercialization partner for Sumavel DosePro in the European Union and three other countries, Desitin Arzneimittel GmbH, or Desitin, may not successfully develop, obtain approval for or commercialize Sumavel DosePro in those territories, which may adversely affect our ability to commercialize Sumavel DosePro both inside and outside the United States.

In March 2008, we entered into a licensing and distribution agreement with Desitin pursuant to which we granted Desitin the exclusive right under our intellectual property rights related to Sumavel DosePro to develop, use, distribute, sell, offer for sale, and import Sumavel DosePro and any potential modified versions of Sumavel DosePro in the European Union, Norway, Switzerland and Turkey. In that regard, Desitin is not obligated under the agreement to pursue regulatory approval or commercialization of Sumavel DosePro in any of these countries except for Germany. Since we will depend on Desitin to develop, obtain regulatory approval for and, if regulatory approval is granted, commercialize Sumavel DosePro in these countries, we will have limited control over the success of Desitin s development, regulatory approval and commercialization efforts. Desitin submitted a Marketing Authorization Application for Sumavel DosePro to the Federal Institute for Drugs and

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Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)) in Germany, the reference member state, through the Decentralized Procedure in October 2009, following completion of a European pivotal bioequivalence trial comparing needle-free Sumavel DosePro to a traditional needle-based autoinjector, Imigran-Inject, the European brand of Imitrex STATdose. In November 2010, Denmark became the first member of the European Union to approve marketing of Sumavel DosePro in that country. Subsequently, Sumavel DosePro has received marketing approval in Germany, Sweden, the United Kingdom, Norway and France.

Any additional clinical studies Desitin may be required to conduct as part of the regulatory approval process may not corroborate the results of the clinical studies we have conducted or may have adverse results or effects on our ability to maintain regulatory approvals in the United States or obtain them in other countries. In addition, although we believe that the U.S. market represents the largest commercial opportunity for Sumavel DosePro, Desitin may not develop Sumavel DosePro as fast or generate as large of a market as we would like or as the market may expect and Desitin may not seek to develop, obtain approval for or commercialize Sumavel DosePro in countries for which it has exclusive rights, other than in Germany, where Desitin is required to develop, seek approval for and commercialize Sumavel DosePro. Any failure by Desitin to successfully commercialize Sumavel DosePro or to successfully obtain applicable foreign regulatory approval for Sumavel DosePro would limit our opportunity to receive revenue from the territories licensed to Desitin. Furthermore, negative developments occurring in those territories controlled by Desitin could have a negative impact on physician and patient impressions of our product in the United States and elsewhere.

Our failure to successfully establish new partnerships with pharmaceutical companies or contract sales organizations to co-promote Sumavel DosePro and any additional product candidates that may receive regulatory approval may impair our ability to effectively market and sell such product candidates.*

Major pharmaceutical companies usually employ groups of sales representatives numbering in the thousands to call on the large number of primary care physicians. In connection with the launch of Sumavel DosePro in January 2010 we built a sales and marketing organization to promote Sumavel DosePro in the United States, including a focused sales force currently comprised of approximately 95 representatives primarily targeting neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. In July 2009, we entered into an exclusive agreement with Astellas under which Sumavel DosePro was also being marketed by Astellas in the United States and promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists by approximately 400 Astellas sales representatives. Our Astellas agreement terminated on March 31, 2012. In June 2012, in order to maintain and expand the market opportunity for Sumavel DosePro into the broader primary care physician audiences, we entered into a new co-exclusive (with us) co-promotion agreement with Mallinckrodt under which in August 2012 Mallinckrodt began promoting Sumavel DosePro to its customer base of prescribers.

In addition, in order to promote any additional product candidates that receive regulatory approval to these broader primary care physician audiences we will, need to expand our sales and marketing personnel and commercial infrastructure and/or establish partnerships with pharmaceutical companies or contract sales organizations to co-promote such additional products. We currently, and on an ongoing basis will have to, compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. We also face competition in our search for collaborators and potential co-promoters. To the extent we rely on additional third parties to co-promote or otherwise commercialize any product and/or product candidates that may receive regulatory approval, we are likely to receive less revenue than if we commercialized these products ourselves. Further, by entering into strategic partnerships or similar arrangements, we may rely in part on such third parties for financial and commercialization resources. Even if we are able to identify suitable partners to assist in the commercialization of our product and/or product candidates, they may fail to devote the resources necessary to realize the full commercial potential of our products. In addition, we may lack the financial and managerial resources to increase the size of our sales and marketing organization to adequately promote and commercialize Sumavel DosePro and any product candidates that may be approved, and any increase in our sales force would result in an increase in our expenses, which could be significant before we generate revenues from any newly approved product candidate. If we are unable to expand our sales and marketing infrastructure or enter into a third-party arrangement, we would not be able to successfully commercialize any approved products. Even if we are able to expand our sales and marketing personnel or successfully establish partnership arrangements, such sales force and marketing teams may not be successful in commercializing our products, which would adversely affect our ability to generate revenue for such products, which will have a material adverse effect on our business, results of operations, financial condition and prospects.

Our failure to successfully acquire, develop and market additional product candidates or approved products would impair our ability to grow our business. In that regard, our DosePro delivery system in its present form cannot be used with drug formulation volumes greater than 0.5 mL, which will likely limit its use with drugs requiring larger formulation volumes.*

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As part of our growth strategy we intend to seek to expand our product pipeline by exploring acquisition or in-licensing opportunities of proven drugs that can be paired with our DosePro needle-free drug delivery system. However, the current version of our DosePro drug delivery system cannot be used with drug formulation volumes greater than 0.5 mL. Many marketed and development-stage injectable products, including most biologics, have formulation volumes greater than 0.5 mL and would require reformulation, if possible, to accommodate the approved doses in smaller volumes that are compatible with DosePro. Any reformulation may increase the risk of failure during development, extend the development timelines, increase development costs and add complexity to the regulatory approval process and in some cases reformulation may not be possible. If we are not able to identify additional drug compounds that can be delivered via the current version of our DosePro technology, or if we are unable to successfully develop higher dose versions of this technology, our ability to develop additional product candidates and grow our business would be adversely affected. We and Battelle Memorial Institute, or Battelle, our technology co-marketing partner, are also seeking opportunities to out-license the DosePro technology to partners seeking to enhance, differentiate, or extend the life-cycle of their injectable products. However, there can be no assurance that our or Battelle s efforts to secure such a partnership will be successful. If we are unable to secure partnerships with companies that have compounds that can be delivered via the current version of our DosePro technology, or if we are unable to successfully develop higher dose versions of this technology, we will not be able to generate revenues from out-licensing our DosePro technology.

We have initiated early stage design and development of a larger volume, second generation version of our DosePro technology to accommodate drug formulation volumes greater than 0.5 mL, which if successfully developed, would allow for a broader range of potential applications for our technology. However, the full development of such technology will require substantial investment and we may enter into a third-party collaboration in order to obtain additional financing to help fully develop such technology. For example, under our co-marketing and option agreement with Battelle, we granted Battelle an option to enter into an exclusive co-development and commercialization arrangement with us related to a 1.2 mL DosePro drug delivery technology. There is no guarantee that we or any potential future third-party collaborator, including Battelle should it exercise its option, will be able to successfully develop such a device technology, whether for financial or technical reasons or otherwise.

In addition, we continue to examine potential improvements to the DosePro needle-free delivery system but cannot be certain that any improvements will obtain the necessary regulatory approvals or actually increase product sales. For example, we submitted a Prior Approval Supplement to the FDA regarding the implementation of a minor change designed to soften the sound upon administration of Sumavel DosePro. The FDA issued a complete response letter requesting more information. We plan to meet with the FDA to understand their position and agree on the additional steps required to implement this improvement. The complete response letter has no impact on the current Sumavel DosePro product.

Furthermore, we intend to in-license, acquire, develop and/or market additional products and product candidates in the areas of pain and central nervous system, or CNS, disorders. For example, in July 2011, we entered into a development and license agreement with Durect Corporation for a proprietary, long-acting, injectable formulation of *risperidone* using Durect s SABER controlled-release formulation technology in combination with our DosePro technology. Durect will be responsible for non-clinical, formulation and CMC development responsibilities. As a result, we will be dependent on Durect s successful completion of its responsibilities for Relday. In addition, because our internal research and development capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify and select promising pharmaceutical product candidates and products, negotiate licensing or acquisition agreements with their current owners and finance these arrangements.

The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing, sales and other resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates, or license the rights to our DosePro technology, on terms that we find acceptable, or at all.

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including pre-clinical or clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any products that we develop or approved products that we acquire will be manufactured or sold profitably or achieve market acceptance.

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If we are unable to license or acquire additional product candidates or approved products and successfully develop and commercialize them, or if we are otherwise unable to pair our DosePro delivery system with other drugs or out-license the DosePro technology to others, it would likely have a material adverse effect on our business, results of operations, financial condition and prospects.

We may need to continue to increase the size of our organization, and we may experience difficulties in managing and financing growth.*

We increased our full-time employees from 48 as of October 31, 2009 to 155 as of September 30, 2012. In addition, we have expanded our sales force in the United States from approximately 80 sales representatives to approximately 95 sales representatives as of September 30, 2012 and we intend to increase our sales force if Zohydro ER is approved by the FDA. Any such increases in our sales force could substantially increase our expenses. We may need to continue to expand our managerial, operational and other resources in order to grow, manage and fund our existing business. Our management and personnel, systems and facilities currently in place may not be adequate to support this recent and any future growth, and we may be unable to fund the costs and expenses required to increase our necessary headcount and infrastructure. Our need to effectively manage our operations, any future growth and various projects requires that we:

- manage our internal and external commercialization efforts for Sumavel DosePro effectively while carrying out our contractual obligations to third parties and complying with all applicable laws, rules and regulations;
- manage our internal development efforts for Zohydro ER, Relday and our other product candidates effectively while carrying out our contractual obligations to licensors, collaborators and other third parties and complying with all applicable laws, rules and regulations;
- continue to improve our operational, financial and management controls, reporting systems and procedures; and
- attract and retain sufficient numbers of talented employees.

We may be unable to successfully implement or fund these tasks on a larger scale and, accordingly, may not achieve our commercialization and development goals. In addition, our management may have to divert a disproportionate amount of its attention away from day-to-day activities and towards managing these growth-related activities. Likewise, any increase in our sales force would increase our expenses, perhaps substantially. Our future financial performance and our ability to execute on our business plan will depend, in part, on our ability to effectively manage any future growth and our failure to effectively manage any growth could have a material adverse effect on our business, results of operations, financial condition and prospects.

If we are unable to attract and retain key personnel, we may not be able to manage our business effectively or develop our product candidates or commercialize our product.

Our success depends on our continued ability to attract, retain and motivate highly qualified management and key clinical development, regulatory, sales and marketing and other personnel. We are highly dependent on the development, regulatory, commercial and financial expertise of our senior management team. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the areas in Southern and Northern California, where we currently operate. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercialization objectives, our ability to raise additional capital and our ability to implement our business strategy. The loss of the services of any members of our senior management team, especially our Chief Executive Officer, Roger L. Hawley, and President and Chief Operating Officer, Stephen J. Farr, Ph.D., could negatively impact the commercialization of Sumavel DosePro and could delay or prevent the development and commercialization of any other product candidates, including Zohydro ER or Relday. Further, if we lose any members of our senior management team, we may not be able to find suitable replacements, and our business may be harmed as a result. In addition to the competition for personnel, our locations in California in particular are characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Although we have employment agreements with each of our executive officers, these agreements are terminable by them at will at any time with or without notice and, therefore, do not provide any assurance that we will be able to retain their services. We do not maintain key man insurance policies on the lives of our senior management team or the lives of any of our other employees. In addition, we have clinical advisors who assist us in formulating our clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with ours. If we are unable to attract and retain key personnel, our business, results of operations, financial condition and prospects will be adversely affected.

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We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time we may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of products, product candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management s time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- higher than expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

If we are unable to achieve and maintain adequate levels of coverage and reimbursement for Sumavel DosePro, or Zohydro ER, if approved, or any of our other product candidates for which we may receive regulatory approval on reasonable pricing terms, their commercial success may be severely hindered.

Successful sales of our products depend on the availability of adequate coverage and reimbursement from third-party payors. Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant

portion of the cost of our products.

In addition, the market for our products will depend significantly on access to third-party payors drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Third-party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor.

Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third-party coverage and reimbursement for Sumavel DosePro or any of our other

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product candidates for which we may receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability if our insurance coverage for those claims is inadequate.

The commercial use of our product and clinical use of our product and product candidates expose us to the risk of product liability claims. This risk exists even if a product is approved for commercial sale by the FDA and manufactured in facilities licensed and regulated by the FDA, such as the case with Sumavel DosePro, or an applicable foreign regulatory authority. Our product and product candidates are designed to affect important bodily functions and processes. Any side effects, manufacturing defects, misuse or abuse associated with Sumavel DosePro or our product candidates could result in injury to a patient or even death. For example, because our DosePro technology is designed to be self-administered by patients, it is possible that a patient could fail to follow instructions and as a result apply a dose in a manner that results in injury. In addition, Zohydro ER is an opioid pain reliever that contains *hydrocodone*, which is a regulated controlled substance under the Controlled Substances Act of 1970, or CSA, and could result in harm to patients relating to its potential for abuse. In addition, a liability claim may be brought against us even if our product or product candidates merely appear to have caused an injury. Product liability claims may be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our product or product candidates, among others. If we cannot successfully defend ourselves against product liability claims we will incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

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

We have obtained product liability insurance coverage for commercial product sales and clinical trials with a $10 million per occurrence and a $10 million annual aggregate coverage limit. Our insurance coverage may not be sufficient to cover all of our product liability related expenses or losses and may not cover 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, in sufficient amounts or upon adequate terms to protect us against losses due to product liability. If we determine that it is prudent to increase our product liability coverage based on sales of Sumavel DosePro, approval of Zohydro ER or otherwise, we may be unable to obtain this increased product liability insurance on commercially reasonable terms or at all. Large judgments have been awarded in class action or individual lawsuits based on drugs that had unanticipated side effects, including side effects that are less severe than those of Sumavel DosePro and our product candidates. 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 decrease our cash and have a material adverse affect our business, results of operations, financial condition and prospects.

We may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters and other facilities are located in San Diego and the San Francisco Bay Area, which in the past have both experienced severe earthquakes. We do not carry earthquake insurance. As a result, earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

Our enterprise financial systems are located in our San Diego, California headquarters. Our manufacturing resource planning and enterprise quality systems are located in our Emeryville, California facility. If a disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters or our Emeryville facility, that damaged critical infrastructure, such as enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations at either location, it may be difficult or, in certain cases, impossible

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for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and our third-party manufacturers and suppliers activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product and product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers facilities pending use and disposal. We cannot completely eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, injury to our employees and others, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources. We do not currently carry biological or hazardous waste insurance coverage.

In connection with the reporting of our financial condition and results of operations, we are required to make estimates and judgments which involve uncertainties, and any significant differences between our estimates and actual results could have an adverse impact on our financial position, results of operations and cash flows.

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosure of contingent assets and liabilities. In particular, as part of our revenue recognition policy, our estimates of product returns, rebates and chargebacks require our most subjective and complex judgment due to the need to make estimates about matters that are inherently uncertain. Any significant differences between our actual results and our estimates and assumptions could negatively impact our financial position, results of operations and cash flows.

Changes in accounting standards and their interpretations could adversely affect our operating results.

GAAP are subject to interpretation by the Financial Accounting Standards Board, the American Institute of Certified Public Accountants, the SEC, and various other bodies that promulgate and interpret appropriate accounting principles. These principles and related implementation guidelines and interpretations can be highly complex and involve subjective judgments. A change in these principles or interpretations could have a significant effect on our reported financial results, and could affect the reporting of transactions completed before the announcement of a change.

Fluctuations in the value of the Euro or U.K. pound sterling could negatively impact our results of operations and increase our costs.*

Payments to our material suppliers and contract manufacturers are denominated in the Euro and U.K. pound sterling. Our reporting currency is the U.S. dollar and to date all of the revenues generated by sales of Sumavel DosePro have been in U.S. dollars. For the nine months ended September 30, 2012, $12.5 million (based on exchange rates as of September 30, 2012) of our materials purchased, contract manufacturing costs and other manufacturing-related costs were denominated in foreign currencies. As a result, we are exposed to foreign exchange risk, and our results of operations may be negatively impacted by fluctuations in the exchange rate between the U.S. dollar and the Euro or U.K. pound sterling. A significant appreciation in the Euro or U.K. pound sterling relative to the U.S. dollar will result in higher expenses and cause increases in our net losses. Likewise, to the extent that we generate any revenues denominated in foreign currencies, or become required to make payments in other foreign currencies, fluctuations in the exchange rate between the U.S. dollar and those foreign currencies could also negatively impact our results of operations. We currently have not entered into any foreign currency hedging contracts to reduce the effect of changes in foreign currency exchange rates, and foreign currency hedging is inherently risky and may result in unanticipated losses.

Our operating results are partially dependent on freight costs and our costs may increase significantly if we are unable to ship and transport finished products efficiently and economically across long distances and international borders.

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Our Sumavel DosePro product is manufactured in Europe and we transport significant volumes of that product across long distances and international borders. As a result, our operating results can be affected by changes in transportation costs. We generally ship our product by air freight, and freight rates can vary significantly due to a large number of factors beyond our control, including changes in fuel prices or general economic conditions. If demand for air freight should increase substantially, it could make it difficult for us to procure transportation space at prices we consider acceptable.

Because our products must cross international borders, we are subject to risk of delay due to customs inspection, if our documentation does not comply with customs rules and regulations or for similar reasons. In addition, any increases in customs duties or tariffs, as a result of changes to existing trade agreements between countries or otherwise, could increase our costs or the final cost of our products to our customers or increase our expenses. The laws governing customs and tariffs in many countries are complex, subject to many interpretations and often includes substantial penalties for noncompliance.

Risks Related to Our Financial Position and Capital Requirements

We have never generated net income or positive cash flow from operations and are dependent upon external sources of financing to fund our business and development.*

We launched our only approved product, Sumavel DosePro, in January 2010. Without a long history of sales, we may not accurately predict future sales, and we may never be able to significantly increase these sales, especially in light of the termination of our partnership with Astellas in March 2012 to co-promote Sumavel DosePro and our future reliance on our new co-promotion partner, Mallinckrodt. We have financed our operations almost exclusively through the proceeds from the issuance of our common and preferred stock, including the proceeds from our initial public offering completed in November 2010, our follow-on public offerings completed in September 2011 and July 2012, and debt, and have incurred losses and negative cash flow from operations in each year since our inception. Our net loss was $46.7 million during the nine months ended September 30, 2012, $83.9 million in 2011 and $73.6 million in 2010, and our cash used in operating activities was $43.7 million in the nine months ended September 30, 2012, $80.5 million in 2011 and $72.0 million in 2010. As of September 30, 2012, we had an accumulated deficit of $328.7 million. These losses and negative cash flow from operations have had a material adverse effect on our stockholders equity and working capital. Further, despite the revenues from Sumavel DosePro, we expect our losses to continue for at least the next several years primarily as a result of the expenses incurred in connection with our efforts in seeking marketing approval for Zohydro ER, the potential additional clinical development for Relay, any additional required testing for Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro ER. As a result, we may remain dependent upon external sources of financing to finance our business and the development and commercialization of our approved product and product candidates. To the extent we need to raise additional capital in the future, we cannot ensure that debt or equity financing will be available to us in amounts, at times or on terms that will be acceptable to us, or at all. Any shortfall in our cash resources could require that we delay or abandon certain development and commercialization activities and could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Our level of indebtedness could adversely affect our ability to raise additional capital to fund our operations, limit our ability to react to changes in the economy or our industry and prevent us from meeting our obligations.*

As of September 30, 2012, the principal amount of our total indebtedness was $30.0 million. On July 30, 2012, we terminated the term loan and revolving credit facility with Oxford and SVB, which consisted of a $25.0 million term loan and a $10.0 million revolving credit facility and repaid all outstanding amounts thereunder in full. Following such repayment, our outstanding indebtedness consists solely of $30.0 million under our financing agreement Healthcare Royalty, or the Healthcare Royalty financing agreement. Our outstanding debt and related debt service obligations could have important adverse consequences to us, including:

- heightening our vulnerability to downturns in our business or our industry or the general economy and restricting us from making improvements or acquisitions, or exploring business opportunities;

- requiring a significant portion of our available cash to be dedicated to the payment of revenue interest and fixed payments and interest on our indebtedness, therefore reducing our ability to use our available cash to fund our operations, capital expenditures and future business opportunities;

limiting our ability to obtain additional financing for working capital, capital expenditures, debt service requirements, acquisitions and general corporate or other purposes;

limiting our ability to adjust to changing market conditions and placing us at a competitive disadvantage compared to our competitors who have greater capital resources; and

subjecting us to financial and other restrictive covenants in our debt instruments, the failure with which to comply could result in an event of default under the applicable debt instrument that allows the lender to demand immediate repayment of the related debt.

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If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay product development, sales and marketing, capital and other expenditures, sell assets, seek additional capital or restructure or refinance our indebtedness. These alternative measures may not be successful and may not permit us to meet our scheduled debt service obligations.

Our debt instrument with Healthcare Royalty contains a number of financial covenants and other provisions, including a requirement that we attain specified future levels of revenues, which, if violated, could result in the immediate acceleration of our outstanding indebtedness.

Pursuant to the terms of our $30.0 million Healthcare Royalty financing agreement, we are required to make payments to Healthcare Royalty of $10.0 million on each of January 31, 2015, 2016 and 2017, as well as fixed percentages of amounts received (in the case of co-promotion revenues and license fees) or recorded (in the case of net products sales).

Our obligations under the Healthcare Royalty financing agreement are secured by a security interest in substantially all of our personal property (including, among other things, accounts receivable, equipment, inventory, contract rights or rights to payment of money, license agreements, general intangibles, including all intellectual property, and cash), to the extent necessary or used to commercialize our products. The security interest will be extinguished once the aggregate payments made by us to Healthcare Royalty equals $75.0 million. If we are unable to repay the indebtedness or other amounts when due, whether at maturity, upon termination or if declared due and payable by the lender following a default, Healthcare Royalty generally has the right to seize and sell the collateral securing the indebtedness, and other amounts owing to it thereunder.

We have the option to terminate the Healthcare Royalty financing agreement at our election prior to the termination date in connection with a change of control of our company, as defined in the Healthcare Royalty financing agreement, upon the payment of a base amount of $52.5 million, or, if higher, an amount that generates a 19% internal rate of return on the borrowed amount as of the date of prepayment, in each case reduced by the revenue interest and fixed payments received by Healthcare Royalty up to the date of such prepayment. In addition, Healthcare Royalty has the option to terminate the Healthcare Royalty financing agreement at its election in connection with a change of control of our company, as defined in the Healthcare Royalty financing agreement, the sale of all or substantially all of our assets (which includes the sale, transfer, assignment or licensing of our rights in the United States to either Sumavel DosePro or Zohydro ER), or an event of default (which includes the occurrence of a bankruptcy event or other material adverse change in our business), as defined in the Healthcare Royalty financing agreement, occurring thereunder. Upon such a termination by Healthcare Royalty prior to the maturity date specified in the Healthcare Royalty financing agreement, we are obligated to make a payment of a base amount of $45.0 million, or, if higher, an amount that generates a 17% internal rate of return on the borrowed amount as of the date of prepayment, in each case reduced by the revenue interests and fixed payments received by Healthcare Royalty up to the date of prepayment. If we were required to accelerate the payment of these amounts upon a default, we would be required to find an alternate source of capital from which to draw funds and there can be no assurances that we would be able to do so on terms acceptable to us, or at all.

There can be no assurance that we will not breach the terms of, or that an event of default or termination event will not occur under, our Healthcare Royalty financing agreement and, if a breach or event of default or termination event occurs, there can be no assurance that we will be able to obtain necessary waivers or amendments from Healthcare Royalty or refinance the related indebtedness or other amounts due and payable on terms we find acceptable, or at all.

As a result, any failure to pay our debt service obligations when due, any breach or default of our obligations under our Healthcare Royalty financing agreement, or any other event that allows Healthcare Royalty to demand immediate repayment of borrowings or termination payments, could have a material adverse effect on our business, results of operations, financial condition and prospects. Furthermore, the arrangement under the Healthcare Royalty financing agreement may make us significantly less attractive to potential acquirers, and in the event that we exercised our change of control pay-off option in order to carry out a change of control, the payment of such funds out of our available cash or acquisition proceeds would reduce acquisition proceeds for our stockholders.

Our results of operations and liquidity needs could be materially negatively affected by market fluctuations and economic downturn.

Our results of operations and liquidity could be materially negatively affected by economic conditions generally, both in the United States and elsewhere around the world. Domestic and international equity and debt markets have experienced

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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 or worsen and the markets continue to remain volatile, our results of operations and liquidity 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 decline. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are not federally insured. If economic instability continues, we cannot provide assurance that we will not experience losses on these investments.

Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

We may need to raise additional funds through public or private equity offerings, debt financings, receivables or royalty financings or corporate collaboration and licensing arrangements. To the extent that we raise additional capital by issuing equity securities or convertible debt, your ownership interest in us will be diluted. Debt financing typically contains covenants that restrict operating activities. Our obligations under the Healthcare Royalty financing agreement are secured by a security interest in substantially all of our personal property (including, among other things, accounts receivable, equipment, inventory, contract rights or rights to payment of money, license agreements, general intangibles, including all intellectual property, and cash). The security interest will be extinguished once the aggregate payments made by us to Healthcare Royalty equals $75.0 million.

The Healthcare Royalty financing agreement contains provisions which allows Healthcare Royalty to accelerate the debt and seize and sell the collateral if, among other things, we fail to pay revenue interest payments and fixed payments when due or breach our obligations under the agreement or if a material adverse change in our business or any other event of default occurs. Any future debt financing we enter into may involve more onerous covenants that restrict our operations, may be secured by some or all of our assets, and will likely allow the lenders to accelerate the debt and seize and sell any collateral following a default. Our obligations under our outstanding Healthcare Royalty financing agreement or any future debt financing will need to be repaid, which creates additional financial risk for our company, particularly if our business or prevailing financial market conditions are not conducive to paying-off or refinancing our outstanding debt obligations.

If we raise additional funds through collaboration, licensing or other similar arrangements, it may be necessary to relinquish potentially valuable rights to our current product or product candidates or proprietary technologies, or grant licenses on terms that are not favorable to us. If adequate funds are not available, our ability to achieve profitability or to respond to competitive pressures would be significantly limited and we may be required to delay, significantly curtail or eliminate the commercialization and development of our product or product candidates.

Our ability to utilize our net operating loss and research and development income tax credit carryforwards may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the IRC, substantial changes in our ownership may limit the amount of net operating loss and research and development income tax credit carryforwards (collectively, tax attributes) that could be utilized annually in the future to offset taxable income, if any. Specifically, this limitation may arise in the event of a cumulative change in ownership of our company of more than 50% within a three-year period as determined under the IRC, which we refer to as an ownership change. Any such annual limitation may significantly reduce the utilization of these tax attributes before they expire. Prior to our initial public offering in November 2010, we performed an IRC Section 382 and 383 analysis and determined that we had one ownership change, which occurred in August 2006 upon the issuance of convertible preferred stock. We performed an additional IRC Section 382 and 383 analysis upon the issuance of common stock in our follow-on public offering in September 2011, and together with the issuance of common stock in our initial public offering and certain other transactions involving our common stock, resulted in an additional ownership change. As a result of these ownership changes, our ability to use our then existing tax attributes to offset future taxable income, if any, was limited.

We expect the issuance of common stock and warrants in our public offering in July 2012 will result in an additional ownership change, which will further limit the amount of the tax attributes we may use to offset future taxable income, if any. In addition, any future equity financing transactions, private placements and other transactions that occur within the specified three-year period may trigger additional ownership changes, which could further limit our use of such tax attributes. Any such limitations, whether as the result of prior or future offerings of our common stock or sales of common stock by our existing stockholders, could have an adverse effect on our consolidated results of operations in future years.

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Risks Related to Regulation of our Product and Product Candidates

Our currently marketed product, Sumavel DosePro, is and any of our other product candidates that receive regulatory approval will be subject to ongoing and continued regulatory review, which may result in significant expense and limit our ability to commercialize such products.

Even after we achieve U.S. regulatory approval for a product, the FDA may still impose significant restrictions on the approved indicated uses for which the product may be marketed or on the conditions of approval. For example, a product s approval may contain requirements for potentially costly post-approval studies and surveillance, including Phase 4 clinical trials, to monitor the safety and efficacy of the product. We will also be subject to ongoing FDA obligations and continued regulatory review with respect to the manufacturing, processing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and with GCPs and good laboratory practices, which are regulations and guidelines enforced by the FDA for all of our products in clinical and pre-clinical development, and for any clinical trials that we conduct post-approval. To the extent that a product is approved for sale in other countries, we may be subject to similar restrictions and requirements imposed by laws and government regulators in those countries.

In the case of Zohydro ER and any other product candidates or products containing controlled substances, we and our contract manufacturers will also be subject to ongoing DEA regulatory obligations, including, among other things, annual registration renewal, security, recordkeeping, theft and loss reporting, periodic inspection and annual quota allotments for the raw material for commercial production of our products. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations, QSR requirements for medical device components or similar requirements, if applicable. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where, or processes by which, the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturer or us, including requiring product recall, notice to physicians, withdrawal of the product from the market or suspension of manufacturing. In that regard, because all of our contract manufacturers for Sumavel DosePro are located outside the United States, they may be subject to foreign laws and regulations governing the manufacture of drugs and devices, and any failure by them to comply with those laws and regulations may delay or interrupt supplies of our product.

If we, our product or product candidates or the manufacturing facilities for our product or product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- impose restrictions on the marketing or manufacturing of the product, suspend or withdraw product approvals or revoke necessary licenses;
- issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;
- commence criminal investigations and prosecutions;
- impose injunctions, suspensions or revocations of necessary approvals or other licenses;
- impose fines or other civil or criminal penalties;
- suspend any ongoing clinical trials;
- deny or reduce quota allotments for the raw material for commercial production of our controlled substance products;

delay or refuse to approve pending applications or supplements to approved applications filed by us;

refuse to permit drugs or precursor chemicals to be imported or exported to or from the United States;

suspend or impose restrictions on operations, including costly new manufacturing requirements; or

seize or detain products or require us to initiate a product recall.

In addition, our product labeling, advertising and promotion are subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription drug products. In particular, a drug may not be promoted for uses that are not approved by the FDA as reflected in the product s approved labeling, although the FDA does not regulate the prescribing practices of physicians. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including substantial monetary penalties and criminal prosecution.

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The FDA s regulations, policies or guidance may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. If we are not able to achieve and maintain regulatory compliance, we may not be permitted to market our drugs, which would adversely affect our ability to generate revenue and achieve or maintain profitability.

Sumavel DosePro, Zohydro ER, Relday and our other product candidates may cause undesirable side effects or have other unexpected properties that could result in post-approval regulatory action.

If we or others identify undesirable side effects, or other previously unknown problems, caused by our products, other products or our product candidates with the same or related active ingredients, after obtaining U.S. regulatory approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require us to recall product;
- regulatory authorities may require the addition of warnings in the product label or narrowing of the indication in the product label;
- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way the product is administered or modify the product in some other way;
- the FDA may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety or efficacy of the product;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

The most common treatment-emergent adverse reactions (reported by at least 5% of patients) for *sumatriptan* injection as described in the Sumavel DosePro Prescribing Information summarizing two large placebo-controlled clinical trials were injection site reaction (59%), atypical sensations (42%), dizziness (12%), flushing (7%), chest discomfort (5%), weakness (5%), and neck pain/stiffness (5%).

The incidence of adverse events was 33.7% and 28.8% in the open label titration and double blind treatment periods of our Phase 3 efficacy trial for Zohydro ER, respectively. Overall, the most commonly reported adverse events (>2%) in this trial were constipation, nausea, somnolence, vomiting, diarrhea, insomnia, fatigue, headache, dizziness and dry mouth. These are typical adverse events associated with chronic opioid therapy.

Any of the above events resulting from undesirable side effects or other previously unknown problems could prevent us from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our product candidates.

Our development and commercialization strategy for Zohydro ER depends upon the FDA s prior findings of safety and effectiveness of Zohydro ER based on data not developed by us, but which the FDA may rely upon in reviewing our NDA.

The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the FFDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Under this statutory provision, the FDA may rely, for purposes of approving an NDA, on findings of safety and effectiveness based on data not developed by the filer of the NDA. Similar to Sumavel DosePro, we submitted the NDA for Zohydro ER under Section 505(b)(2), and as such the NDA will rely, in part, on the FDA s previous findings of safety and effectiveness for *hydrocodone*. Even though we may be able to take advantage of Section 505(b)(2) to support potential U.S. approval for Zohydro ER, the FDA may require us, and did require us with respect to Sumavel DosePro, to perform additional studies or measurements to support approval. In addition, the FDA s interpretation and use of Section 505(b)(2) has been controversial and has previously been challenged in court, but without a definitive ruling on the propriety of the FDA s approach. Future challenges, including a direct challenge to the approval of our products, may be possible and, if successful, could limit or eliminate our ability to rely on the Section 505(b)(2) pathway for the approval of our products. Such a result could require us to conduct additional testing and costly clinical trials, which could substantially delay or prevent the approval and launch of our products.

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Zohydro ER will be subject to DEA regulations and, failure to comply with these regulations, or the cost of compliance with these regulations, may adversely affect our business.

Zohydro ER contains *hydrocodone*, a regulated controlled substance under the CSA, which establishes, among other things, certain registration, production quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Zohydro ER, because it is a single-entity *hydrocodone* product, is expected to be regulated by the DEA as a Schedule II controlled substance under the CSA. All Schedule II substance prescriptions, such as prescriptions for Zohydro ER, must be in writing and signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription.

The manufacture, shipment, storage, sale and use, among other things, of controlled substances that are pharmaceutical products are subject to a high degree of regulation, including security, record-keeping and reporting obligations enforced by the DEA. Our failure to comply with these requirements could result in the loss of our DEA registration, significant restrictions on Zohydro ER, civil penalties or criminal prosecution.

The DEA, and some states, also conduct periodic inspections of registered establishments that handle controlled substances. Facilities that conduct research, manufacture, store, distribute, import or export controlled substances must be registered to perform these activities and have the security, control and inventory mechanisms required by the DEA to prevent drug loss and diversion. Failure to maintain compliance, particularly non-compliance resulting in loss or diversion, can result in regulatory action that could have a material adverse effect on our business, results of operations, financial condition and prospects. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal proceedings.

Individual states also have controlled substances laws. Though state controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule drugs, as well. While some states automatically schedule a drug when the DEA does so, in other states there has to be rulemaking or a legislative action. State scheduling may delay commercial sale of any controlled substance drug product for which we obtain federal regulatory approval and adverse scheduling could have a material adverse effect on the commercial attractiveness of such product. We or our partners must also obtain separate state registrations in order to be able to obtain, handle, and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions from the states in addition to those from the DEA or otherwise arising under federal law.

The FDA, in consultation with the DEA, will require us to develop a comprehensive risk management program to reduce the inappropriate use of our product candidate, including restrictions on the manner in which it is marketed and sold, so as to reduce the risk of improper patient selection and diversion or abuse of the product. We submitted a REMS at the time of the NDA submission for Zohydro ER and developing such a program in consultation with the FDA may be a time-consuming process and could delay approval of our product candidate. Such a program or delays of any approval from the FDA could limit market acceptance of the product.

Under the terms of our license agreement with Alkermes, Alkermes has the exclusive right to manufacture and supply both clinical and commercial supplies of Zohydro ER. While Alkermes is required to comply with applicable laws and regulations regarding controlled substances, we do not have any direct control over Alkermes compliance in these regards, and any failure by Alkermes to comply with those laws and regulations could result in a reduction or cessation of production of Zohydro ER.

Annual DEA quotas on the amount of hydrocodone allowed to be produced in the United States and our specific allocation of hydrocodone by the DEA could significantly limit any additional clinical development of Zohydro ER, if required, as well as the production or sale of Zohydro ER even if we obtain FDA approval.

The DEA limits the availability and production of all Schedule II substances through a quota system which includes a national aggregate quota and individual quotas. Because *hydrocodone* is subject to the DEA s production and procurement quota scheme, the DEA establishes annually an aggregate quota for how much *hydrocodone* may be produced in total in the United States based on the DEA s estimate of the quantity needed to meet legitimate scientific and medicinal needs. This limited aggregate amount of *hydrocodone* that the DEA allows to be produced in the United States each year is allocated among individual companies, who must submit applications annually to the DEA for individual production and procurement quotas. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make

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such adjustments. Alkermes, which has licensed us the right to sell Zohydro ER in the United States, if approved, was allocated a sufficient quantity of *hydrocodone* to meet our planned clinical and pre-clinical needs during 2011. However, in future years, we will need significantly greater amounts of *hydrocodone* to implement our commercialization plans if the FDA approves Zohydro ER.

Moreover, we do not know what amounts of *hydrocodone* other companies developing product candidates containing *hydrocodone* may request for future years. The DEA, in assessing factors such as medical need, abuse and diversion potential and other policy considerations, may choose to set the aggregate *hydrocodone* quota lower than the total amount requested by the companies. Alkermes is permitted to petition the DEA to increase the annual aggregate quota after it is initially established, but there is no guarantee that the DEA would act favorably upon such a petition. Our procurement quota of *hydrocodone* may not be sufficient to meet any future clinical development needs or commercial demand if we receive regulatory approval for Zohydro ER. Any delay or refusal by the DEA in establishing the procurement quota or a reduction in our quota for *hydrocodone* or a failure to increase it over time as we anticipate could delay or stop any additional clinical development of Zohydro ER, if required, or, if approved, the product launch or commercial sale of Zohydro ER or cause us to fail to achieve our expected operating results, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

We will need to obtain FDA approval of our proposed product trade names and any failure or delay associated with such approval may adversely impact our business.

Any trade name we intend to use for our products will require approval from the FDA regardless of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office, or PTO. The FDA typically conducts a rigorous review of proposed trade names, including an evaluation of potential for confusion with other trade names. The FDA may also object to a trade name if it believes the name inappropriately implies medical claims. If the FDA objects to our proposed trade names, we may be required to adopt an alternative name for our product candidate. If we adopt an alternative name, we would lose the benefit of our existing trademark applications and may be required to expend significant additional resources in an effort to identify a suitable trade name that would qualify under applicable trademark laws, and not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to generate revenues from our products.

Even though Sumavel DosePro has received regulatory approval in the United States and a limited number of foreign countries, we, Desitin, or any other potential partners may never receive approval in other countries or commercialize our products anywhere outside of the United States.

We have established an exclusive commercial partnership for Sumavel DosePro with Desitin in the European Union and three other countries in order to seek to accelerate the development and regulatory approvals in those territories. We may also seek to establish commercial partnerships for Sumavel DosePro in other foreign countries. In order to market Sumavel DosePro or any other products outside of the United States, we, Desitin, or any potential partner must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our products. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed in these Risk Factors and elsewhere in this Quarterly Report on Form 10-Q regarding FDA approval in the United States, as well as other risks. For example, legislation analogous to Section 505(b)(2) of the FFDCA in the United States does not exist in other countries. In territories where data is not freely available, we or our partners may not have the ability to commercialize our products without negotiating rights from third parties to refer to their clinical data in our regulatory applications, which could require the expenditure of significant additional funds. We, Desitin, or any potential partner may be unable to obtain rights to the necessary clinical data and may be required to develop our own proprietary safety effectiveness dossiers. Desitin submitted a Marketing Authorization Application for Sumavel DosePro to the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)) in Germany, the reference member state, through the Decentralized Procedure in October 2009, following completion of a European pivotal bioequivalence trial comparing needle-free Sumavel DosePro to a traditional needle-based autoinjector, Imigran-Inject, the European brand of Imitrex STATdose. However, regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others.

Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed in these Risk Factors and elsewhere in this Quarterly Report on Form 10-Q regarding FDA approval in the United States. As described above, such effects include the risks that our product and product candidates may not be approved at all or for all requested indications, which could limit the uses of our product and product candidates and have an adverse effect on their commercial potential or require costly, post-marketing studies. In addition, we, Desitin, or any potential partner may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution if we fail to comply with applicable foreign regulatory requirements.

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Health care reform measures and changes in policies, funding, staffing and leadership at the FDA and other agencies could hinder or prevent the commercial success of Sumavel DosePro and any of our product candidates that may be approved by the FDA.

In the United States, there have been a number of legislative and regulatory changes to the healthcare system in ways that could affect our future results of operations and the future results of operations of our potential customers. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established the Part D prescription drug benefit, which became effective January 1, 2006. Under the prescription drug benefit, Medicare beneficiaries can obtain prescription drug coverage from private sector plans that are permitted to limit the number of prescription drugs that are covered in each therapeutic category and class on their formularies. If Sumavel DosePro or any of our product candidates that are approved by the FDA are not widely included on the formularies of these plans, our ability to market our products to the Medicare population could suffer.

Furthermore, there have been and continue to be a number of initiatives at the federal and state levels that seek to reduce healthcare costs. Most recently, in March 2010, President Obama signed into law the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA, which includes measures to significantly change the way health care is financed by both governmental and private insurers. Among the provisions of the PPACA of greatest importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, beginning in 2011;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23% and 13% of the average manufacturer price for most branded and generic drugs, respectively;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D, beginning in 2011;

- extension of manufacturers Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, effective March 23, 2010;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in April 2010 and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing both the volume of sales and manufacturers Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program, effective in January 2010;

- new requirements to report certain financial arrangements with physicians and others, including reporting any transfer of value made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year beginning in 2013;

- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012;

a licensure framework for follow-on biologic products;

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

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 and those recommendations could have the effect of law even if Congress does not act on the recommendations; and

establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending beginning by January 1, 2011.

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Many of the details regarding the implementation of the PPACA are yet to be determined, and at this time, it remains unclear the full effect that the PPACA would have on our business. Since its passage, a number of state governors have strenuously opposed certain of the PPACA s provisions, in particular the mandate that all individuals must obtain insurance, and initiated lawsuits challenging its constitutionality. These challenges are pending final adjudication in several jurisdictions, including the United States Supreme Court. Congress has also proposed a number of legislative initiatives, including possible repeal of the PPACA. At this time, it remains unclear whether there will be any changes made to the PPACA, whether to certain provisions or its entirety.

Additionally, individual states have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects.

In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This can reduce demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

In certain foreign markets, the pricing of prescription drugs is subject to government control and reimbursement and may, in some cases, be unavailable. In the United States, the commercial success of Sumavel DosePro and our product candidates, if and when commercialized, will depend, in part, upon the availability of coverage and reimbursement from third-party payors at the federal, state and private levels. Third-party payors include governmental programs such as Medicare or Medicaid, private insurance plans and managed care plans. These third-party payors may deny coverage or reimbursement for a product or therapy in whole or in part if they determine that the product or therapy was not medically appropriate or necessary. Also, third-party payors have attempted to control costs by limiting coverage through the use of formularies and other cost-containment mechanisms and the amount of reimbursement for particular procedures or drug treatments.

Additionally, given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform, the cost of prescription drugs and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to market our products and generate revenues. In addition, legislation has been introduced in Congress that, if enacted, would permit more widespread importation or re-importation of pharmaceutical products from foreign countries into the United States, including from countries where the products are sold at lower prices than in the United States. Such legislation, or similar regulatory changes, could lead to a decision to decrease our prices to better compete, which, in turn, could adversely affect our business, results of operations, financial condition and prospects. Alternatively, in response to legislation such as this, we might elect not to seek approval for or market our products in foreign jurisdictions in order to minimize the risk of re-importation, which could also reduce the revenue we generate from our product sales. It is also possible that other legislative proposals having similar effects will be adopted.

Furthermore, regulatory authorities assessment of the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects. For example, average review times at the FDA for marketing approval applications have fluctuated over the last ten years, and we cannot predict the review time for any of our submissions with any regulatory authorities. In addition, review times can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes.

We may incur liability if our continuing medical or health education programs and/or product promotions are determined, or are perceived, to be inconsistent with regulatory guidelines.

The FDA provides guidelines with respect to appropriate promotion and continuing medical and health education activities. Although we endeavor to follow these guidelines, the FDA or the Office of the Inspector General of the U.S. Department of Health and Human Services may disagree, and we may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. In addition, management s attention could be diverted and our reputation could be damaged.

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If we fail to comply with federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients rights are and will be applicable to our business. We could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Law, which constrains our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, and which may apply to entities like us which provide coding and billing advice to customers;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, and its implementing regulations, and the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, which prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also impose certain requirements relating to the privacy, security and transmission of individually identifiable health information;

- federal physician self-referral laws, such as the Stark law, which prohibit a physician from making a referral to a provider of certain health services with which the physician or the physician s family member has a financial interest, and prohibit submission of a claim for reimbursement pursuant to a prohibited referral; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under the U.S. federal Anti-Kickback Statute, it is possible that some of our business activities could be subject to challenge under one or more of such laws. To the extent that any product we make is sold in a foreign country, we may be subject to similar foreign laws and regulations. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in U.S. federal or state health care programs, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management s attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Import/export regulations and tariffs may change and increase our costs.

We are subject to risks associated with the regulations relating to the import and export of products and materials. We cannot predict whether the import and/or export of our products will be adversely affected by changes in, or enactment of, new quotas, duties, taxes or other charges or restrictions imposed by India (where our supplier of the *sumatriptan* used in Sumavel DosePro is located), the United Kingdom (where the assembly of Sumavel DosePro takes place) or any other country in the future. Any of these factors could adversely affect our business, results of operations, financial condition and prospects.

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Risks Related to Intellectual Property

Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our product, Sumavel DosePro, and our product candidates, Zohydro ER and Relday, their respective components, formulations, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing Sumavel DosePro or our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

We in-license certain intellectual property for Zohydro ER from Alkermes, and certain intellectual property for Relday from Durect. We rely on these licensors to file and prosecute patent applications and maintain patents and otherwise protect certain of the intellectual property we license from them. We have not had and do not have primary control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, with respect to our license agreements with Alkermes and Durect, we cannot be certain that such activities by Alkermes and Durect have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. Alkermes has retained the first right, but not the obligation, to initiate an infringement proceeding against a third-party infringer of the intellectual property rights that Alkermes has licensed to us, and enforcement of our licensed patents or defense of any claims asserting the invalidity or unenforceability of these patents would also be subject to the control or cooperation of Alkermes. Similarly, Durect has retained the first right, but not the obligation, to initiate an infringement proceeding against a third-party infringer of certain of the intellectual property rights that Durect has licensed to us, and enforcement of certain of our licensed patents or defense of any claims asserting the invalidity or unenforceability of these patents would also be subject to the control or cooperation of Durect. We are not entitled to control the manner in which Alkermes or Durect may defend certain of the intellectual property that is licensed to us and it is possible that their defense activities may be less vigorous than had we conducted the defense ourselves.

Most of our patents related to DosePro were acquired from Aradigm, who acquired those patents from a predecessor owner. Our patents related to Zohydro ER are licensed from Alkermes. Thus, most of our patents, as well as many of our pending patent applications, were not written by us or our attorneys, and we did not have control over the drafting and prosecution of these patents. Further, the former patent owners and our licensors might not have given the same attention to the drafting and prosecution of these patents and applications as we would have if we had been the owners of the patents and applications and had control over the drafting and prosecution. In addition, the former patent owners and Alkermes may not have been completely familiar with U.S. patent law, possibly resulting in inadequate disclosure and/or claims. This could possibly result in findings of invalidity or unenforceability of the patents we own and in-license, patents issuing with reduced claim scope, or in pending applications not issuing as patents.

In addition, as part of the agreement where we acquired patents related to DosePro from Aradigm, Aradigm retained, and we granted to Aradigm, a non-exclusive, worldwide, royalty free license to the acquired patents solely for purposes of the delivery of one or more aerosolized APIs directly into the bronchia or lungs. The agreement with Aradigm also includes a covenant not to compete with us regarding technologies or products for the delivery of one or more APIs via needle free injection. That covenant expired on August 26, 2010, giving Aradigm or its licensees the right to develop and sell other needle-free injection technologies and products.

The patent positions of pharmaceutical, biopharmaceutical and medical device 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 patents in these fields has emerged to date in the United States. There have been recent changes regarding how patent laws are interpreted, and both the PTO and Congress have recently proposed radical changes to the patent system. We cannot accurately predict future changes in the interpretation of patent laws or changes to patent laws which might be enacted into law. Those changes may materially affect our patents, our ability to obtain patents and/or the patents and applications of our collaborators and licensors. The patent situation in these fields 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 or narrow the scope of our patent protection. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in the patents we own or to which we have a license or third-party patents.

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The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the pharmaceutical compounds used in Sumavel DosePro and our product candidates but that are not covered by the claims of our patents;
- the APIs in Sumavel DosePro and our current product candidates are, or will soon become, commercially available in generic drug products, and no patent protection will be available without regard to formulation or method of use;
- we or our licensors, as the case may be, may not be able to detect infringement against our in-licensed patents, which may be especially difficult for manufacturing processes or formulation patents;
- we or our licensors, as the case may be, might not have been the first to make the inventions covered by our owned or in-licensed issued patents or pending patent applications;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are dominating patents to Sumavel DosePro or our product candidates of which we are not aware;
- it is possible that there are prior public disclosures that could invalidate our or our licensors inventions, as the case may be, or parts of our or their inventions of which we or they are not aware;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors , as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our device or product candidates;

our owned or in-licensed issued patents may not provide us with any competitive advantages, or may be narrowed in scope, be held invalid or unenforceable as a result of legal challenges by third parties;

we may not develop additional proprietary technologies for which we can obtain patent protection; or

the patents of others may have an adverse effect on our business.

We also may rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect, and we have limited control over the protection of trade secrets used by our licensors, collaborators and suppliers. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If our confidential or proprietary information is divulged to or acquired by third parties, including our competitors, our competitive position in the marketplace will be harmed and our ability to successfully penetrate our target markets could be severely compromised.

If any of our owned or in-licensed patents are found to be invalid or unenforceable, or if we are otherwise unable to adequately protect our rights, it could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Likewise, our patents covering certain technology used in our DosePro device are expected to expire on various dates from 2014 through 2026 and the patents licensed to us by Alkermes are expected to expire in 2019. As of September 30, 2012, our patent portfolio included twelve issued U.S. patents, four pending U.S. patent applications, 40 issued foreign patents and four pending foreign patent applications relating to various aspects of Sumavel DosePro and our DosePro technology. Nine of our U.S. patents relating to our DosePro technology, U.S. Patent Nos. 5,891,086, 5,957,886, 6,135,979, 7,776,007, 7,901,385, 8,267,903, 8,118,771, 8,241,243 and 8,241,244 are expected to expire in 2014, 2016, 2017, 2026, 2026, 2023, 2023, 2025 and 2022, respectively. U.S. Patent No. 5,891,086 covers a particular actuator mechanism forming a part of the needleless injector device; U.S. Patent No. 5,957,886 claims a needleless injector system using a viscous damping medium; U.S. Patent No. 6,135,979 covers the needleless injector with particular

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safety mechanisms; U.S. Patent Number 7,776,007 covers the cap and latch mechanism; U.S. Patent Nos. 7,901,385 and 8,267,903 encompass various embodiments of the casing for enclosing the injection devices; and U.S. Patent Nos. 8,118,771, 8,241,243 and 8,241,244 cover a method of reducing breakage of glass capsules used in the Sumavel DosePro device. Upon the expiration of these patents, we will lose the right to exclude others from practicing these inventions. Additionally, since these nine patents are the only patents currently listed in the FDA Orange Book for Sumavel DosePro, their expiration will mean that we lose certain advantages that come with Orange Book listing of patents. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects. Moreover, if Alkermes or Durect decides not to commence or continue any action relating to the defense of the patents they have licensed to us, they are required to notify us and we have the right to initiate proceedings after receiving their notice. Such proceedings will require the assistance of Alkermes or Durect, as applicable, and we have limited control over the amount or timing of resources Alkermes or Durect devotes on our behalf or the priority they place on enforcing these patent rights.

If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to a license agreement with Alkermes, pursuant to which we license key intellectual property for Zohydro ER. We have also entered into a license agreement with Durect, pursuant to which we license key intellectual property for Relday. These existing licenses impose various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate the license, in which event we would not be able to develop or market the affected products. If we lose such license rights, our business, results of operations, financial condition and prospects may be materially adversely affected. We may enter into additional licenses in the future and if we fail to comply with obligations under those agreements, we could suffer similar consequences.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and we may be unable to protect our rights to our products and technology.

If we or our collaborators or licensors choose to go to court to stop a third party from using the inventions claimed in our owned or in-licensed patents, that third party may ask the court to rule that the patents are invalid and/or should not be enforced against that third party. These lawsuits are expensive and would consume time and other resources even if we or they, as the case may be, were successful in stopping the infringement of these patents. In addition, there is a risk that the court will decide that these patents are not valid and that we or they, as the case may be, do not have the right to stop others from using the inventions.

There is also the risk that, even if the validity of these patents is upheld, the court will refuse to stop the third party on the ground that such third-party s activities do not infringe our owned or in-licensed patents. In addition, the U.S. Supreme Court has recently changed some tests regarding granting patents and assessing the validity of patents. As a consequence, issued patents may be found to contain invalid claims according to the newly revised standards. Some of our own or in-licensed patents may be subject to challenge and subsequent invalidation or significant narrowing of claim scope in a reexamination proceeding before the PTO, or during litigation, under the revised criteria which make it more difficult to obtain patents.

We may also not be able to detect infringement of our own or in-licensed patents, which may be especially difficult for methods of manufacturing or formulation products. While we intend to take actions reasonably necessary to enforce our patent rights, we depend, in part, on our licensors and collaborators to protect a substantial portion of our proprietary rights. For example, Alkermes, our licensor, is primarily responsible for the enforcement of the intellectual property rights related to Zohydro ER. Under the agreement, Alkermes has the first right, but not the obligation, to initiate an infringement proceeding against a third-party infringer. If Alkermes decides not to commence or continue any action, they are required to notify us and grant us step in rights to enforce the in-licensed intellectual property. Such enforcement will require the cooperation of Alkermes, and we will be responsible for Alkermes reasonable expenses and attorney s fees incurred as a result of that cooperation. We have limited control over the amount or timing of resources Alkermes devotes on our behalf or the priority they place on enforcing these patent rights to our advantage. Similarly, Durect, our licensor, is primarily responsible for the enforcement of certain of the intellectual property rights it licenses to us related to Relday. Under the agreement, Durect has the first right, but not the obligation, to initiate an infringement proceeding against a third-party infringer of those intellectual property rights through the use, marketing, sale or import of a product that is competitive to Relday. If Durect decides not to commence or continue any such action, we have the right, but not the duty, to do so and such enforcement will require the cooperation of Durect. We have limited control over the amount or timing of resources Durect devotes on our behalf or the priority it places on enforcing these patent rights to our advantage.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

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Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our device and product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields relating to Sumavel DosePro and our product candidates. As the medical device, biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert our product or product candidates infringe the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of medical devices, drugs, products or their methods of use. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product, product candidates, technology or methods.

In addition, there may be issued patents of third parties of which we are currently unaware, that are infringed or are alleged to be infringed by our product, product candidates or proprietary technologies. Because some patent applications in the United States may be maintained in secrecy until the patents are issued, because patent applications in the United States and many foreign jurisdictions are typically not published until eighteen months after filing, and because publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding declared by the PTO to determine priority of invention in the United States. If another party has reason to assert a substantial new question of patentability against any of our claims in our owned and in-licensed U.S. patents, the third party can request that the PTO reexamine the patent claims, which may result in a loss of scope of some claims or a loss of the entire patent. In addition to potential infringement claims, interference and reexamination proceedings, we may become a party to patent opposition proceedings in the European Patent Office where either our patents are challenged, or we are challenging the patents of others. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if the other party had independently arrived at the same or similar invention prior to our own or, if applicable, our licensor s invention, resulting in a loss of our U.S. patent position with respect to such inventions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our device and/or product candidates and/or proprietary technologies infringe their intellectual property rights. These lawsuits are costly and could adversely affect our results of operations and divert the attention of managerial and technical personnel. There is a risk that a court would decide that we or our commercialization partners are infringing the third party s patents and would order us or our partners to stop the activities covered by the patents. In addition, there is a risk that a court will order us or our partners to pay the other party damages for having violated the other party s patents.

If a third-party s patents was found to cover our device and/or product candidates, proprietary technologies or their uses, we or our collaborators could be enjoined by a court and required to pay damages and could be unable to commercialize Sumavel DosePro or our product candidates or use our proprietary technologies unless we or they obtained a license to the patent. A license may not be available to us or our collaborators on acceptable terms, if at all. In addition, during litigation, the patent holder could obtain a preliminary injunction or other equitable relief which could prohibit us from making, using or selling our products, technologies or methods pending a trial on the merits, which could be years away.

There is a substantial amount of litigation involving patent and other intellectual property rights in the device, biotechnology and pharmaceutical industries generally. If a third party claims that we or our collaborators infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management s attention from our core business;

- substantial damages for infringement, which we may have to pay if a court decides that the product at issue infringes on or violates the third party s rights, and if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner s attorneys fees;

- a court prohibiting us from selling or licensing the product unless the third party licenses its product rights to us, which it is not required to do;

if a license is available from a third party, we may have to pay substantial royalties, upfront fees and/or grant cross-licenses to intellectual property rights for our products; and

redesigning our products or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

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Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Although we own worldwide rights to Sumavel DosePro, we do not have patent protection for the product in a significant number of countries, and we will be unable to prevent infringement in those countries.

Our patent portfolio related to DosePro includes patents in the United States, Canada, Germany, Spain, France, the United Kingdom, Italy, and Japan. The covered technology and the scope of coverage varies from country to country. For those countries where we do not have granted patents, we have no ability to prevent the unauthorized use of our intellectual property, and third parties in those countries may be able to make, use, or sell products identical to, or substantially similar to DosePro.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on our owned and in-licensed patents are due to be paid to the PTO in several stages over the lifetime of the patents. Future maintenance fees will also need to be paid on other patents which may be issued to us. We have systems in place to remind us to pay these fees, and we employ outside firms to remind us or our in-licensor to pay annuity fees due to foreign patent agencies on our pending foreign patent applications. The PTO 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. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, 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. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business. For the patents and patent applications related to Zohydro ER, Alkermes is obligated to maintain our in-licensed patents in the United States under our license agreement. Should Alkermes fail to pursue maintenance of our licensed patents and patent applications, Alkermes is obligated to notify us and, at that time, we will be granted an opportunity to maintain the prosecution and avoid withdrawal, cancellation, expiration or abandonment of the licensed U.S. patents and applications. For the patents and patent applications related to Relday, Durect is obligated to maintain certain of our in-licensed patents on a worldwide basis, using commercially reasonable efforts, under our license agreement. Should Durect fail to pursue maintenance of certain of those licensed patents and patent applications, Durect is obligated to notify us and, at that time, we will be granted an opportunity to maintain the prosecution and avoid withdrawal, cancellation, expiration or abandonment of those licensed patents and applications.

We also may rely on trade secrets and confidentiality agreements to protect our technology and know-how, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect, and we have limited control over the protection of trade secrets used by our licensors, collaborators and suppliers. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If our confidential or proprietary information is divulged to or acquired by third parties, including our competitors, our competitive position in the marketplace will be harmed and our ability to successfully generate revenues from Sumavel DosePro and, if approved by the FDA or other regulatory authorities, our product candidates could be adversely affected.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the device, biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other device, biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management, which would adversely affect our financial condition.

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Risks Relating to the Securities Markets and an Investment in Our Stock

The market price of our common stock has fluctuated and is likely to continue to fluctuate substantially.*

The market prices for securities of biotechnology and pharmaceutical companies have historically been highly volatile, and the market has recently experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. Since the commencement of trading in connection with our initial public offering in November 2010, the publicly traded shares of our common stock have themselves experienced significant price and volume fluctuations. During the quarter ended September 30, 2012, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price of $1.99 to a high sale price of $2.86. This market volatility is likely to continue. These and other factors could reduce the market price of our common stock, regardless of our operating performance. In addition, the trading price of our common stock could change significantly, both over short periods of time and the longer term, due to many factors, including those described elsewhere in this Risk Factors section and the following:

announcements concerning our and Mallinckrodt s commercial progress in promoting and selling Sumavel DosePro, including sales and revenue trends;

announcements concerning our NDA for Zohydro ER;

FDA or international regulatory actions, including results and announcements from FDA advisory committee meetings convened with respect to the Zohydro ER NDA or hydrocodone generally and whether and when we receive regulatory approval for Zohydro ER or any of our other product candidates;

the development status of Relday or any of our other product candidates, including the results from our clinical trials;

other regulatory developments, including the FDA s potential grant of regulatory exclusivity to a competitor who receives FDA approval before us for an extended-release *hydrocodone* product, which could significantly delay our ability to receive approval for Zohydro ER;

announcements of the introduction of new products by us or our competitors;

announcements concerning product development results or intellectual property rights of others;

announcements relating to litigation, intellectual property or our business, and the public s response to press releases or other public announcements by us or third parties;

variations in the level of expenses related to Zohydro ER, Relday or any of our other product candidates or clinical development programs, including relating to the timing of invoices from, and other billing practices of, our CROs and clinical trial sites;

market conditions or trends in the pharmaceutical sector or the economy as a whole;

changes in operating performance and stock market valuations of other pharmaceutical companies and price and volume fluctuations in the overall stock market;

litigation or public concern about the safety of Sumavel DosePro or our product candidates;

actual and anticipated fluctuations in our quarterly operating results;

the financial projections we may provide to the public, any changes in these projections or our failure to meet these projections;

deviations from securities analysts estimates or the impact of other analyst comments;

ratings downgrades by any securities analysts who follow our common stock;

additions or departures of key personnel;

third-party payor coverage and reimbursement policies;

developments concerning current or future strategic collaborations, and the timing of payments we may make or receive under these arrangements;

developments affecting our contract manufacturers, component fabricators and service providers;

the development and sustainability of an active trading market for our common stock;

future sales of our common stock by our officers, directors and significant stockholders;

other events or factors, including those resulting from war, incidents of terrorism, natural disasters, security breaches, system failures or responses to these events;

changes in accounting principles; and

discussion of us or our stock price by the financial and scientific press and in online investor communities.

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In addition, the stock markets, and in particular the Nasdaq Global Market, have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many pharmaceutical companies. Stock prices of many pharmaceutical companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. The realization of any of the above risks or any of a broad range of other risks, including those described in these Risk Factors could have a dramatic and material adverse impact on the market price of our common stock.

There may not be a viable public market for our common stock.

Our common stock had not been publicly traded prior to our initial public offering in November 2010, the trading volume of our common stock on the Nasdaq Global Market has been limited and an active trading market may not be developed or sustained. We cannot predict the extent to which investor interest in our company will lead to the development of an active trading market on the Nasdaq Global Market or otherwise or how liquid that market might become. If an active public market does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at a price that is attractive to you, or at all. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products, product candidates or technologies by using our shares of common stock as consideration.

We may invest or spend our cash in ways with which you may not agree or in ways which may not yield a significant return.

Our management has considerable discretion in the use of our cash. Our cash may be used for purposes that do not increase our operating results or market value. Until the cash is used, it may be placed in investments that do not produce significant income or that may lose value. The failure of our management to invest or spend our cash effectively could result in unfavorable returns and uncertainty about our prospects, each of which could cause the price of our common stock to decline.

Our quarterly operating results may fluctuate significantly.*

Our quarterly operating results are difficult to predict and may fluctuate significantly from period to period, particularly because the commercial success of, and demand for, Sumavel DosePro, as well as the success and costs of our Zohydro ER, Relday and other product candidate development programs are uncertain and therefore our future prospects are uncertain. Our net loss and other operating results will be affected by numerous factors, including:

- fluctuations in the quarterly revenues of Sumavel DosePro, including fluctuations resulting from the performance of Mallinckrodt under our new co-promotion agreement, and from our distributors inventory management practices and buying patterns;
- the level of underlying demand for Sumavel DosePro or any of our other product candidates that may receive regulatory approval;
- our ability to control production spending and underutilization of production capacity;
- variations in the level of development and /or regulatory expenses related to Zohydro ER, Relday or other development programs;
- results of clinical trials for Zohydro ER, Relday or any other of our product candidates;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments and legislative changes, including healthcare reform, affecting our product and product candidates or those of our competitors; and

our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

We may become involved in securities class action litigation that could divert management s attention and adversely affect our business and could subject us to significant liabilities.

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The stock markets have recently experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations as well a broad range of other factors, including the realization of any of the risks described in these Risk Factors, may cause the market price of our common stock to decline. 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 biotechnology and pharmaceutical companies generally experience significant stock price volatility. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management s attention and resources, which could adversely affect our business. Any adverse determination in any such litigation or any amounts paid to settle any such actual or threatened litigation could require that we make significant payments.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.*

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. As of September 30, 2012, we had research coverage by only five securities analysts. If these securities analysts cease coverage of our company, the trading price for our stock would be negatively impacted. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

Our executive officers and directors and their affiliates will exercise significant control over stockholder voting matters in a manner that may not be in the best interests of all of our stockholders.*

Our executive officers and directors and their affiliates together control approximately 29% of our outstanding common stock, assuming no exercise of outstanding options or warrants, as of September 30, 2012. Four of our non-employee directors are, or are representatives designated by, significant stockholders and two of our directors are executive officers. As a result, these stockholders will collectively be able to significantly influence and may be able to control all matters requiring approval of our stockholders, including the election of directors and approval of significant corporate transactions such as mergers, consolidations or the sale of all or substantially all of our assets. The concentration of ownership may delay, prevent or deter a change in control of our company even when such a change may be in the best interests of some stockholders, impede a merger, consolidation, takeover or other business combination involving us, or could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might adversely affect the prevailing market price of our common stock.

In addition, sales of shares beneficially owned by executive officers and directors and their affiliates could be viewed negatively by third parties and have a negative impact on our stock price. Moreover, we cannot assure you as to how these shares will may be distributed and subsequently voted.

Future sales of our common stock or securities convertible or exchangeable for our common stock may depress our stock price.*

Persons who were our stockholders prior to the sale of shares in our initial public offering in November 2010 continue to hold a substantial number of shares of our common stock that they are able to sell in the public market, subject in some cases to certain legal restrictions. Significant portions of these shares are held by a small number of stockholders. If these stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. The perception in the market that these sales may occur could also cause the trading price of our common stock to decline. As of September 30, 2012, we had 100,666,197 shares of common stock outstanding. Of these shares, approximately 71,721,000 are freely tradable, without restriction, in the public market.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans are eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act, and, in any event, we have filed a registration statement permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of shares of our common stock, warrants to purchase our common stock and the shares of common stock issuable upon exercise of those warrants are entitled to rights with respect to the registration of their shares 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, except for shares purchased by our affiliates. In addition, our directors and

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executive officers may establish programmed selling plans under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for the purpose of effecting sales of our common stock. Any sales of securities by these stockholders, or the perception that those sales may occur, including the entry into such programmed selling plans, could have a material adverse effect on the trading price of our common stock.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than $66\,^{2}/_{3}\%$ of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than $66\,^{2}/_{3}\%$ of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

We have never paid dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.

The continued operation and expansion of our business will require substantial funding. Investors seeking cash dividends in the foreseeable future should not purchase our common stock. We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our available cash to fund the development and growth of our business. Any determination to pay dividends in the future will be at the discretion of our board of directors and will depend upon results of operations, financial condition, contractual restrictions, restrictions

imposed by applicable law and other factors our board of directors deems relevant. In addition, our ability to pay cash dividends is currently prohibited by the terms of our loan and security agreements. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any return to stockholders will therefore be limited to the appreciation in the market price of their stock, which may never occur.

We have incurred and will continue to incur significant increased costs as a result of operating as a public company, and our management is required to devote substantial time to meet compliance obligations.*

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the Nasdaq Stock Market, or Nasdaq, that impose significant requirements on public companies, including requiring establishment and

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maintenance of effective disclosure and financial controls and changes in corporate governance practices. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and financial condition. In addition, on July 21, 2010, the Dodd-Frank Wall Street Reform and Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation-related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas. The requirements of these rules and regulations have increased and will continue to increase our legal and financial compliance costs, make some activities more difficult, time-consuming or costly and may also place considerable strain on our personnel, systems and resources. Our management and other personnel have devoted and will continue to devote a substantial amount of time to these new compliance initiatives. In addition, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. Ensuring that we have adequate internal financial and accounting controls and procedures in place is a costly and time-consuming effort that needs to be re-evaluated frequently. In particular, commencing in fiscal 2011, we performed system and process evaluation and testing of our internal controls over financial reporting which allowed management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act, or Section 404. Our future testing may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. We expect to incur significant expense and devote substantial management effort toward ensuring compliance with Section 404. Pursuant to Section 404(c) of the Sarbanes-Oxley Act, our independent registered public accounting firm will be required to deliver an attestation report on the effectiveness of our internal control over financial reporting for the year ending December 31, 2012 as we will be an accelerated filer. We currently do not have an internal audit function, and we may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Implementing any appropriate changes to our internal controls may require specific compliance training for our directors, officers and employees, entail substantial costs to modify our existing accounting systems, and take a significant period of time to complete. Such changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate consolidated financial statements or other reports on a timely basis, could increase our operating costs and could materially impair our ability to operate our business. Moreover, effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent fraud. If we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal controls that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would entail expenditure of additional financial and management resources.

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

Unregistered Sales of Equity Securities

Not applicable.

Use of Proceeds

Not applicable.

Item 3. Defaults Upon Senior Securities

Not applicable.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

Not applicable.

Item 6. Exhibits

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EXHIBIT INDEX

Exhibit Number	Description
3.1(2)	Fifth Amended and Restated Certificate of Incorporation of the Registrant
3.2	Certificate of Amendment of Fifth Amended and Restated Certificate of Incorporation of the Registrant
3.3(2)	Amended and Restated Bylaws of the Registrant
4.1(3)	Form of the Registrant s Common Stock Certificate
4.2(1)	Third Amended and Restated Investors Rights Agreement dated December 2, 2009
4.3(1)	Amendment to Third Amended and Restated Investors Rights Agreement dated as of July 1, 2010
4.4(4)	Second Amendment to Third Amended and Restated Investors Rights Agreement dated June 30, 2011
4.5(1)	Warrant dated March 5, 2007 issued by the Registrant to General Electric Capital Corporation
4.6(1)	Warrant dated June 30, 2008 issued by the Registrant to Oxford Finance Corporation
4.7(1)	Warrant dated June 30, 2008 issued by the Registrant to CIT Healthcare LLC (subsequently transferred to The CIT Group/Equity Investments, Inc.)
4.8(1)	Transfer of Warrant dated March 24, 2009 from CIT Healthcare LLC to The CIT Group/Equity Investments, Inc.
4.9(1)	Warrant dated July 1, 2010 issued by the Registrant to Oxford Finance Corporation
4.10(1)	Warrant dated July 1, 2010 issued by the Registrant to Silicon Valley Bank
4.11(4)	Warrant dated June 30, 2011 issued by the Registrant to Oxford Finance LLC
4.12(4)	Warrant dated June 30, 2011 issued by the Registrant to Silicon Valley Bank
4.13(4)	Warrant dated July 18, 2011 issued by the Registrant to Healthcare Royalty Partners (formerly Cowen Healthcare Royalty Partners II, L.P.)
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
32.1*	Certification of Chief Executive Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
32.2*	Certification of Chief Financial Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
101**	The following financial statements from the Registrant s Quarterly Report on form 10-Q for the period ended September 30, 2012, formatted in XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statements of Cash Flows, and (iv) the Notes to Consolidated Financial Statements.

(1) Filed with the Registrant s Registration Statement on Form S-1 on September 3, 2010.
(2) Filed with Amendment No. 2 to Registrant s Registration Statement on Form S-1 on October 27, 2010.
(3) Filed with Amendment No. 3 to the Registrant s Registration Statement on Form S-1 on November 4, 2010.
(4) Filed with the Registrant s Quarterly Report on Form 10-Q on August 11, 2011.

* These certifications are being furnished solely to accompany this quarterly report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not subject to the liability of that section. These certifications are not to be incorporated by reference into any filing of Zogenix, Inc., whether made before or after the date hereof,

regardless of any general incorporation language in such filing.

** Pursuant to Rule 406T of Regulation S-T, these interactive data files are deemed not filed or part of a registration statement or prospectus for purposes of Section 11 or 12 of the Securities Act of 1933, are deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, and otherwise are not subject to liability under these sections.

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SIGNATURES

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

ZOGENIX, INC.

Date: November 8, 2012

By: /s/ Roger L. Hawley
Chief Executive Officer

Date: November 8, 2012

By: /s/ Ann D. Rhoads
Executive Vice President, Chief Financial Officer, Treasurer and Secretary