ZOGENIX, INC.
Form 10-Q
November 04, 2013
Table of Contents

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, 2013
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 (Address of Principal Executive Offices)	92130 (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 x
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined in 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, 2013 was 107,792,467.

Table of Contents

ZOGENIX, INC.
FORM 10-Q
For the Quarterly Period Ended September 30, 2013
Table of Contents

Table of Contents

PART I – FINANCIAL INFORMATION
Item 1. Financial Statements
Zogenix, Inc.
Consolidated Balance Sheets
(In Thousands)

	September 30, 2013 (Unaudited)	December 31, 2012
Assets		
Current assets:		
Cash and cash equivalents	$17,352	$41,228
Trade accounts receivable, net	6,161	5,643
Inventory, net	12,089	12,886
Prepaid expenses and other current assets	1,772	2,254
Total current assets	37,374	62,011
Property and equipment, net	12,943	13,561
Other assets	4,316	5,114
Total assets	$54,633	$80,686
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$2,972	$4,592
Accrued expenses	16,145	14,343
Common stock warrant liabilities	12,273	9,493
Accrued compensation	2,901	4,226
Total current liabilities	34,291	32,654
Long-term debt, less current portion	28,719	28,481
Other long-term liabilities	5,512	5,078
Commitments and contingencies		
Stockholders' equity (deficit):		
Common stock	108	101
Additional paid-in capital	360,634	343,763
Accumulated deficit	(374,631)	(329,391)
Total stockholders' (deficit) equity	(13,889)	14,473
Total liabilities and stockholders' equity	$54,633	$80,686

See accompanying notes.

Table of Contents

Zogenix, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In Thousands, except Per Share Amounts)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2013	2012	2013	2012
Revenue:				
Net product revenue	$6,897	$8,453	$22,693	$26,368
Contract revenue	—	—	—	8,462
Service and other revenue	271	—	398	—
Total revenue	7,168	8,453	23,091	34,830
Operating expenses:				
Cost of sales	5,354	4,249	14,144	13,478
Royalty expense	281	325	901	997
Research and development	2,544	3,660	9,358	16,005
Selling, general and administrative	10,011	10,857	36,491	37,574
Restructuring	—	—	876	—
Total operating expenses	18,190	19,091	61,770	68,054
Loss from operations	(11,022)	(10,638)	(38,679)	(33,224)
Other income (expense):				
Interest income	1	11	12	40
Interest expense	(1,587)	(3,463)	(4,795)	(8,730)
Change in fair value of warrant liabilities	215	(3,569)	(2,780)	(3,611)
Change in fair value of embedded derivatives	1,474	(202)	912	166
Other income (expense)	67	(1,421)	90	(1,379)
Total other income (expense)	170	(8,644)	(6,561)	(13,514)
Net loss before income taxes	(10,852)	(19,282)	(45,240)	(46,738)
Provision for income taxes	—	—	—	(5)
Net loss	$(10,852)	$(19,282)	$(45,240)	$(46,743)
Net loss per share, basic and diluted	$(0.10)	$(0.21)	$(0.44)	$(0.63)
Weighted average shares outstanding, basic and diluted	104,682	90,370	102,136	73,790
Comprehensive loss	$(10,852)	$(19,282)	$(45,240)	$(46,743)

See accompanying notes.

Table of Contents

Zogenix, Inc.
Consolidated Statements of Cash Flows
(In Thousands)
(Unaudited)

	Nine Months Ended September 30,	
	2013	2012
Operating activities:		
Net loss	$(45,240)	$(46,743)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	5,579	4,538
Stock-based compensation, restructuring	201	—
Depreciation and amortization	1,395	1,172
Amortization of debt issuance costs and non-cash interest	422	1,898
Change in fair value of warrant liabilities	2,780	3,611
Change in fair value of embedded derivatives	(912)	(166)
Changes in operating assets and liabilities:		
Trade accounts receivable	(518)	(591)
Inventory, net	797	2,546
Prepaid expenses and other current assets	482	(469)
Other assets	614	(286)
Accounts payable and accrued expenses	205	(756)
Restructuring liabilities	6	—
Deferred revenue	—	(8,462)
Net cash used in operating activities	(34,189)	(43,708)
Investing activities:		
Purchases of property and equipment	(785)	(255)
Net cash used in investing activities	(785)	(255)
Financing activities:		
Proceeds from revolving credit facility	—	9,900
Payments on borrowings of debt	—	(40,051)
Proceeds from exercise of common stock options	—	27
Proceeds from issuance of common stock and common stock warrants	11,098	67,114
Net cash provided by financing activities	11,098	36,990
Net decrease in cash and cash equivalents	(23,876)	(6,973)
Cash and cash equivalents at beginning of period	41,228	56,525
Cash and cash equivalents at end of period	$17,352	$49,552

See accompanying notes.

Table of Contents

Zogenix, Inc.
Notes to Consolidated Financial Statements

1. Organization and Basis of Presentation

Zogenix, Inc. (the Company) is a pharmaceutical company developing and commercializing 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, 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 (FDA) that allows for the needle-free, subcutaneous delivery of medication. The Company commercializes Sumavel DosePro through its internal sales and marketing organization and in collaboration with Mallinckrodt LLC, the Company's co-promotion partner. On October 25, 2013, the Company received FDA marketing approval for Zohydro™ ER (hydrocodone bitartrate) extended-release capsules, the first extended-release oral formulation of hydrocodone without acetaminophen. Zohydro ER is an opioid agonist for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The Company plans to launch Zohydro ER in March 2014.

The Company was incorporated in the state of Delaware on May 11, 2006 as SJ2Therapeutics, 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. These conditions raise substantial doubt about the Company's ability to continue as a going concern. The accompanying financial statements have been prepared assuming that the Company will continue as a going concern and do not include any adjustments that might result from the outcome of this uncertainty. This basis of accounting contemplates the recovery of the Company's assets and the satisfaction of liabilities in the normal course of business.

Management expects operating losses and negative cash flows to continue for at least the next year as the Company continues to incur costs related to the continued development of its product candidates and commercialization of its approved products. Management intends to pursue additional opportunities to raise additional capital, if required, through public or private equity offerings, including through a controlled equity offering program, debt financings, receivables financings or through collaborations or partnerships with other companies 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. If the Company is unsuccessful in raising additional required funds, it may be required to significantly delay, reduce the scope of or eliminate one or more of its development programs or its commercialization efforts, or cease operating as a going concern. The Company also may be required to relinquish, license or otherwise dispose of rights to product candidates or products that it would otherwise seek to develop or commercialize itself on terms that are less favorable than might otherwise be available.

On March 27, 2013, the Company entered into a controlled equity offering sales agreement, or the sales agreement, with Cantor Fitzgerald & Co., or Cantor, as sales agent, under which the Company can issue and sell shares of its common stock having an aggregate offering price of up to $25.0 million from time to time through Cantor. The sales of common stock made under the controlled equity offering sales agreement will be made in "at-the-market" offerings as defined in Rule 415 of the Securities Act of 1933, as amended, or the Securities Act. During the nine months ended September 30, 2013, the Company issued 6.8 million shares of its common stock pursuant to the sales agreement at an average stock issuance price of $1.66 per share, resulting in net proceeds of approximately $10.9 million. As of September 30, 2013, the Company had the capacity to issue up to $13.8 million in shares of its common stock under the sales agreement. However, there can be no assurance that Cantor will be successful in consummating further sales based on prevailing market conditions or in the quantities or at the prices that management deems appropriate.

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.

Table of Contents

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, 2012 filed with the SEC on March 15, 2013.

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.

The Company has monitored actual product return history for Sumavel DosePro since product launch. Based on the Company's product returns analysis, which considers actual product returns on an individual product lot basis, and factors such as the dating of the Company's product at the time of shipment into the distribution channel, prescription trends, trends in customer purchases and their inventory management practices, and changes in the estimated levels of inventory within the distribution channel, the Company increased its estimate for product returns, resulting in adjustments of $1,226,000 in the first quarter of 2013 and $2,408,000 in the third quarter of 2013, which led to decreases in net product revenue for the respective periods. Further, as a result of the Company’s third quarter 2013 product returns analysis, the Company expects to utilize a higher product returns rate for future Sumavel DosePro sales.

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, and accrued compensation 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 liability for the annual tail payments due to Astellas Pharma US, Inc. (Astellas) (see Note 4) for the termination of the Company’s co-promotion agreement was measured at fair value in December 2011 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.

The Company classifies its cash equivalents within Level 1 of the fair value hierarchy because it values its cash equivalents using quoted market prices. The Company classifies its 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, 2013 and December 31, 2012 are as follows (in thousands):

Table of Contents

	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, 2013				
Assets				
Cash equivalents[1]	$8,116	—	—	$8,116
Liabilities				
Common stock warrant liabilities[2]	$—	—	12,273	$12,273
Embedded derivative liabilities[3]	$—	—	80	$80
At December 31, 2012				
Assets				
Cash equivalents[1]	$37,605	—	—	$37,605
Liabilities				
Common stock warrant liabilities[2]	$—	—	9,493	$9,493
Embedded derivative liabilities[3]	$—	—	992	$992

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

(2) Common stock warrant liabilities include liabilities associated with warrants issued in connection with the Company's July 2012 public offering of common stock and warrants (see Note 6) and warrants issued in connection with the Healthcare Royalty financing agreement (see Note 4), which are measured at fair value using the Black-Scholes option pricing valuation model. The assumptions used in the Black-Scholes option pricing valuation model for both common stock warrant liabilities 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 Company's historical volatility, supplemented with 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 common stock warrant liabilities associated with the Healthcare Royalty financing agreement is the expected volatility. Significant increases in volatility would result in a higher fair value measurement. 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 public 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 equal to the lesser of 40% and the 180-day volatility rate obtained from the HVT function on Bloomberg as of the trading day immediately following the public announcement of an extraordinary transaction. The significant unobservable inputs used in measuring the fair value of the common stock warrant liabilities associated with the July 2012 public offering are the expected volatility and the probability of the occurrence of an extraordinary event. Significant increases in volatility would result in a higher fair value measurement and 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. Management's revenue projections used in the September 30, 2013 valuation model significantly increased from prior periods as they included an increase in projected Zohydro ER revenues based on the October 2013 Zohydro ER NDA approval date. This significant increase in management's revenue projections led to a significant decrease in the fair value of embedded derivative liabilities as of September 30, 2013.

Table of Contents

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, 2013 (in thousands):

	Common Stock Warrant Liabilities	Embedded Derivative Liabilities
Balance at December 31, 2012	$9,493	$992
Changes in fair value	2,780	(912)
Balance at September 30, 2013	$12,273	$80

Changes in fair value of the liabilities shown in the table above are recorded through 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 and comprehensive loss.

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.

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,	
	2013	2012	2013	2012
Numerator				
Net loss	$(10,852)	$(19,282)	$(45,240)	$(46,743)
Denominator				
Weighted average common shares outstanding, basic and diluted	104,682	90,370	102,136	73,790
Basic and diluted net loss per share	$(0.10)	$(0.21)	$(0.44)	$(0.63)

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,	
	2013	2012
Common stock options and restricted stock units	1,776	6,542
Common stock warrants	—	15,784
	1,776	22,326

Segment Reporting

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

9

Table of Contents

Recent Accounting Pronouncements

In February 2013, the Financial Accounting Standards Board issued an Accounting Standards Update which requires entities to separately present amounts reclassified out of accumulated other comprehensive income (AOCI) for each component of AOCI and to disclose, for each affected line item in the income statement, the amount of AOCI that has been reclassified into that line item. For AOCI reclassification items that are not reclassified in their entirety into net income, it is acceptable to cross reference that amount to another footnote that provides the required disclosure. The updated guidance became effective for fiscal and interim periods beginning after December 15, 2012. The Company adopted this guidance on January 1, 2013 and it did not have a material impact on the Company's results of operations.

3. Inventory, net (in thousands)

	September 30, 2013	December 31, 2012
Raw materials	$3,329	$4,867
Work in process	4,863	6,134
Finished goods	3,897	1,885
	$12,089	$12,886

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 pays 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 Co-Promotion 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 Co-Promotion 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.

Amounts payable to Mallinckrodt for service fees are reflected as selling, general and administrative expenses. For the three and nine months ended September 30, 2013, the Company incurred $249,000 and $618,000, respectively, in service fee expenses under the Co-Promotion Agreement. For each of the three and nine months ended September 30, 2012, the Company incurred $92,000 in service fee expenses under the Co-Promotion Agreement.

Table of Contents

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. In December 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

revenue in the consolidated statement of operations and comprehensive loss 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 as contract revenue during the three months ended March 31, 2012.

The Company is required to make two annual tail payments to Astellas, calculated as decreasing fixed percentages 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 is being accreted through interest expense through the dates of payment in July 2013 and July 2014. The first tail payment of $2,032,000 was made in July 2013. As of September 30, 2013 and December 31, 2012, the tail payment liability was $1,090,000 and $2,795,000 (including the service fee reduction discussed below), respectively. During the three months ended September 30, 2013 and 2012, $40,000 and $93,000 of related interest expense was recognized, respectively, and $327,000 and $414,000 of related interest expense was recognized during the nine months ended September 30, 2013 and 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 Astellas Co-Promotion 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 offsets 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 twelve months ended December 31, 2012, and an offset to the tail payment liability. The fair

value of the service fee receivable and tail payment reduction for each of the tail payments will be accreted through interest expense through the dates of the two tail payments in July 2013 and July 2014.

For the three months ended September 30, 2013 and 2012, the Company did not recognize any shared marketing expense under the Astellas Co-Promotion Agreement. For the nine months ended September 30, 2013 and 2012, the Company recognized shared marketing expense of $0 and $253,000, respectively.

For the three months ended September 30, 2013 and 2012, the Company did not recognize any service fee expenses under the Astellas Co-Promotion Agreement. For the nine months ended September 30, 2013 and 2012, and prior to the final reconciliation of service fees, the Company incurred service fee expenses of $0 and $1,757,000, respectively.

Table of Contents

Valeant Pharmaceuticals North America LLC Co-Promotion Agreement

On June 27, 2013, the Company entered into a co-promotion agreement (the Valeant Agreement) with Valeant Pharmaceuticals North America LLC (Valeant). Under the terms of the Valeant Agreement, the Company was granted the exclusive right (with Valeant or any of its affiliates) to promote Migranal® (dihydroergotamine mesylate) Nasal Spray (Migranal) to a prescriber audience of physicians and other health care practitioners in the United States. The Company's sales team began promoting Migranal to prescribers in August 2013. The term of the Valeant Agreement will run through December 31, 2015 (unless otherwise terminated), and can be extended by mutual agreement of the parties in additional twelve month increments. Valeant remains responsible for the manufacture, supply and distribution of Migranal for sale in the United States. In addition, Valeant will supply the Company with a specified amount of product samples every six months, and the Company will reimburse Valeant for the cost of additional samples and any promotional materials ordered by the Company. The cost of any additional samples and any promotional materials ordered by the Company will be recognized as selling, general and administrative expenses.

In partial consideration of the Company's sales efforts, Valeant will pay the Company a co-promotion fee on a quarterly basis that represents specified percentages of net sales generated by the Company over defined baseline amounts of net sales (Baseline Forecast or Adjusted Baseline Forecast). In addition, upon completion of the co-promotion term, and only if the Valeant Agreement is not terminated by Valeant due to a bankruptcy event (as defined in the Valeant Agreement) or a material failure by the Company to comply with its material obligations under the Valeant Agreement, Valeant will be required to pay the Company an additional tail payment calculated as a fixed percentage of the Company's net sales over the Baseline Forecast (or Adjusted Baseline Forecast) during the first full six months following the last day of the term.

The Company may terminate the Valeant Agreement in the event of a Valeant supply failure (as defined in the Valeant Agreement) or material product recall, or if the net sales price in a fiscal quarter is less than a specified percentage of the net sales price in the immediately preceding quarter, if the reduction in such net sales price would have a material adverse effect on the Company's financial return as a result of performance of its obligation under the Valeant Agreement.

Either party may terminate the Valeant Agreement with six months' notice, provided that neither party may provide notice of termination before January 1, 2014. Either party may terminate the Valeant Agreement with 30 days' prior notice if the Company's net sales within a fiscal quarter fall below the Baseline Forecast (or Adjusted Baseline Forecast) for one or more fiscal quarters, or following the commercial introduction of a generic product to Migranal promoted or otherwise commercialized by a third party in the United States. In addition, either party may terminate the Valeant Agreement in the event of a change of control of itself or the other party (upon 90 days' prior written notice), upon any action taken or objection raised by governmental authority that prevents either party from performing its obligations under the Valeant Agreement, upon the filing of an action alleging patent infringement, in connection with the material breach of the other party's material obligations, or if a bankruptcy event of the other party occurs.

The Company recognizes co-promotion fees received under the Valeant Agreement as service revenue in the period in which its promotional activities generate net sales over the Baseline Forecast or Adjusted Baseline Forecast. For each of the three and nine months ended September 30, 2013, the Company recognized service revenue of $232,000 under the Valeant Agreement.

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).

Table of Contents

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);
- 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.

As security for the payment of the Company's obligations under the Financing Agreement, the Company also entered into a security agreement whereby the Company granted to Healthcare Royalty 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 may include 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, as well as the change in the Revenue Interest rate from 5% to 5.75% in connection with the early termination of the Astellas Co-Promotion Agreement, 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, 2013 and December 31, 2012 was $80,000 and $992,000, respectively, 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 $(8,000) and $(23,000) for the three months ended September 30, 2013 and 2012, respectively, and $(43,000) and $(65,000) for the nine months ended September 30, 2013 and 2012, respectively, in the statement of operations and comprehensive loss. The Company has recognized other income (expense) in relation to the change in the fair value of the Healthcare Royalty embedded derivatives of $1,474,000 and $(202,000) for the three months ended September 30, 2013 and

Table of Contents

2012, respectively, and $912,000 and $166,000 for the nine months ended September 30, 2013 and 2012, respectively, in the statement of operations and comprehensive loss.

Term Debt

In June 2008, the Company entered into a Loan and Security Agreement with Oxford and CIT Healthcare LLC (the Oxford Agreement) under which it borrowed $18,000,000. The obligations under the Oxford Agreement were collateralized by personal property excluding certain intellectual property and all equipment pledged to secure an equipment financing. 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.

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.

On July 30, 2012, the Company exercised its right to terminate the Amended Oxford/SVB Agreement prior to the loan maturity date of January 2, 2014 and repaid $19,492,000 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.

5. Restructuring

In May 2013, the Company commenced a restructuring of its workforce, resulting in a reduction in force of 55 employees across all functional areas of the Company. During the three months ended June 30, 2013, the Company recorded restructuring charges of $876,000 consisting primarily of employee-related compensation charges. The Company did not record any restructuring charges during the three months ended September 30, 2013. The following table summarizes the components of the restructuring charges for the nine months ended September 30, 2013 (in thousands):

	Nine Months Ended September 30, 2013		
	Accruals	Non-cash items	Total
Employee-related charges	$663	$201	$864
Other restructuring charges	12	—	12
	$675	$201	$876

The following table sets forth activity in the restructuring liability for the nine months ended September 30, 2013, which is primarily comprised of employee severance costs (in thousands):

	Employee severance costs	Other restructuring charges	Total
Balance at December 31, 2012	$—	$—	$—
Accruals	663	12	675
Payments	(657)	(12)	(669)
Balance at September 30, 2013	$6	$—	$6

The balance of the restructuring liability at September 30, 2013 is anticipated to be fully distributed by June 2014.

Table of Contents

6. Common Stock Warrants

In July 2012, in connection with a public offering of common stock and warrants, the Company sold warrants to purchase 15,784,200 shares of common stock (including over-allotment purchase). The warrants are exercisable at an exercise price of $2.50 per share and will expire on July 27, 2017, which is 5 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 (see Note 2). The fair value of the warrants was approximately $12,045,000 and $9,308,000 as of September 30, 2013 and December 31, 2012, respectively.

In July 2011, upon the closing of and in connection with the Financing Agreement (see Note 4), the Company issued to Healthcare 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 (see Note 2). The fair value of the warrant was approximately $228,000 as of September 30, 2013 and $185,000 as of December 31, 2012.

In June 2011, and in connection with entering into the Amended Oxford/SVB Agreement (see Note 4), 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.

7. 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, 2013 and 2012 are as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2013	2012	2013	2012
Risk free interest rate	1.5% to 1.7%	0.7% to 0.9%	0.8% to 1.7%	0.2% to 1.2%
Expected term	5.1 to 6.0 years	5.0 to 6.1 years	5.0 to 6.1 years	5.0 to 6.1 years
Expected volatility	82.8% to 83.9%	80.1% to 81.7%	82.8% to 87.9%	80.1% to 82.8%
Expected dividend yield	— %	— %	— %	— %

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 Company's historical volatility, supplemented with historical volatility of comparable companies whose share prices are 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,	
	2013	2012	2013	2012
Cost of sales	$119	$53	$227	$130
Research and development	316	256	782	687
Selling, general and administrative	1,780	1,433	4,570	3,721
Restructuring	—	—	201	—

Total	$2,215	$1,742	$5,780	$4,538

As of September 30, 2013, there was approximately $12,898,000 of total unrecognized compensation costs related to outstanding options, which is expected to be recognized over a weighted average period of 2.7 years.

Table of Contents

8. Subsequent Event

On November 1, 2013, the Company entered into a Development and Option Agreement (the Development Agreement) with Altus Formulation Inc. (Altus). Under the Development Agreement, Altus will be responsible for the development of abuse deterrent formulations of hydrocodone using Altus' Intellitab™ drug delivery platform and will be reimbursed by the Company for its development efforts on the product. The Company is responsible for the conduct of the clinical development of the product and will pay a non-refundable upfront fee to Altus of $750,000. The Company is also obligated to pay Altus up to $3,500,000 in total future milestone payments upon the achievement of various development and regulatory milestones.

Pursuant to the Development Agreement, the Company was granted an option to obtain an exclusive, royalty-bearing license, with the right to sublicense, to certain Altus intellectual property rights to make, have made, import, use, sell, have sold, offer for sale and import an abuse deterrent formulation of hydrocodone for the treatment or relief of pain in the United States. However, the Company will need to obtain the consent of Alkermes or otherwise amend its license agreement with Alkermes for Zohydro ER in order to exercise the option and ultimately commercialize the Altus abuse deterrent formulation of hydrocodone. If the Company exercises this option, Altus will be eligible to receive additional regulatory and sales milestones and a royalty based on net sales of the licensed product.

The term of the Development Agreement will end upon expiration of the earlier of (1) the date upon which a NDA or similar application for regulatory approval is submitted by the Company for the Altus abuse resistant formulation of hydrocodone, or (2) November 1, 2016. The Company may terminate the Development Agreement upon 30 days' written notice or upon written notice of a material uncured breach by Altus. In addition, the Company may terminate any work plan under the Development Agreement upon written notice. Altus may only terminate the Development Agreement upon the occurrence of certain bankruptcy events with respect to the Company. Altus may also terminate a work plan under the Development Agreement upon written notice of the Company's material uncured breach.

Table of Contents

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;
- the timing of the launch of Zohydro ER;
- our ability to successfully execute our sales and marketing strategy for the commercialization of Sumavel DosePro and Zohydro ER;
- the progress and timing of clinical trials for Relday and our other product candidates;
- adverse side effects or inadequate therapeutic efficacy of Sumavel DosePro or Zohydro ER that could result in product recalls, market withdrawals or product liability claims;
- the safety and efficacy of our product candidates;
- the market potential for migraine treatments, and our ability to compete within that market;
- the market potential for extended-release/long-acting (ER/LA) opioid products, 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;
- the ability to develop an abuse deterrent formulation of Zohydro ER;
- estimates of the capacity of manufacturing and other facilities to support our products and product candidates;
- our ability to ensure adequate and continued supply of Sumavel DosePro and Zohydro ER to successfully meet anticipated market demand;
- 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, Zohydro ER, or any of our 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," "an "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparab 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.

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.

Table of Contents

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, 2012 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, 2012.

Overview

Background

We are a pharmaceutical company developing and commercializing products for the treatment of central nervous system disorders and pain. On October 25, 2013, we received marketing approval from the U.S. Food and Drug Administration, or FDA, for Zohydro™ ER (hydrocodone bitartrate) extended-release capsules, an opioid agonist, extended-release oral formulation of hydrocodone without acetaminophen, for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Zohydro ER is the first extended-release oral formulation of hydrocodone without acetaminophen. We currently expect to launch Zohydro ER in March 2014. In addition, we are currently commercializing Sumavel® DosePro® (sumatriptan injection) Needle-free Delivery System. 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 FDA that allows for the needle-free, subcutaneous delivery of medication. We commercialize Sumavel DosePro through our internal sales and marketing organization and in collaboration with Mallinckrodt LLC, our co-promotion partner.

Sumavel DosePro and Zohydro ER each have the potential to address significant unmet medical needs and become important and widely-used additions to the treatment options available to patients and physicians in the United States' multi-billion dollar migraine and chronic pain markets, respectively.

We are also developing Relday™, a proprietary, long-acting injectable formulation of risperidone using Durect Corporation's SABER™ controlled-release formulation technology through a development and license agreement with Durect, or the Durect License Agreement. 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 subcutaneous antipsychotic product that allows for once-monthly dosing. In May 2012, we filed an investigational new drug, or IND, application with the FDA. In July 2012, we initiated our first clinical trial for Relday. This Phase 1 clinical trial was a single-center, open-label, safety and pharmacokinetic trial of 30 patients with chronic, stable schizophrenia or schizoaffective disorder. We announced positive single-dose pharmacokinetic results from the Phase 1 clinical trial on January 3, 2013. Based on the favorable safety and pharmacokinetic profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, we extended the study to include an additional cohort of 10 patients at a 100 mg dose of the same formulation. We announced positive top-line results from the extended Phase 1 clinical trial on May 2, 2013. The results for the extended Phase 1 clinical trial showed risperidone blood concentrations in the therapeutic range were achieved on the first day of dosing and maintained throughout the one-month period. In addition, dose proportionality has now been established across the full dose range that would be anticipated to be used in clinical practice (50 to 100 mg). The positive results from this study extension position us to begin a multi-dose clinical trial, which will provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies. We plan to commence this multi-dose clinical trial in the second half of 2014.

The development of Relday will first focus on its delivery by conventional needle and syringe in order to allow the administration of different volumes of the same formulation of Relday by a healthcare professional. We anticipate that the introduction of our DosePro needle-free technology for administration of Relday can occur later in development or as part of life cycle management after further work involving formulation development, technology enhancements, and applicable regulatory approvals.

We have experienced net losses and negative cash flow from operating activities since inception, and as of September 30, 2013, we had an accumulated deficit of $374.6 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next year primarily as a result of the expenses incurred in connection with our efforts to commercialize Zohydro ER, the clinical development for Relday, required post-market

testing for Zohydro ER, additional activities with respect to Zohydro ER, including the development of an abuse deterrent formulation of Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro and Zohydro ER. As of September 30, 2013, we had cash and cash equivalents of $17.4 million.

On March 27, 2013, we entered into a controlled equity offering sales agreement with Cantor Fitzgerald & Co., or Cantor, as sales agent, under which we can issue and sell shares of our common stock having an aggregate offering price of up to $25.0 million from time to time through Cantor. The sales of common stock made under the controlled equity offering sales agreement will be made in “at-the-market” offerings as defined in Rule 415 of the Securities Act of 1933, as amended, or the

Table of Contents

Securities Act. During the nine months ended September 30, 2013, we issued 6.8 million shares of our common stock pursuant to the sales agreement at an average stock issuance price of $1.66 per share, resulting in net proceeds of approximately $10.9 million. As of September 30, 2013, we had the capacity to issue up to $13.8 million in shares of our common stock under the sales agreement. However, there can be no assurance that Cantor will be successful in consummating further sales based on prevailing market conditions or in the quantities or at the prices that we deem appropriate.

Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of September 30, 2013, and our projected product revenues from Sumavel DosePro, will be sufficient to fund our operations into the first quarter of 2014. We will need to obtain additional capital to finance our operations beyond that point, or possibly earlier. We intend to raise additional capital, if necessary, through public or private equity offerings, including through our controlled equity offering program, debt financings, receivables financings or through collaborations or partnerships with other companies. 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. In its report on our consolidated financial statements for the year ended December 31, 2012, 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 entered into a co-promotion agreement with Mallinckrodt. 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 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, 2013, we incurred service fee expenses of $0.2 million and $0.6 million, respectively, under the co-promotion agreement. For the three and nine months ended September 30, 2012, 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, whereby the agreement terminated on March 31, 2012. As a result of the agreement termination, and pursuant to a promotion transition plan, beginning in the second quarter of 2012, our field sales force assumed full responsibility from the 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.

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 were recorded as deferred revenues on our

Table of Contents

consolidated balance sheet at December 31, 2011, and beginning with the launch of Sumavel DosePro in January 2010, we began recognizing these proceeds as contract revenues over the term of the agreement. Upon amendment of the Astellas co-promotion agreement in December 2011, the remaining deferred proceeds were recognized as contract revenues on a ratable basis over 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 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. The first tail payment of $2.0 million was made in July 2013 and the second tail payment of $1.1 million as of September 30, 2013, which includes the service fee reduction discussed below, is payable in July 2014. The fair value of each of the tail payments is accreted through interest expense on a monthly basis through the date of payment. There was $40,000 and $0.3 million of related interest expense recognized during the three and nine months ended September 30, 2013, respectively.

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 co-promotion 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 twelve months ended December 31, 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 expense through the dates of the two tail payments in July 2013 and July 2014.

For the three months ended September 30, 2013 and 2012, we did not recognize any shared marketing expense under the Astellas co-promotion agreement. For the nine months ended September 30, 2013 and 2012, we recognized shared marketing expense of $0 and $0.3 million, respectively.

For the three months ended September 30, 2013 and 2012, we did not recognize any service fee expenses under the Astellas co-promotion agreement. For the nine months ended September 30, 2013 and 2012, and prior to the final reconciliation of service fees, we incurred service fee expenses of $0 and $1.8 million, respectively.

Valeant Co-Promotion Agreement

In June 2013, we entered into a co-promotion agreement, or the Valeant agreement, with Valeant Pharmaceuticals North America LLC, or Valeant. Under the terms of the Valeant agreement, we were granted the exclusive right (with Valeant or any of its affiliates) to promote Migranal® (dihydroergotamine mesylate) Nasal Spray, or Migranal, to a prescriber audience of physicians and other health care practitioners in the United States. Our sales team began promoting Migranal to prescribers in August 2013. The term of the Valeant agreement will run through December 31, 2015 (unless otherwise terminated), and can be extended by mutual agreement of the parties in additional twelve month increments. Valeant remains responsible for the manufacture, supply and distribution of Migranal for sale in the United States. In addition, Valeant will supply us with a specified amount of product samples every six months, and we will reimburse Valeant for the cost of additional samples and any promotional materials ordered by us. The cost of any additional samples and any promotional materials ordered by us will be recognized as selling, general and administrative expenses.

In partial consideration of our sales efforts, Valeant will pay us a co-promotion fee on a quarterly basis that represents specified percentages of net sales generated by us over defined baseline amounts of net sales. In addition, upon completion of the co-promotion term, and only if the Valeant agreement is not terminated by Valeant due to a

bankruptcy event (as defined in the Valeant agreement) or a material failure by us to comply with our material obligations under the Valeant agreement, Valeant will be required to pay us an additional tail payment calculated as a fixed percentage of our net sales over a baseline forecast during the first full six months following the last day of the term. For each of the three and nine months ended September 30, 2013, we recognized service revenue of $0.2 million under the Valeant Agreement.

Table of Contents

Critical Accounting Policies and Estimates

There have been no significant changes in critical accounting policies during the nine months ended September 30, 2013, 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 Estimates" in our Annual Report on Form 10-K for the year ended December 31, 2012.

Results of Operations

Comparison of the three and nine months ended September 30, 2013 to the three and nine months ended September 30, 2012

Revenue. We recognize net product sales upon the shipment of product to wholesale pharmaceutical distributors and retail pharmacies. Revenue for the three months ended September 30, 2013 and 2012 was $7.2 million and $8.5 million, respectively, and revenue for the nine months ended September 30, 2013 and 2012 was $23.1 million and $34.8 million, respectively. Net product revenue for the three months ended September 30, 2013 and 2012 was $6.9 million and $8.5 million, respectively, and net product revenue for the nine months ended September 30, 2013 and 2012 was $22.7 million and $26.4 million, respectively.

The aggregate $1.6 million, or 18%, decrease in net product revenue during the three months ended September 30, 2013 compared to 2012 was primarily due to a decrease in average net selling price of 22%, slightly offset by an increase in unit volume of 4%. The decrease in our average net selling price was primarily due to an increase in our estimate for Sumavel DosePro product returns. Based on our analysis of actual product return history, which considers actual product returns on an individual product lot basis since product launch, and factors such as the dating of our product at the time of shipment into the distribution channel, prescription trends, trends in customer purchases and their inventory management practices and changes in the estimated levels of inventory within the distribution channel, we increased our estimate for product returns, resulting in an adjustment of $2.4 million, which decreased our net product sales in the third quarter of 2013.

The aggregate $3.7 million, or 14%, decrease in net product revenue during the nine months ended September 30, 2013 compared to 2012 was primarily due to a decrease in unit volume of 8% and the adjustment booked to increase our estimate for product returns, partially offset by an increase in our whole acquisition cost. The decrease in unit volume was primarily due to the resetting of health insurance co-pays and co-insurance at the beginning of 2013, which slowed patient volumes in the first quarter of 2013 to a greater degree than in previous years.

There was no contract revenue recognized for the three months ended September 30, 2013 and 2012. Contract revenue for the nine months ended September 30, 2013 and 2012 was $0 and $8.5 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. In December 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.

Service and other revenue for the three and nine months ended September 30, 2013 was $0.3 million and $0.4 million, respectively. We did not recognize any service and other revenue during the three and nine months ended September 30, 2012. Service and other revenue is primarily comprised of the co-promotion fee that is earned for our Migranal sales efforts under the Valeant Agreement.

Cost of Sales. Cost of sales consists 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. It represents the cost of Sumavel DosePro units recognized as net product revenues in the period and the impact of underutilized production capacity and other manufacturing variances. Cost of sales for the three months ended September 30, 2013 and 2012 was $5.4 million and $4.2 million, respectively. Cost of sales for the nine months ended September 30, 2013 and 2012 was $14.1 million and $13.5 million, respectively. Product gross margin for the three months ended September 30, 2013 and 2012 was 22% and

50%, respectively, and product gross margin was 38% and 49% for the nine months ended September 30, 2013 and 2012, respectively. The decrease in product gross margin for the three months ended September 30, 2013 compared to 2012 was due to the lower average net selling price

Table of Contents

as well as a one-time scrap charge and excess capacity charge, and the decrease in product gross margin for the nine months ended September 30, 2013 compared to 2012 was primarily due to the one-time scrap charge and excess capacity charge.

Royalty Expense. Royalty expense consists of royalties payable to Aradigm Corporation based on net sales of Sumavel DosePro by us or one of our licensees and the amortization of the $4.0 million milestone payment paid by us to Aradigm upon the first commercial sale of Sumavel DosePro in the United States (which occurred in January 2010). We are not required to make any further milestone payments to Aradigm. We are required to pay to Aradigm a 3% royalty on global net sales of Sumavel DosePro, by us or one of our licensees, if any, until the expiration of the last valid claim of the transferred patents covering the manufacture, use, or sale of the product. During the three months ended September 30, 2013 and 2012, we recorded $0.3 million in royalty expense, and during the nine months ended September 30, 2013 and 2012 we recorded $0.9 million and $1.0 million, respectively, in royalty expense.

Research and Development Expenses. Research and development expenses consist of expenses incurred in developing, testing and seeking marketing approval of our product candidates, including: license and milestone payments; payments made to third-party clinical research organizations, or CROs, and investigational sites, which conduct our trials on our behalf, and consultants; 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; 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.

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.

The table below sets forth information regarding our research and development expenses for our major development programs. The period over period variances for our major development programs are explained in the narrative beneath the table.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2013	2012	2013	2012
Research and development expenses (in thousands):				
Zohydro	$843	$1,253	$2,858	$8,380
Relday	121	700	1,400	2,779
Sumavel DosePro	390	236	881	581
Other[(1)]	1,190	1,471	4,219	4,265
Total	$2,544	$3,660	$9,358	$16,005

(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.

Research and development expenses decreased by $1.1 million for the three months ended September 30, 2013 compared to 2012, and decreased by $6.6 million for the nine months ended September 30, 2103 compared to 2012. The decrease in research and development expenses during the three months ended September 30, 2013 compared to 2012 was primarily due to a decrease in development activities for Relday and Zohydro ER. The decrease in research and development expenses during the nine months ended September 30, 2013 compared to 2012 was primarily due to greater Zohydro ER development expenses during the first half of 2012 as expenses were incurred for preparation of the Zohydro ER NDA that we submitted to the FDA in May 2012.

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.

We expect our research and development expenses for the remainder of 2013 to continue to decrease over amounts incurred in 2012 as we incurred costs in 2012 related to our Zohydro ER NDA submission and costs related to preparation for and participation in the December 2012 FDA advisory committee meeting for Zohydro ER, which we do not expect to recur in 2013.

Table of Contents

Selling, General and Administrative Expenses. 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, service fees under our Mallinckrodt co-promotion agreement, sample product costs, and consulting fees. 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.

Selling, general and administrative expenses decreased to $10.0 million for the three months ended September 30, 2013 compared to $10.9 million for the three months ended September 30, 2012. Selling, general and administrative expenses decreased to $36.5 million for the nine months ended September 30, 2013 compared to $37.6 million for the nine months ended September 30, 2012.

Selling expenses were $6.3 million and $24.9 million for the three and nine months ended September 30, 2013, respectively, compared to $7.3 million and $27.4 million for the three and nine months ended September 30, 2012, respectively. General and administrative expenses were $3.7 million and $11.6 million for the three and nine months ended September 30, 2013, respectively, compared to $3.6 million and $10.2 million for the three and nine months ended September 30, 2012, respectively.

The decrease in selling, general and administrative expenses for the three months ended September 30, 2013 compared to 2012 was the result of a decrease of $1.0 million in sales and marketing expenses, partially offset by an increase of $0.1 million in general and administrative expenses.

- The decrease in sales and marketing expenses is primarily the result of a decrease in salaries and sample product expenses, partially offset by an increase in co-promotion fees resulting from the reduction of the service fee and tail payment liability under the Astellas co-promotion agreement as a result of the final reconciliation completed in August 2012 following the termination of the Astellas co-promotion agreement on March 31, 2012.
- The increase in general and administrative expenses is primarily the result of an increase in professional service related costs, such as legal and accounting and advisory services.

The decrease in selling, general and administrative expenses for the nine months ended September 30, 2013 was the result of a decrease of $2.5 million in sales and marketing expenses, offset by an increase of $1.4 million in general and administrative expenses.

- The decrease in sales and marketing expenses is primarily the result of a decrease in salaries and sales incentive compensation.
- The increase in general and administrative expenses is primarily the result of an increase in professional service related costs, such as legal and accounting and advisory services.

We do not expect a significant change in general and administrative expenses throughout the remainder of 2013 as compared to 2012 levels; however, our selling expenses may increase during the fourth quarter of 2013 as we prepare for the launch of Zohydro ER.

Restructuring Expenses. Restructuring expenses of $0.9 million were recorded during the nine months ended September 30, 2013, and consist of the costs incurred in connection with the restructuring of our workforce, which commenced in May 2013. These restructuring expenses primarily consist of cash charges of $0.7 million in severance costs and $0.2 million in non-cash stock-based compensation charges.

Interest Income. During the three months ended September 30, 2013 and 2012, interest income was $1,000 and $11,000, respectively. During the nine months ended September 30, 2013 and 2012, interest income was $12,000 and $40,000, respectively. The decrease in interest income during the three and nine months ended September 30, 2013 compared to the same periods in 2012 was primarily driven by a decrease in average cash and cash equivalent balances during the respective periods.

Interest Expense. Interest expense consists of interest expense incurred in connection with our financing agreements and certain other arrangements, including the following:

- our $30.0 million financing agreement, or the Healthcare Royalty financing agreement, with Healthcare Royalty Partners (formerly Cowen Healthcare Royalty Partners II, LP), or Healthcare Royalty;
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our $10.0 million revolving credit facility with Oxford Finance Corporation, or Oxford, and Silicon Valley Bank, or SVB (terminated in July 2012);

Table of Contents

- our $25.0 million loan and security agreement with Oxford and SVB, or the amended Oxford/SVB loan agreement (terminated in July 2012); and
- imputed interest from the two annual tail payments to Astellas.

Interest expense was $1.6 million and $4.8 million for the three and nine months ended September 30, 2013, respectively, compared to $3.5 million and $8.7 million for the three and nine months ended September 30, 2012, respectively. The decrease in interest expense during the three and nine months ended September 30, 2013 compared to the same periods in 2012 was primarily due to the termination of our amended Oxford/SVB loan agreement in July 2012.

We expect that interest expense throughout the remainder of 2013 will decrease from 2012 levels due to the repayment in full and termination of our revolving credit facility and amended Oxford/SVB loan agreement in July 2012.

Change in Fair Value of Warrant Liabilities. The change in fair value of warrant liabilities relates to a fair value adjustment recorded on 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. See Note 6 to our consolidated financial statements.

Change in Fair Value of Embedded Derivatives. The change in fair value of embedded derivatives relates to a fair value adjustment recorded on the embedded derivatives associated with the Healthcare Royalty financing agreement. See Note 4 to our consolidated financial statements.

Other Income (Expense). Other income (expense) for the three and nine months ended September 30, 2013 and 2012 consists primarily of foreign currency transaction gains and losses.

Provision for Income Tax Expense. Provision for income tax expense is primarily related to the taxable income generated by our wholly-owned subsidiary, Zogenix Europe Limited.

Liquidity and Capital Resources

We have experienced net losses and negative cash flow from operations since inception, and as of September 30, 2013, had an accumulated deficit of $374.6 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next year primarily as a result of the expenses incurred in connection with the commercialization of Zohydro ER, the clinical development for Relday, required post-market testing for Zohydro ER, additional activities with respect to Zohydro ER, including the development of an abuse deterrent formulation of Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro and Zohydro ER. As of September 30, 2013, we had cash and cash equivalents of $17.4 million.

In May 2013, we commenced a restructuring of our workforce, resulting in a reduction in force of approximately 37%, or 55 employees, across all functional areas of our company. We took this step as part of our initiative to extend our cash runway to reach key business milestones, including gaining FDA approval for our NDA for Zohydro ER, which occurred in October 2013, securing a development partner for Relday, and out-licensing our proprietary DosePro needle-free delivery technology.

Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of September 30, 2013, and our projected product revenues from Sumavel DosePro, will be sufficient to fund our operations into the first quarter of 2014. We will need to obtain additional capital to finance our operations beyond that point, or possibly earlier. We intend to raise additional capital, if necessary, through public or private equity offerings, including through our controlled equity offering program, debt financings, receivables financings or through collaborations or partnerships with other companies. 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.

In its report on our consolidated financial statements for the year ended December 31, 2012, 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. Our ability to continue as a going concern depends, in large part, on our ability to generate positive cash flow from operations and obtain additional financing, neither of which is certain. If we are unable to achieve these goals, our business would be jeopardized and we may not be able to continue operations and have to liquidate our assets and may receive less than the value at which those assets were carried on our financial statements, and it is likely that investors will lose all or part of their investment.

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, 2013, we received aggregate net cash proceeds of approximately $352.1 million from the sale of shares of our preferred and common stock, including sales through our controlled equity offering program and our financing in July 2012. In July 2012, we issued and sold a total of 35,058,300 shares of common stock and warrants to purchase 15,784,200 shares of common stock in a public offering, including the underwriters' over-allotment purchase, for aggregate net proceeds of $65.4 million.

On March 27, 2013, we entered into a controlled equity offering sales agreement, or sales agreement, with Cantor, as sales agent, to create a controlled equity offering program under which we may, from time to time, sell shares of common stock up to an aggregate offering price of $25.0 million. Sales of the common stock made pursuant to the sales agreement will be made by methods deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act, including sales made directly on the Nasdaq Global Market, on any other existing trading market for the common stock or to or through a market marker under our currently-effective Registration Statement on Form S-3. In addition, Cantor may sell the common stock by any other method permitted by law, including in privately negotiated transactions. We pay Cantor a commission equal to 3% of the gross proceeds from the sale of shares of our common stock under the sales agreement and have agreed to provide Cantor with customary indemnification and contribution rights. We have also agreed to reimburse Cantor for certain specified expenses, including the fees and disbursements of its legal counsel, in an amount not to exceed $50,000. The offering of common stock pursuant to the sales agreement will terminate upon the earlier of (a) the sale of all of the shares of common stock under the sales agreement having an aggregate offering price of $25.0 million and (b) the termination of the sales agreement by us or Cantor as permitted therein. The sales agreement may be terminated by us or Cantor at any time upon 10 days' prior written notice to the other party, or by Cantor at any time in certain circumstances, including the occurrence of a material adverse change in our company. There can be no assurance that Cantor will be successful in consummating sales of our common stock based on prevailing market conditions or in the quantities or at the prices that we deem appropriate. During the nine months ended September 30, 2013, we issued 6.8 million shares of our common stock pursuant to the sales agreement at an average stock price of $1.66 per share, resulting in net proceeds of approximately $10.9 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 a result of the termination of the amended Oxford/SVB loan agreement, the lenders 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.

Table of Contents

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.

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.

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 may include 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.

Cash and Cash Equivalents. Cash and cash equivalents totaled $17.4 million and $41.2 million at September 30, 2013 and December 31, 2012, respectively.

The following table summarizes our cash flows used in operating, investing and financing activities for the nine months ended September 30, 2013 and 2012:

	Nine Months Ended September 30,	
	2013	2012
	(In Thousands)	
Statement of Cash Flows Data		
Total cash provided by (used in):		
Operating activities	$(34,189)	$(43,708)
Investing activities	(785)	(255)
Financing activities	11,098	36,990
Decrease in cash and cash equivalents	$(23,876)	$(6,973)

Operating Activities: Net cash used in operating activities was $34.2 million and $43.7 million for the nine months ended September 30, 2013 and 2012, respectively. Net cash used for the nine months ended September 30, 2013 primarily reflects the use of cash for operations, adjusted for non-cash charges including a $2.8 million change in fair value of warrant liabilities and $5.8 million in stock-based compensation (which includes $0.2 million in stock-based compensation from restructuring), partially offset by a $(0.9) million change in fair value of embedded derivatives. Significant working capital uses of cash for the nine months ended September 30, 2013 includes personnel-related costs, sales and marketing expenses for Sumavel DosePro, research and development costs (primarily for employee and infrastructure resources) and other professional services.

Net cash used for the nine months ended September 30, 2012 primarily reflects the use of cash for operations, adjusted for non-cash charges including $4.5 million in stock-based compensation and a $3.6 million change in fair value of warrant liabilities, offset by a reduction in commercial inventory of $2.5 million and a reduction in deferred revenue of $8.5 million due to the termination of the Astellas co-promotion agreement. Significant working capital uses of cash for the nine months ended September 30, 2012 includes personnel related costs, research and development costs (primarily for Zohydro ER and Relday), sales and marketing expenses for Sumavel DosePro, and other professional services.

Investing Activities. Net cash used in investing activities was $0.8 million and $0.3 million for the nine months ended September 30, 2013 and 2012, respectively. These amounts are the result of the purchase of property and equipment primarily for use in manufacturing Sumavel DosePro.

Table of Contents

We expect to incur additional capital expenditures of up to $1.0 million in the fourth quarter of 2013. These planned capital expenditures primarily relate to further investments in our manufacturing operations for Sumavel DosePro and toward enhancing our existing manufacturing technology and equipment.

Financing Activities. Net cash provided by financing activities during the nine months ended September 30, 2013 was $11.1 million, which is primarily related to proceeds received under our controlled equity offering program. Net cash provided by financing activities was $37.0 million for the nine months ended September 30, 2012, which 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 related to our debt, including a $21.1 million to terminate our $25.0 million term debt with Oxford/SVB and a $0.1 million payment to terminate our revolving credit facility with Oxford/SVB.

Our sources of liquidity include our cash balances and cash receipts from the sale of Sumavel DosePro. Through September 30, 2013, we received aggregate net cash proceeds of approximately $352.1 million from the sale of shares of our preferred and common stock. As of September 30, 2013, we had $17.4 million in cash and cash equivalents. Other potential sources of near-term liquidity include (i) equity offerings, including through our controlled equity offering program, debt or other financing, (ii) entering into a commercialization agreement for Zohydro ER, or a licensing arrangement for Relday, or (iii) further leveraging our sales force capacity to promote Migranal or another new product.

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 and Zohydro ER 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.

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 2012, 2011 and 2010 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 products 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 through commercialization, and as we potentially advance Relday through clinical development.

Recent Accounting Pronouncements

In February 2013, the Financial Accounting Standards Board issued an Accounting Standards Update which requires entities to separately present amounts reclassified out of accumulated other comprehensive income, or AOCI, for each

component of AOCI and to disclose, for each affected line item in the income statement, the amount of AOCI that has been reclassified into that line item. For AOCI reclassification items that are not reclassified in their entirety into net income, it is acceptable to cross reference that amount to another footnote that provides the required disclosure. The updated guidance became effective for fiscal and interim periods beginning after December 15, 2012. We adopted this guidance on January 1, 2013 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.

Table of Contents

Item 3. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

Our cash and cash equivalents as of September 30, 2013 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, 2013, approximately $15.1 million (based on exchange rates as of September 30, 2013) 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 in our cash flows 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, 2013 would have resulted in approximately $0.6 million or $0.9 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, 2013 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 September 30, 2013 that have materially affected, or are reasonably likely to materially affect, our internal control over financial

reporting.

Table of Contents

PART II – OTHER INFORMATION

Item 1. Legal Proceedings

We are not currently a party to any legal proceedings.

Item 1A. Risk Factors

There have been no material changes to the risk factors included in "Item 1A. Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2012, other than those set forth below, which should be read in conjunction with the risk factors disclosed therein.

Risks Related to Our Business and Industry

We 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 year.

We were organized in 2006 and began commercialization of Sumavel DosePro in January 2010 and we plan to launch the commercial sale of Zohydro ER in the United States in March 2014. Our business and prospects must be considered in light of the risks and uncertainties frequently encountered by pharmaceutical companies commercializing a new product.

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, 2013 and the years ended December 31, 2012 and 2011, we incurred net losses of $45.2 million, $47.4 million and $83.9 million, respectively, our net cash used in operating activities was $34.2 million, $52.2 million and $80.5 million, respectively, and, at September 30, 2013, our accumulated deficit was $374.6 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next year primarily as a result of the expenses incurred in connection with our efforts to commercialize Zohydro ER, the clinical development for Relday, required post-market testing for Zohydro ER, additional development activities with respect to Zohydro ER, including the development of an abuse deterrent formulation of Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro and Zohydro ER. Our ability to generate revenues from Sumavel DosePro, Zohydro ER or any of our product candidates will depend on a number of factors including, in the case of Sumavel DosePro and Zohydro ER, the factors described in risk factors below and, in the case of our product candidates, including an abuse deterrent formulation of Zohydro ER, 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 commercialization and product development 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. If we do not increase sales of Sumavel DosePro or successfully commercialize Zohydro ER or any of our product candidates that may receive regulatory approval, a material adverse effect would likely impact our business, results of operations, financial condition and prospects and could result in our inability to continue operations.

We will 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.

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 financing agreements. In addition, we have funded our operations through the proceeds from the sales and issuances of our common stock pursuant to the controlled equity offering program that we established on March 27, 2013 with Cantor Fitzgerald & Co., or Cantor, as sales agent, under which we may, from time to time, sell shares of common stock up to an aggregate offering price of $25.0 million. During the nine months ended September 30, 2013, we issued 6.8 million shares of our common stock under the controlled equity offering program at an average stock issuance price of $1.66 per share, resulting in net proceeds of approximately $10.9 million; however, there can be no assurance that Cantor will be successful in consummating further sales under the

program based on prevailing market conditions or in the quantities or at the prices that we deem appropriate. Cantor or we are permitted to terminate the controlled equity offering sales agreement, or sales agreement, at any time upon 10 days' prior written notice, and Cantor is also permitted to terminate the sales agreement at any time in certain circumstances, including the occurrence of a material adverse change in our company.

Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of September 30, 2013, and our projected product revenues from Sumavel DosePro, will be sufficient to fund our operations into

Table of Contents

the first quarter of 2014. We will need to obtain additional funds to finance our operations beyond that point, or possibly earlier, in order to:

- 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 such product candidates receive regulatory approval;
- expand our sales and marketing infrastructure to support our safe use initiatives while reaching the appropriate prescribers of extended-release opioids for Zohydro ER and continue our promotion of Sumavel DosePro to headache specialists;
- establish and maintain our sales and marketing activities for Zohydro ER and Sumavel DosePro;
- qualify secondary sources for the manufacturing of Sumavel DosePro; and
- fund our operations and fund required post-market testing of Zohydro ER and additional development activities with respect to Zohydro ER, including the development of an abuse deterrent formulation of Zohydro ER, as well as further development of Relday and development of any other product candidate to support potential regulatory approval of marketing applications.

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 and Zohydro ER;
- the costs of maintaining and expanding our sales and marketing infrastructure or establishing distribution capabilities;
- the timing of regulatory approval, if granted, of any 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 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, 2012, 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, including through our controlled equity offering program, 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.

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

Our ability to generate revenues and become profitable will depend in large part on the commercial success of our approved products, Sumavel DosePro and Zohydro ER. We launched the commercial sale of Sumavel DosePro in the United States in January 2010 and we plan to launch the commercial sale of Zohydro ER in the United States in March 2014. The commercial success of our products depends on several factors, including our ability to:

Table of Contents

- successfully maintain and increase market demand for, and sales of, Sumavel DosePro through our sales and marketing efforts and those of Mallinckrodt LLC, our collaboration partner;
- successfully launch and educate prescribers on safe use initiatives for Zohydro ER through our own marketing and sales activities;
- expand our sales and marketing infrastructure to support our safe use initiatives while reaching the appropriate prescribers of extended-release opioids for Zohydro ER and continue our promotion of Sumavel DosePro to headache specialists;
- obtain greater acceptance of Sumavel DosePro by physicians and patients;
- create market demand for Zohydro ER through our own marketing and sales activities, and any other arrangements to promote this product that we may later establish;
- establish and maintain adequate levels of coverage and reimbursement for Zohydro ER and Sumavel DosePro, respectively, 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 Zohydro ER and manufacture commercial quantities at acceptable cost levels; and
- successfully maintain intellectual property protection for Sumavel DosePro and Zohydro ER.

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, we have at certain times experienced a reduction in total and new prescriptions month over month. If we and Mallinckrodt are unable to successfully maintain and increase sales of Sumavel DosePro, or we are unable to commercialize Zohydro ER in a timely manner or at all, 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 our products, in which case 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 focused on marketing and selling Sumavel DosePro primarily to physicians, nurses and other healthcare professionals in the United States. In May 2013, we commenced a restructuring of our workforce, including our field sales force, which was comprised of approximately 80 field sales personnel as of March 31, 2013 and was reduced to approximately 51 field sales personnel as of September 30, 2013. Our current sales force will continue to promote Sumavel DosePro primarily to neurologists and other prescribers of migraine medications, including headache clinics and headache specialists in the United States. With the approval of Zohydro ER, we now intend to conduct a staged expansion of our sales force to support broader reach to prescribers of extended-release opioids for Zohydro ER, and headache specialists for Sumavel DosePro.

To complement our existing sales force, we entered into a 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 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. We also intend to explore commercial strategies including co-promotion and other partnering opportunities for Zohydro ER.

The ability to generate revenue from our arrangement with Mallinckrodt and any future co-promoters depends on such co-promoter’s efforts in promoting our products and its ability to achieve broad market acceptance and prescribing of our products in its targeted physician segment.

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

- Mallinckrodt could unsuccessfully devote sufficient resources to the promotion of Sumavel DosePro, including by failing to develop, deploy or expand its sales force as necessary;
- Mallinckrodt could unsuccessfully 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

Table of Contents

- 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' written 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.

We may terminate the co-promotion agreement with 60 days' notice if Mallinckrodt does not achieve an agreed-upon minimums 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.

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 for any of our products, our portion of retained product revenues is likely to be lower than if we directly marketed and sold our products 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 our products through our sales, marketing and commercialization efforts and the efforts of any co-promoters, including 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, Zohydro ER, and, if approved, 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, Zohydro ER, and, if approved, 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 products by third-party payors are also necessary for commercial success. The degree of market acceptance of Sumavel DosePro, Zohydro ER and any 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;
- the clinical indications for which the product is approved;

Table of Contents

- in the case of Zohydro ER and 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 and 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 like Zohydro ER, 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. For example, in September 2013, the FDA announced class-wide safety labeling changes and new post-market study requirements for all extended-release and long-acting opioid analgesics intended to treat pain. Because of the risks of addiction, abuse, and misuse, even at recommended doses, and because of the greater risks of overdose and death, the FDA determined that these drugs should be reserved for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. In addition, the FDA is requiring the drug companies that make these drugs to conduct further studies and clinical trials to assess the known serious risks of misuse, abuse, increased sensitivity to pain (hyperalgesia), addiction, overdose and death.

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 is 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 marketing of Zohydro ER may generate public controversy that may adversely affect market acceptance of Zohydro ER. Due to the concerns regarding abuse of opioids like Zohydro ER, we are developing an abuse deterrent formulation of Zohydro ER.

Our efforts to educate the medical community and third-party payors on the benefits of Sumavel DosePro, Zohydro ER, and, if approved, 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 in the past experienced failures in our information systems and computer servers, 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 and post-market study compliance 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 products 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 Zohydro ER and development of Relday or any of our other product candidates could be delayed.

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

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

Table of Contents

organization, conducting product development activities for our products and product candidates, in-licensing rights to Zohydro ER and Relday, commercializing Sumavel DosePro and preparing to commercialize Zohydro ER. In January 2010, we launched Sumavel DosePro and began generating revenues. We are currently preparing to commercialize Zohydro ER. 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, Cardinal Health, Inc. and McKesson Corporation, individually comprised 34% and 28%, respectively, of our total gross sales of Sumavel DosePro for the nine months ended September 30, 2013, 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 assure you 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 products 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. In addition, Allergan, Inc., is now marketing BOTOX botulinum toxin for the treatment of chronic migraine. 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 Pharmaceutical Industries Limited in June 2011. Although these products may not be

Table of Contents

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.

Zohydro ER will 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 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 Actavis, 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, Merck & Co., Allergan, Inc. and Avanir Pharmaceuticals, Inc. In addition, Nupathe, Inc. received FDA approval for its migraine patch, Zecuity, in January 2013. Zohydro ER will also compete with a significant number of opioid product candidates under development, including abuse deterrent 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, which include abuse deterrent and tamper resistant formulations, 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, 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, Zyprexa Relprevv marketed by Eli Lilly & Company, Abilify Maintena (apripiprazole) marketed by Otsuka Pharmaceutical Co., Ltd. and H. Lundbeck A/S. 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, Endo Health Solutions Inc., Laboratorios Farmaceuticos Rovi SA, Novartis AG, and Reckitt Benckiser Group plc, each of which has announced they are developing long-acting antipsychotic product candidates.

We expect Sumavel DosePro, Zohydro ER, and, if approved, 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. The competition that we will encounter with respect to Zohydro ER and any of our product candidates that receive the requisite regulatory approval and classification and are marketed, 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, Zohydro ER and our product candidates could be significantly harmed if competitors are able to develop alternative formulations and/or

Table of Contents

drug delivery technologies outside the scope of our products. Compared to us, many of our potential competitors have substantially greater:

- capital resources;
- 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, Zohydro ER or any of our product candidates that are approved, our business, results of operations, financial condition and prospects may be materially adversely affected.

We can offer no assurances that Zohydro ER will be granted three-year Hatch-Waxman exclusivity, or if granted, that such exclusivity will effectively prevent or otherwise limit competition from other hydrocodone products, either generic or otherwise.

In addition to patent protection, we intend to rely, in part, on Hatch-Waxman marketing exclusivity (if granted by the FDA) for the commercialization of Zohydro ER in the United States. Under the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, newly approved drugs may benefit from certain statutory periods of non-patent marketing exclusivity in the United States. Exclusivity provides the holder of an approved application limited protection from new competition in the marketplace for the innovation represented by its approved drug product.

We believe that a three-year period of Hatch-Waxman exclusivity may be available for Zohydro ER. A three-year period of exclusivity is available for a drug product that contains an active ingredient that has been previously approved and the application contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the applicant that were essential to approval of the application. Changes to an approved drug product that may qualify for this exclusivity include changes that affect the product's active ingredient(s), strength, dosage form, route of administration, or conditions of use, so long as clinical investigations were essential to approval of the application containing those changes. The exclusivity prevents FDA from approving other applications for the same change for three years from the date of the new product's approval.

In this context, we believe Zohydro ER as the first single entity hydrocodone product approved for the treatment of chronic pain on the basis of a comprehensive Phase 3 safety and efficacy program conducted by us, will qualify for three-year Hatch-Waxman data exclusivity, but there can be no assurance that such exclusivity will be granted, or that if granted such exclusivity will effectively prevent or otherwise limit competition from other hydrocodone products, either generic or otherwise. Such competition by other hydrocodone products, including other 505(b)(2) applications for different conditions of use or other changes to the hydrocodone products that would not be restricted by the three-year exclusivity, could have a significantly negative impact on our future revenues from Zohydro ER.

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 Zohydro ER and for the clinical supply of 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, or Patheon, 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. We have identified alternative suppliers for these services and are currently working on a plan to transfer the manufacturing processes that are presently handled by Patheon to a new supplier in advance of the expected closure date of the Swindon, United Kingdom facility. In addition, Nypro Limited, located in Bray, Ireland, manufactures the actuator assemblies and injection molded

Table of Contents

components for our DosePro device and Nipro Glass, Germany AG (formerly 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. An affiliate of Alkermes, Alkermes Pharma Ireland Limited, or APIL, is the exclusive manufacturer and supplier (subject to certain exceptions) for Zohydro ER. We also outsource all manufacturing and packaging of the clinical trial materials for 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, APIL 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 clinical trials and, if approved, commercial production. We have restrictions on establishing a second source of supply under our agreement with APIL, 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 products 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, including obtaining regulatory approval to utilize the new manufacturer or supplier. 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.

Reliance on third-party manufacturers and suppliers entails risks to which we would not be subject if we manufactured Sumavel DosePro, Zohydro ER 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.

Production capacity to support launch and initial forecast demand for Zohydro ER is installed and pending final packaging qualification. In order to meet future anticipated growth in demand for Zohydro ER, APIL has initiated activities to qualify additional production lines and expand the manufacturing capacity for Zohydro ER. However, if APIL or our other contract manufacturers or suppliers are unable to deliver the required commercial quantities of our products and their various components, the quantities of our 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 products, 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 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, as well as the performance of services to support our safe use initiatives for Zohydro ER.

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 also rely on GENCO and Inmar Inc. to process our product returns. We place substantial reliance on these providers 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

Table of Contents

service providers are unable to comply with applicable laws and regulations, are unable 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 other third parties to perform various other services for us relating to drug safety monitoring and surveillance, sample accountability and regulatory monitoring, including adverse event reporting, education regarding the safe use of our products, 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.

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

The commercialization of Zohydro ER will require that we expand our sales force, which could substantially increase our expenses. We will need to expand our managerial, operational and other resources in order to grow, manage and fund our existing business and support the commercialization of Zohydro ER. Our management and personnel, systems and facilities currently in place may not be adequate to support 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 and Zohydro ER 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 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 inability 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 products.

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. In May 2013, we commenced a restructuring of our workforce, resulting in a reduction in force of approximately 37%, or 55 employees, across all functional areas of our company. We took this step as part of our initiative to extend our cash runway to reach key business milestones that may occur over the remainder of 2013, which included the approval of our NDA for Zohydro ER in October 2013. In June 2013, we implemented a company-wide retention program pursuant to which restricted stock units were granted to our executives and all other full time personnel; however, this new program may not be effective in retaining our 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, our ability to implement our business strategy and our ability to maintain effective internal controls for financial reporting and disclosure controls and procedures as required by the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act. 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 Zohydro ER and could delay or prevent the development and commercialization of any of our product candidates, including 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

Table of Contents

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.

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

We currently are developing Relday for the treatment of the symptoms of schizophrenia as well an abuse deterrent formulation of Zohydro ER. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products, among other things, are subject to extensive regulation by the FDA and other regulatory authorities in the United States. We are not permitted to market 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 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, as renewed by the Food and Drug Administration Safety and Innovation Act, or FDASIA, the FDA is subject to a two-tiered system of review times for new drugs - Standard Review and Priority Review. For drugs subject to standard review that do not contain a new molecular entity, such as Relday, 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 review process and the PDUFA target action date may be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission. The FDA's review goals are subject to change, and the duration of the FDA's review may depend on the number and type of other NDAs that are submitted to the FDA around the same time period. For example, in February 2013, the FDA informed us that we were unlikely to receive an action letter for our NDA for Zohydro ER by the PDUFA target action date of March 1, 2013. Subsequently, we did not receive NDA approval until October 25, 2013.

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. Although the FDA is not bound by the recommendation of an advisory committee, the matters discussed at the advisory committee meeting, and in particular any concerns regarding safety, could limit our ability to successfully commercialize our product candidates subject to advisory committee review.

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, or CRL, 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 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.

Product candidates such as Relday 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

Table of Contents

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. For example, the approval of our NDA for Zohydro ER was associated with post-market study and REMS requirements due to the risks of misuse, abuse, addiction, overdose and death associated with the active ingredient hydrocodone.

Relday and any of our other product candidates may not achieve their specified endpoints in clinical trials. We initiated a Phase 1 safety and pharmacokinetic clinical trial for Relday in July 2012 and announced positive single-dose pharmacokinetic results from this trial in January 2013. Based on the favorable safety and pharmacokinetic profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, we extended the study to include an additional cohort of 10 patients at a 100 mg dose of the same formulation and announced positive top-line results from the extended Phase 1 clinical trial in May 2013. The positive results from this study extension position us to begin a multi-dose clinical trial, which would provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies. We plan to commence this multi-dose clinical trial in the second half of 2014.

If we are unable to obtain regulatory approval for Relday, an abuse deterrent formulation of Zohydro ER or any other product candidates on the timeline we anticipate, we may not be able to execute our business strategy effectively and our ability to generate additional revenues beyond Sumavel DosePro and Zohydro ER may be limited.

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

Relday and any of our 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 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 our product candidates 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, recent amendments to the FFDCA over the past several years have granted 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. 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. 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 Relday or any of our other product candidates are not shown to be safe and effective in clinical trials, the programs 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 clinical testing for Relday or pre-clinical or clinical testing for 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 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 and announced positive single-dose pharmacokinetic results from the Phase 1 clinical trial in January 2013. Based on the favorable safety and pharmacokinetic profile demonstrated in the Phase 1 trial, we extended the study to include an additional dose of the same formulation and announced positive top-line results in May 2013. The positive results from this study extension position us to begin a multi-dose clinical trial, which will provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies. We plan to commence this multi-dose clinical trial in the second half of 2014. We do not know whether any of our other pre-clinical or clinical trials will begin on time or be

Table of Contents

completed on schedule, if at all. 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 similar indications;
- 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. If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for 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.

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 prior clinical trials under agreements with third-party CROs, and we anticipate that we may enter into agreements with third-party CROs in the future regarding 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

Table of Contents

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.

The implementation of a REMS for Zohydro ER will add additional 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 would require a class-wide REMS for all long-acting and sustained-release opioid drug products. The central component of the extended-release/long-acting opioid REMS program is an education program for prescribers and patients. Specifically, the REMS for these products includes 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 healthcare professionals 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 manufacturers. 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 is available at www.ER-LA-opioidrems.com for use by continuing education providers in developing continuing education courses. Moreover, REMS assessments must be submitted to the FDA at 6 months and 12 months after the initial approval date of the REMS (July 9, 2012), and annually thereafter, 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.

As an extended-release formulation of hydrocodone, Zohydro ER is required to have a REMS that contains the elements of the FDA-approved class-wide REMS, 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.

Table of Contents

Our inability to successfully establish new partnerships with pharmaceutical companies or contract sales organizations to co-promote Sumavel DosePro, Zohydro ER 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, which as of September 30, 2013 was comprised of approximately 51 field sales personnel, primarily targeting neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. 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 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 Zohydro ER and any 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 products 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 products and/or product candidates, they may be unable 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, Zohydro ER 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.

If we are unable to further amend our license agreement with Alkermes or obtain its consent, we will be unable to license, market and sell an abuse deterrent formulation of Zohydro ER that makes use of another party's formulation technology.

We recently entered into a development and option Agreement with Altus Formulation Inc., or Altus, to develop abuse deterrent formulations of hydrocodone. Pursuant to the agreement, we have been granted an option to obtain an exclusive, royalty-bearing license, with the right to sublicense, to certain Altus intellectual property rights to make, have made, import, use, sell, have sold, offer for sale and import an abuse deterrent formulation of hydrocodone for the treatment or relief of pain in the United States. However, during the term of our license agreement with Alkermes for Zohydro ER, we are precluded from licensing, marketing or selling in the United States any oral controlled release capsule or tablet formulation whose sole active ingredient is hydrocodone, other than Zohydro ER. Accordingly, we will need Alkermes' cooperation in order to exercise our option with Altus and ultimately commercialize an abuse deterrent formulation of hydrocodone. If we are unable to obtain this consent or otherwise amend our license agreement with Alkermes, we will not be able to license or commercialize any abuse deterrent formulation under development with Altus or any other abuse deterrent formulation of hydrocodone, unless we pursue the development or commercialization of such abuse deterrent formulation with Alkermes. We believe it is in the mutual interest of Alkermes and our company to proceed with the abuse deterrent formulation from Altus and that we can ultimately come to an agreement with Alkermes to do so. However, we can provide no assurance that we will reach such an

agreement. Our inability to obtain Alkermes' consent could have a negative impact on the long term opportunity for Zohydro ER, and even if we are successful, we may need to compensate Alkermes for its consent, which may include increased compensation in the form of royalties or other payments and other concessions compared to our existing license terms.

If we are unable to achieve and maintain adequate levels of coverage and reimbursement for Sumavel DosePro, Zohydro ER, 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

Table of Contents

governmental healthcare programs, such as Medicare and Medicaid, and commercial payors are 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.

In addition, regional healthcare authorities and individual hospitals are increasingly using competitive 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.

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, Zohydro ER or any of our 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 products and clinical use of our products 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 and Zohydro ER, or an applicable foreign regulatory authority. Our products and product candidates are designed to affect important bodily functions and processes. Any side effects, manufacturing defects, misuse or abuse associated with Sumavel DosePro, Zohydro ER 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 products 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 products 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 products or product candidates;
- decreased demand for our products 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 $15 million annual aggregate coverage limit. Our insurance coverage may not be sufficient to cover all of

Table of Contents

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 and Zohydro ER, approval of Relday 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, Zohydro ER 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 effect on our business, results of operations, financial condition and prospects.

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, 2013, $15.1 million (based on exchange rates as of September 30, 2013) of our materials purchased and contract manufacturing 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.

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 Sumavel DosePro in January 2010 and expect to launch Zohydro ER in March 2014. Given on our limited sales history for Sumavel DosePro and our lack of sales history for Zohydro ER, we may not accurately predict future sales, and we may never be able to significantly increase sales, especially in light of our reliance on our co-promotion partner for Sumavel DosePro, 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. For example, for the nine months ending September 30, 2013 and the years ended December 31, 2012 and 2011, we incurred net losses of $45.2 million, $47.4 million and $83.9 million, respectively, our net cash used in operating activities was $34.2 million, $52.2 million and $80.5 million, respectively, and, at September 30, 2013, our accumulated deficit was $374.6 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 and any future revenue from Zohydro ER, we expect our losses to continue for at least the next year primarily as a result of the expenses incurred in connection with our efforts to commercialize Zohydro ER, the potential additional clinical development of Relday, post-market testing for Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro and 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 products 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.

We may not be able to sell shares of our common stock under our controlled equity offering program with Cantor at times, prices or quantities that we desire, and if such sales do occur, they may result in dilution to our existing stockholders.

On March 27, 2013, we entered into the sales agreement with Cantor. Under the terms of the sales agreement, Cantor will use its commercially reasonable efforts, consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the Nasdaq Global Market, to sell shares of our common stock designated by us. However, there can be no assurance that Cantor will be successful in consummating such sales based on prevailing market conditions or in the quantities or at the prices that we deem appropriate. In addition, we will not be able to make sales of our common stock pursuant to the sales agreement unless certain conditions are met, which include the accuracy of representations

Table of Contents

and warranties made to Cantor under the sales agreement; compliance with laws; and the continued listing of our stock on the Nasdaq Global Market. In addition, Cantor is permitted to terminate the sales agreement at any time. If we are unable to access funds through sales under the sales agreement, or it is terminated by Cantor, we may be unable to access capital on favorable terms or at all.

During the nine months ended September 30, 2013, we issued 6.8 million shares of our common stock pursuant to the sales agreement, which had a dilutive effect on holdings of our existing stockholders as of September 30, 2013. Should we sell additional shares pursuant to the sales agreement, it will further dilute the holdings of our existing stockholders, and may result in downward pressure on the price of our common stock. If we sell shares under the sales agreement at a time when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Issuances in the face of a declining share price will have an even greater dilutive effect than if our share price were stable or increasing, and may further decrease our share price.

Risks Related to Regulation of our Products and Product Candidates

Our currently approved products, Sumavel DosePro and Zohydro ER, are, 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, or the restriction in a REMS program. The Zohydro ER approval requires us to conduct post-marketing studies and implement the extended-release and long-acting opioid class-wide REMS with respect to our product. We are also 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 our product. These requirements include submissions of safety and other post-marketing information and reports, drug listing, as well as continued compliance with cGMPs for our marketed and investigational products, 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 product candidates 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 products or product candidates or the manufacturing facilities for our products 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;

Table of Contents

- 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.

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. For example, the FDASIA requires the FDA to issue new guidance on permissible forms of internet and social media promotion of regulated medical products, and the FDA may soon specify new restrictions on this type of promotion. 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.

Our development strategy for Relday depends upon the FDA’s prior findings of safety and effectiveness of risperidone based on data not developed by us, but which the FDA may rely upon in reviewing any future NDA.

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 and Zohydro ER, we plan to submit an NDA for Relday 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 risperidone. Even though we may be able to take advantage of Section 505(b)(2) to support potential U.S. approval for Relday, the FDA may require us, and did require us with respect to Sumavel DosePro and Zohydro ER, 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 and product candidates, 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 Relday and our other product candidates. 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 Relday and our other product candidates.

Zohydro ER is a controlled substance 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 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 ability

to supply Zohydro ER, 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

Table of Contents

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, required us to develop a comprehensive REMS containing the elements of the class-wide extended-release and long-acting opioid REMS to reduce the inappropriate use of Zohydro ER, 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. The restrictions of this program could limit market acceptance of the product.

Pursuant to the terms of our license agreement with Alkermes, we entered into a commercial manufacturing and supply agreement for Zohydro ER with APIL. APIL has the exclusive right to manufacture and supply both clinical and commercial supplies of Zohydro ER (subject to certain exceptions). While APIL is required to comply with applicable laws and regulations regarding controlled substances, we do not have any direct control over APIL's compliance in these regards, and any failure by APIL 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 the production or sale of Zohydro ER.

The DEA limits the availability and production of all Schedule II substances through a quota system which includes a national aggregate quota and individual procurement 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 procurement 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 such adjustments. Alkermes, which has licensed us the right to sell Zohydro ER in the United States, was allocated a sufficient quantity of hydrocodone to meet our planned clinical, pre-clinical and launch requirements through 2013. However, we will need significantly greater amounts of hydrocodone to meet expected demand for Zohydro ER in the second half of 2014.

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.

Alkermes procurement quota of hydrocodone may not be sufficient to meet any future clinical development needs or commercial demand for Zohydro ER. Any delay or refusal by the DEA in establishing the procurement quota or a reduction in Alkermes quota for hydrocodone or a failure to increase it over time as we anticipate could delay or stop commercial sale of Zohydro ER or cause us not to achieve our expected operating results, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

States.

In March 2008, we established an exclusive commercial partnership for Sumavel DosePro with Desitin in the European Union, Norway, Switzerland and Turkey, in order to seek to accelerate the development and regulatory approvals in those territories. However, on August 5, 2013, we agreed with Desitin to terminate the licensing and distribution agreement effective October 1, 2013. Following the termination of the licensing and distribution agreement, we assumed the rights to exclusive development and commercialization of Sumavel DosePro for the European Union, Norway, Switzerland and Turkey. We may seek to establish commercial partnerships for Sumavel DosePro in other foreign countries, and we may also seek to establish a new commercial partnership in the European Union, Norway, Switzerland and Turkey. In order to market Sumavel DosePro or

Table of Contents

any other products outside of the United States, we, 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 the "Risk Factors" set forth in our Annual Report on Form 10-K for the fiscal year ended December 31, 2012 regarding FDA approval in the United States, as well as other risks. For example, in the European Economic Area, or EEA (comprised of the 27 European Union, or EU, member states plus Iceland, Liechtenstein, and Norway), we can take advantage of the hybrid application pathway of the EU Centralized Procedure, which is similar to the FDA’s 505(b)(2) pathway. Hybrid applications may rely in part on the results of pre-clinical tests and clinical trials contained in the authorization dossier of the reference product, but must be supplemented with additional data. 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, 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.

Inability 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” 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, 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 are unable to comply with applicable foreign regulatory requirements.

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, Zohydro ER 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 customers. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established a new 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, Zohydro ER 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. In March 2010, President Obama signed into law the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education 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;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program 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;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- 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

Table of Contents

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;
- 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, with manufacturers being required to begin data collection on August 1, 2013 and report such data to the Centers for Medicare & Medicaid Services, or CMS, by March 31, 2014 and the 90th day of each subsequent calendar year;
- 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 CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

Other legislative changes have also been proposed and adopted in the United States since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. On March 1, 2013, the President signed an executive order implementing sequestration, and on April 1, 2013, the 2% Medicare payment reductions went into effect. The ATRA also, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

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.

Table of Contents

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 Statute, 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, which prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- federal "sunshine" requirements that require drug manufacturers to report and disclose any "transfer of value" made or distributed to physicians and teaching hospitals. Device manufacturers were required to begin collecting data on August 1, 2013 and will be required to submit reports to CMS by March 31, 2014 (and the 90th day of each subsequent calendar year);
- 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. In addition, recent health care reform legislation has strengthened these laws. For example, the PPACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians, including the tracking and reporting of gifts, compensation and other remuneration to physicians. Certain states mandate implementation of commercial compliance programs to ensure compliance with these laws, while other states impose restrictions on device manufacturer marketing practices and tracking and reporting of gifts, compensation and other remuneration to physicians. The shifting commercial compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may be found out of compliance of one or more of the requirements, subjecting us to significant civil monetary penalties.

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.

Table of Contents

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 depends in large part on obtaining and maintaining patent, trademark and trade secret protection of our products, Sumavel DosePro and Zohydro ER, our current product candidate, Relday, and any future product candidates, 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, Zohydro ER 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. 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:

Table of Contents

- others may be able to make or use compounds that are similar to the pharmaceutical compounds used in Sumavel DosePro, Zohydro ER and our product candidates but that are not covered by the claims of our patents;
- the APIs in Sumavel DosePro, Zohydro ER and Relday 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, Zohydro ER or Relday 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, 2013, our patent portfolio included twelve issued U.S. patents, one pending U.S. patent applications, 40 issued foreign patents and two pending foreign patent applications relating to various aspects of Sumavel DosePro, our DosePro technology and Zohydro ER. Eleven 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, 8,241,244, 8,287,489, 8,343,130 and 8,491,524 are expected to expire in 2014, 2016, 2017, 2026, 2026, 2023, 2023, 2025, 2022, 2024, 2022 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 safety mechanisms; U.S. Patent Nos. 7,776,007 and 8,287,489 cover devices with a 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; U.S. Patent Nos. 8,118,771, 8,241,243 and 8,241,244 cover a method of reducing breakage of glass capsules; 8,491,524 relates to a drug capsule filled with a formulation purged with an inert gas; and 8,343,130 covers a method of reducing the propensity to create a shock wave on firing the device as used in the Sumavel DosePro device. U.S. Patent Nos. 6,902,742 and 6,228,398 relating to Zohydro ER covers a modified release composition containing hydrocodone and are expected to expire in November 2019. Upon the expiration of these patents, we or Alkermes, as applicable, will lose the right to exclude others from practicing the claimed inventions. Additionally, since these thirteen patents are the only patents currently listed in the FDA Orange Book for Sumavel DosePro, or will be listed for Zohydro ER, 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

Table of Contents

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.

The patent rights that we have in-licensed covering Zohydro ER are limited to a modified release composition containing hydrocodone. As a result, our market opportunity for this product may be limited by the lack of patent protection for the active ingredient itself and other formulations of hydrocodone.

The active ingredient in Zohydro ER is hydrocodone. Patent protection is not available for the hydrocodone molecule itself in the United States. As a result, competitors who obtain the requisite regulatory approval can offer products with the same active ingredient as Zohydro ER so long as the competitors do not infringe any patents that we have in-licensed from Alkermes. We are the exclusive licensee in the United States and its territories of two U.S. patent and one U.S. patent application owned by Alkermes for oral controlled release hydrocodone products for the treatment or relief of pain, pain syndromes or pain associated with medical conditions or procedures. U.S. Patent Nos. 6,228,398 and 6,902,742 covers a modified release composition containing hydrocodone. These patents both expire in November 2019.

Third parties may challenge the patent covering Zohydro ER, which could result in the invalidation or unenforceability of some or all of the relevant patent claims. For example, invalidity claims have been filed against U.S. Patent No. 6,228,398 for products unrelated to Zohydro ER or hydrocodone.

Moreover, if a third party files an NDA or abbreviated new drug application, or ANDA, for a generic drug product containing hydrocodone and relies in whole or in part on studies conducted by or for us, the third party will be required to certify to the FDA that, in the opinion of that third party, the patents listed in the Orange Book for Zohydro ER are invalid, unenforceable, or will not be infringed by the manufacture, use or sale of the third party's generic drug product. A third party certification that the new product will not infringe the Orange Book-listed patent for Zohydro ER, or that such patents are invalid, is called a Paragraph IV patent certification. If the third party submits a Paragraph IV patent certification to the FDA, a notice of the Paragraph IV patent certification must also be sent to us and Alkermes once the third-party's NDA or ANDA is accepted for filing by the FDA. A lawsuit may then be initiated to defend the patents identified in the notice. The filing of a patent infringement lawsuit within 45 days of the receipt of notice of a Paragraph IV patent certification automatically prevents the FDA from approving the NDA or ANDA until the earlier of the expiration of a 30-month period, the expiration of the patents, the entry of a settlement order stating that the patents are invalid or not infringed, a decision in the infringement case that is favorable to the NDA or ANDA applicant, or such shorter or longer period as the court may order. If a patent infringement lawsuit is not initiated within the required 45-day period, the third-party's NDA or ANDA will not be subject to the 30-month stay.

Alkermes has retained the first right, but not the obligation, to enforce our licensed patent or defend any claims asserting the invalidity or unenforceability of these patents. We are not entitled to control the manner in which Alkermes may defend certain of the intellectual property that is licensed to us and it is possible that Alkermes' defense activities may be less vigorous than had we conducted the defense ourselves. If Alkermes decides not to initiate a patent infringement lawsuit following the receipt of notice of a Paragraph IV patent certification and we decide to do so, such litigation would be very complex in nature and may be very expensive and time-consuming, may divert our management's attention from our core business, and may result in unfavorable results that could adversely impact our ability to prevent third parties from competing with our products. Any adverse outcome of such litigation could result in one or more generic versions of Zohydro ER being launched before the expiration of the patents we have in-licensed from Alkermes, which could adversely affect our ability to successfully execute our business strategy to commercialize Zohydro ER and negatively impact our financial condition and results of operations.

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.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our products 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, Zohydro ER and Relday. As the medical device, biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert our products 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 products, product candidates, technology or methods.

Table of Contents

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 products, product candidate or proprietary technologies. Because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until eighteen months after filing, and 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 products 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 patent was found to cover our products 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, Zohydro ER 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.

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.

Table of Contents

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, Zohydro ER, and, if approved by the FDA or other regulatory authorities, our product candidates could be adversely affected.

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, 2013, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price of $1.50 to a high sale price of $2.24. 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 any co-promoter’s commercial progress in promoting and selling Sumavel DosePro and Zohydro ER, including sales and revenue trends;
-

FDA or international regulatory actions and whether and when we receive regulatory approval for any of our product candidates;

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

Table of Contents

- variations in the level of expenses related to 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, Zohydro ER 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 inability 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.

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” and the "Risk Factors' set forth in our Annual Report on Form 10-K for the fiscal year ended December 31, 2012 could have a dramatic and material adverse impact on the market price of our common stock.

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 and Zohydro ER, as well as the success and costs of our 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, Zohydro ER or any of our product candidates that may receive regulatory approval;
- our ability to successfully market and sell Zohydro ER;
- our ability to control production spending and underutilization of production capacity;
- variations in the level of development and/or regulatory expenses related to Relday or other development programs;
- results of clinical trials for 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 products 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.

Table of Contents

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, as of September 30, 2013, approximately 15% of our outstanding common stock, assuming no exercise of outstanding options or warrants. Two 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, 2013, we had 107,767,008 shares of common stock outstanding. Of these shares, approximately 69,503,004 are freely tradeable, 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.

We have registered under the Securities Act 15,784,200 shares of our common stock issuable upon the exercise of the warrants we issued in July 2012, which warrants became exercisable on July 27, 2013 at an exercise price of $2.50 per share (subject to restrictions on exercise set forth in such warrants), which means that upon exercise of warrants, such shares will be freely tradeable without restriction under the Securities Act, except for shares held by our affiliates. Further, certain holders of shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act, which, if registered, would also become freely tradeable without restriction under the Securities Act, except for shares held by our affiliates. In addition, our directors and 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, warrantholders or executive officers and directors, or the perception that those sales may occur, could have a material adverse effect on the trading price of our common stock.

Table of Contents

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

Employment Transition Agreement with Cynthia Y. Robinson, Ph.D.

On November 1, 2013, we announced that Cynthia Y. Robinson, Ph.D. will be resigning as Chief Development Officer effective as of November 1, 2013, and we entered into an employment transition agreement with Dr. Robinson, or the Transition Agreement. The Transition Agreement supersedes the existing employment agreement between us and Dr. Robinson. Pursuant to the Transition Agreement, effective November 1, 2013, Dr. Robinson will continue to serve as an employee in the role of Advisor to our President through May 31, 2014, or the Expiration Date. During the term of her transition services, Dr. Robinson will be paid a base salary of $24,072.19 per month. Dr. Robinson will be eligible for a target bonus of $75,000 for 2013, but will not be eligible for an annual bonus during 2014. In the event Dr. Robinson's employment is terminated by us without cause prior to the Expiration Date, Dr. Robinson will be eligible to receive (1) a lump sum payment equal to the remaining base salary payable to her under the Transition Agreement through the Expiration Date plus, to the extent such termination occurs prior to the date on which annual bonuses are paid for 2013, an amount equal to her target bonus for 2013 (pro-rated to the extent her termination of employment occurs prior to December 31, 2013), plus (2) continued health benefits at the same cost to her as was in effect on the date of her termination through the Expiration Date (or, if earlier, the date her eligibility for COBRA expires or the date she becomes eligible to receive equivalent or increased healthcare coverage from a subsequent employer). The foregoing severance benefits are conditioned on Dr. Robinson's execution of general release of claims in favor of us.

The above summary of the terms of the Transition Agreement is qualified in its entirety by reference to the full text of the agreement, a copy of which will be filed as an exhibit to the our Annual Report on Form 10-K for the year ending December 31, 2013.

Development and Option Agreement with Altus Formulation Inc.

On November 1, 2013, we entered into a Development and Option Agreement, or the Development Agreement, with Altus Formulation Inc., or Altus. Under the Development Agreement, Altus will be responsible for the development of abuse deterrent formulations of hydrocodone using Altus' Intellitab™ drug delivery platform. We will reimburse Altus for its development efforts on the product and we our responsible for the conduct of clinical development of the product.

Pursuant to the Development Agreement, we have been granted an option to obtain an exclusive, royalty-bearing license, with the right to sublicense, to certain Altus intellectual property rights to make, have made, import, use, sell, have sold, offer for sale and import an abuse deterrent formulation of hydrocodone for the treatment or relief of pain in the United States. We may exercise our option at any time until the earlier of (1) the date upon which a NDA or similar application for regulatory approval is submitted by us for the Altus abuse resistant formulation of hydrocodone, or (2) November 1, 2016. We refer to this period of time as the Option Period. However, we will need to obtain the consent of Alkermes or otherwise amend our license agreement with Alkermes for Zohydro ER in order to exercise the option and ultimately commercialize the Altus abuse deterrent formulation of hydrocodone.

We will pay a non-refundable upfront fee to Altus of $750,000. We are also obligated to pay Altus up to $3.5 million in total future milestone payments upon the achievement of various development and regulatory milestones even if we do not

Table of Contents

exercise our option under the Development Agreement. Altus will be eligible to receive additional regulatory and sales milestones and a royalty based on net sales of the licensed product upon our exercise of the option.

The term of the Development Agreement will end upon expiration of the Option Period. We may terminate the Development Agreement upon 30 days' written notice or upon written notice of a material uncured breach by Altus. In addition, we may terminate any work plan under the Development Agreement upon written notice. Altus may only terminate the Development Agreement upon the occurrence of certain bankruptcy events with respect to us. Altus may also terminate a work plan under the Development Agreement upon written notice of our material uncured breach.

The above summary of the terms of the Development Agreement is qualified in its entirety by reference to the full text of the agreement, a copy of which will be filed as an exhibit to our Annual Report on Form 10-K for the year ending December 31, 2013.

Table of Contents

Item 6. Exhibits
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.)
10.1 †	Amendment #1 to the Manufacturing Services Agreement, dated February 28, 2013 with an effective date of November 1, 2013, by and between the Registrant and Patheon UK Limited
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)

60

Table of Contents

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, 2013, formatted in XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations and Comprehensive Loss, (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.

† Confidential treatment has been requested for portions of this exhibit. These portions have been omitted and filed separately with the Securities and Exchange Commission

* 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.

Table of Contents

SIGNATURES

Pursuant to the requirements 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 4, 2013

By: /s/ Roger L. Hawley
Chief Executive Officer
(Principal Executive Officer)

Date: November 4, 2013

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