

ZOGENIX, INC.  
Form S-1/A  
September 07, 2011  
Table of Contents

As filed with the Securities and Exchange Commission on September 7, 2011

Registration No. 333-176443

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**AMENDMENT NO. 1**  
**TO**  
**FORM S-1**  
**REGISTRATION STATEMENT**  
*Under*  
*The Securities Act of 1933*

**ZOGENIX, INC.**

(Exact name of registrant as specified in its charter)

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**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**2834**  
(Primary Standard Industrial  
Classification Code Number)  
**12671 High Bluff Drive, Suite 200**

**20-5300780**  
(I.R.S. Employer  
Identification Number)

**San Diego, CA 92130**

**(858) 259-1165**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Roger L. Hawley**

**Chief Executive Officer**

**Zogenix, Inc.**

**12671 High Bluff Drive, Suite 200**

**San Diego, CA 92130**

**(858) 259-1165**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

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If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

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

Accelerated filer "  
Smaller reporting company "

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.**

**Table of Contents**

**The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities or the solicitation of an offer to buy these securities in any state or other jurisdiction in which such offer, solicitation or sale is not permitted.**

**SUBJECT TO COMPLETION DATED SEPTEMBER 7, 2011**

**PROSPECTUS**

**12,000,000 Shares of Common Stock**

We are selling 12,000,000 shares of our common stock.

Our common stock is listed on the Nasdaq Global Market under the symbol ZGNX. On September 2, 2011, the last reported sale price of our common stock on the Nasdaq Global Market was \$3.39 per share.

**Investing in our common stock involves a high degree of risk. Before buying any shares you should read the discussion of material risks of investing in our common stock in Risk Factors beginning on page 10.**

	Per Share	Total
Public Offering Price	\$	\$
Underwriting Discounts and Commissions	\$	\$
Proceeds to us, before expenses	\$	\$

We have granted a 30-day option to the underwriters to purchase up to 1,800,000 additional shares of our common stock (15% of the shares sold).

Cowen Healthcare Royalty Partners II, L.P., a current stockholder, Roger L. Hawley, our Chief Executive Officer, and Ann D. Rhoads, our Executive Vice President and Chief Financial Officer, have indicated an interest in purchasing \$1.5 million, \$100,000 and \$100,000 of shares of our common stock in this offering, respectively. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these parties, or any of these parties may determine to purchase more, less or no shares in this offering. The underwriters will not receive an underwriting discount or commission on any sales of shares to these parties.

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

The underwriters expect to deliver the shares on or about \_\_\_\_\_, 2011 through the book-entry facilities of The Depository Trust Company.

**Leerink Swann**

**Wells Fargo Securities**

**Stifel Nicolaus Weisel**

**William Blair & Company**  
The date of this prospectus is \_\_\_\_\_, 2011.

**Oppenheimer & Co.**

**Table of Contents**

We launched our first product, Sumavel® DosePro®, using our proprietary DosePro technology in January 2010.

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**Table of Contents**

**TABLE OF CONTENTS**

	<b>Page</b>
<u>About this Prospectus</u>	1
<u>Prospectus Summary</u>	2
<u>Risk Factors</u>	10
<u>Special Note Regarding Forward-Looking Statements and Market Data</u>	61
<u>Use of Proceeds</u>	63
<u>Price Range of Common Stock</u>	64
<u>Dividend Policy</u>	64
<u>Capitalization</u>	65
<u>Dilution</u>	67
<u>Selected Financial Data</u>	70
<u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	72
<u>Business</u>	99
<u>Management</u>	142
<u>Compensation Discussion and Analysis</u>	151
<u>Principal Stockholders</u>	181
<u>Certain Relationships and Related Party Transactions</u>	185
<u>Description of Capital Stock</u>	190
<u>Shares Eligible for Future Sale</u>	194
<u>Material U.S. Federal Income Tax Consequences to Non-U.S. Holders of Our Common Stock</u>	197
<u>Underwriting</u>	201
<u>Legal Matters</u>	207
<u>Experts</u>	207
<u>Where You Can Find Additional Information</u>	207
<u>Index to Consolidated Financial Statements</u>	F-1

**Table of Contents**

**ABOUT THIS PROSPECTUS**

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of our business and the securities we are offering, you should carefully read the registration statement, including its exhibits and this prospectus before making an investment decision.

You should rely only on the information contained in this prospectus and in any free writing prospectus that we may provide to you in connection with this offering. Neither we nor any of the underwriters has authorized anyone to provide you with information different from, or in addition to, that contained in this prospectus or any such free writing prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. Neither we nor any of the underwriters is making an offer to sell or seeking offers to buy these securities in any jurisdiction where or to any person to whom the offer or sale is not permitted. The information in this prospectus is accurate only as of the date on the front cover of this prospectus and the information in any free writing prospectus that we may provide you in connection with this offering is accurate only as of the date of that free writing prospectus. Our business, financial condition, results of operations and prospects may have changed since those dates.

For investors outside the United States: Neither we nor any of the underwriters has done anything that would permit this offering or possession or distribution of this prospectus or any free writing prospectus we may provide to you in connection with this offering in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus and any such free writing prospectus outside of the United States.



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**Table of Contents**

**PROSPECTUS SUMMARY**

*This summary does not contain all of the information you should consider before buying shares of our common stock. You should read the entire prospectus carefully, especially the Risk Factors section and our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in shares of our common stock. Unless the context requires otherwise, references in this prospectus to Zogenix, we, us and our refer to Zogenix, Inc., including its consolidated subsidiary, Zogenix Europe Limited.*

**Overview**

We are a pharmaceutical company commercializing and developing products for the treatment of central nervous system disorders and pain. Our first commercial product, Sumavel® DosePro® (*sumatriptan* injection) Needle-free Delivery System, was launched in January 2010. Sumavel DosePro offers fast-acting, easy-to-use, needle-free subcutaneous administration of *sumatriptan* for the acute treatment of migraine and cluster headache in a pre-filled, single-use delivery system. Sumavel DosePro is the first drug product approved by the U.S. Food and Drug Administration, or FDA, that allows for the needle-free, subcutaneous delivery of medication. Our lead product candidate, Zohydro, is a novel, oral, single-entity extended-release formulation of *hydrocodone* currently in Phase 3 development for the treatment of moderate to severe chronic pain in patients requiring around-the-clock opioid therapy. We reported positive top-line results from our pivotal Phase 3 efficacy trial for Zohydro in August 2011 and expect to submit a New Drug Application, or NDA, with the FDA by early 2012. Sumavel DosePro and Zohydro each has 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.

Sumavel DosePro may serve as a treatment alternative to oral and nasal triptans and may offer simple, convenient administration when compared to traditional, needle-based *sumatriptan* injection. According to its Prescribing Information, Sumavel DosePro can provide onset of migraine pain relief in as little as ten minutes for some patients. As a result, we believe that Sumavel DosePro has the potential to be prescribed by a broad physician audience, especially for difficult to treat migraine episodes.

Migraine is a syndrome that affects approximately 30 million people in the United States, according to a 2010 National Headache Foundation press release. Triptans are the class of drugs most often prescribed for treating migraines. In the United States in the 12 months ended December 2010, triptans generated sales of approximately \$3.5 billion and *sumatriptan*, including branded and generic forms, represented the largest market share of the seven approved triptans, with sales of approximately \$2.1 billion, according to Wolters Kluwer Pharma Solutions (Source® PHAST Institution/Retail).

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. Our sales and marketing organization is comprised of approximately 100 professionals. Our field sales force of approximately 80 representatives promotes Sumavel DosePro primarily to neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. To build upon our success in growing Sumavel DosePro prescriptions, we have initiated activities to expand our field sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. Our promotional efforts are complemented by our collaboration with Astellas and approximately 400 of its sales representatives, who are promoting Sumavel DosePro primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists in the United States. We also have entered into a partnership for Sumavel DosePro with Desitin Arzneimittel GmbH to accelerate development and regulatory approvals in Europe and further enhance the global commercial potential of Sumavel DosePro.

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## Table of Contents

Sumavel DosePro has demonstrated significant quarterly growth in total prescriptions since its launch in January 2010. For the six months ended June 30, 2011, we recognized \$16.2 million in net product revenue from sales of Sumavel DosePro, represented by more than 32,000 aggregate dispensed prescriptions (Source<sup>®</sup> PHAST Retail, January 2011 – June 2011). Sumavel DosePro continues to add new and repeat prescribers in both the neurology and primary care settings. The product is also gaining use from a range of patient segments, including new triptan users, patients being converted to the product from other migraine drugs and patients who have been prescribed Sumavel DosePro and also have other triptan prescriptions. This experience is consistent with our belief that many patients will selectively use Sumavel DosePro for their more challenging migraine episodes, while continuing to use oral triptans to treat their less severe migraine episodes. Through our ongoing efforts with the largest commercial health plans, Sumavel DosePro is achieving broad coverage in the United States, with a reimbursement claims approval rate of approximately 80% since launch through June 2011 (Source<sup>®</sup> Dynamic Claims January 2010 – June 2011).

Our lead product candidate, Zohydro, is a novel, oral, single-entity extended-release formulation of *hydrocodone* currently in Phase 3 development for the treatment of moderate to severe chronic pain in patients requiring around-the-clock opioid therapy. Zohydro utilizes Elan Pharma International Limited's, or Elan's, proprietary Spheroidal Oral Drug Absorption System, or SODAS<sup>®</sup> technology, which serves to enhance the release profile of *hydrocodone* to provide consistent 12-hour pain relief relative to existing immediate-release combination formulations. Most marketed *hydrocodone* products contain the analgesic combination ingredient *acetaminophen*, which if taken in high quantities over time can cause liver toxicity. In June 2009, the FDA organized a joint advisory committee meeting that highlighted the public health problem of liver injury related to the use of *acetaminophen* in both over-the-counter and prescription products. Zohydro, if approved, may represent the first available extended-release version of *hydrocodone* and also the first *hydrocodone* product that is not combined with another analgesic. As a result, we believe Zohydro could generate sales from both patients who are using immediate-release opioid products on a chronic basis and patients already using extended-release opioids. We initiated the Phase 3 clinical development program for Zohydro in March 2010 and reported positive top-line results from our pivotal Phase 3 efficacy trial in August 2011. The trial successfully met its primary efficacy endpoint in demonstrating a significant difference ( $p=0.008$ ) between the mean changes in daily pain intensity Numeric Rating Scale (NRS) scores between Zohydro and placebo groups. We expect to submit an NDA with the FDA by early 2012. We in-licensed exclusive U.S. rights to Zohydro from Elan in 2007.

The American Pain Society estimated in 1999 that 9% of the U.S. adult population suffers from moderate to severe non-cancer related chronic pain. Chronic pain can be treated with both immediate-release and extended-release opioids. We define our target market for Zohydro as prescription, non-injectable *codeine*-based and extended-release *morphine*-based pain products. This market generated U.S. sales of approximately \$13.5 billion for the year ended December 2010, based on average wholesale price, on approximately 206 million prescriptions. During the same period, existing *hydrocodone* products, the most commonly prescribed pharmaceutical products in the United States, generated \$3.2 billion in sales on approximately 128 million prescriptions. (Source<sup>®</sup> PHAST Retail). We believe Zohydro has the potential to be an important therapeutic alternative to existing *hydrocodone* products, including the branded product Vicodin and its generic equivalents.

We are also developing Relday, a proprietary, long-acting injectable formulation of *risperidone* using Durect Corporation's SABER controlled-release formulation technology in combination with our DosePro needle-free, subcutaneous drug delivery system through a July 2011 development and license agreement with Durect. *Risperidone* is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. If successfully developed and approved, we believe Relday may be the first once-monthly, subcutaneous antipsychotic product available in a needle-free delivery system. The existing long-acting injectable *risperidone* product achieved global net sales of \$1.5 billion in 2010, according to industry reports, and requires twice monthly, 2 mL intramuscular injections with a 21 gauge or larger needle. We believe the combination of our DosePro technology with Durect's SABER controlled-release technology will allow Relday

## **Table of Contents**

to be delivered subcutaneously without a needle on a once-monthly basis with a simplified dosing regimen, improved pharmacokinetic profile and significant reduction in injection volume versus currently marketed long-acting injectable antipsychotics. Based upon these characteristics, Relday may provide an important alternative to currently marketed long-acting injectable antipsychotics as well as a new long-acting treatment option for patients that currently use daily oral antipsychotic products. We intend to initiate clinical studies for Relday in patients with schizophrenia in early 2012 following the filing of an investigational new drug application.

Our DosePro technology is a novel, patent-protected, needle-free drug delivery system designed for self-administration of a pre-filled, single dose of liquid drug. We believe the FDA's approval of Sumavel DosePro represents an important validation of the technology. Results from our pre-clinical and clinical studies demonstrate that DosePro can be used successfully with small molecules and biological products, including protein therapeutics and monoclonal antibodies. We are building our internal product pipeline by investigating proven drugs that can be paired with DosePro to enhance their benefits and commercial attractiveness, such as with Relday. In addition to Relday, we are also evaluating the market potential, formulation requirements and clinical development pathway of an additional central nervous system, or CNS, compound that could be paired with DosePro to enhance its commercial attractiveness. We are also seeking to capitalize on our DosePro technology by out-licensing it to potential partners enabling them to enhance, differentiate or extend the life cycle of their proprietary injectable products. We acquired the DosePro technology and related intellectual property from Aradigm Corporation in August 2006.

Our management team has a proven clinical, regulatory, business development and commercialization track record at Zogenix and prior organizations, as well as significant expertise in CNS disorders and pain. Since our inception in 2006, our management team has successfully acquired, developed, obtained regulatory approval for and launched the commercial sale of Sumavel DosePro and completed a significant primary care co-promotion agreement in the United States and secured a European partnership for the product. We also completed in-licensing transactions for Zohydro and Relday and initiated Phase 3 development for Zohydro.

## **Investment Highlights**

We believe we are differentiated by the unique characteristics of our marketed product, Sumavel DosePro, and our lead product candidate, Zohydro, each of which addresses large market opportunities, as well as our established commercial infrastructure, our innovative technology and the depth of experience of our management team. The following represents the key attributes that help differentiate our company:

Fully-integrated pharmaceutical company with established commercial infrastructure.

Sumavel DosePro, a differentiated entrant in the migraine market that has demonstrated significant quarterly growth in total prescriptions since its launch.

Zohydro, a novel, extended-release chronic pain therapy with positive top-line pivotal Phase 3 efficacy trial results and anticipated NDA submission by early 2012.

Validated, proprietary DosePro technology with broad range of potential applications, including our newest product candidate, Relday, a proprietary, long-acting injectable formulation of *risperidone*.

Experienced management team with unique commercial and development expertise, including CNS sales and marketing experience.

## **Table of Contents**

### **Our Strategy**

Our core strategy is to commercialize and develop differentiated CNS and pain therapeutics that can address significant unmet medical needs and overcome limitations of existing products. Key elements of our strategy include:

Increasing sales and continuing to drive patient and physician adoption of Sumavel DosePro in the United States.

Developing and commercializing Zohydro for the treatment of moderate to severe chronic pain.

Expanding our product pipeline in CNS disorders and/or pain, including through the development of our newest product candidate, Relday.

Obtaining regulatory approvals for Sumavel DosePro outside of the United States.

Out-licensing our proprietary DosePro technology.

Securing rights to complementary products and product candidates that address CNS disorders and/or pain.

### **Our Risks**

Our business and our ability to execute our business strategy are subject to a number of risks that you should be aware of before you decide to buy our common stock. In particular, you should consider the following risks, which are discussed more fully in Risk Factors :

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.

We are largely dependent on the commercial success of Sumavel DosePro. For the six months ended June 30, 2011, we recognized only \$16.2 million in net product revenue from sales of Sumavel DosePro, and we may never significantly increase these sales or become profitable.

We are at an early stage of commercialization and have incurred significant net losses since our inception and anticipate that we will incur continued net losses for at least the next several years. Our net loss attributable to common stockholders was \$45.6 million in 2008, \$45.9 million in 2009, \$73.6 million in 2010 and \$38.2 million for the six months ended June 30, 2011.

We may not be successful in executing our sales and marketing strategy for the commercialization of Sumavel DosePro and, as part of this strategy, we are dependent on our collaboration with Astellas to promote Sumavel DosePro primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists. If we are unable to successfully execute such strategy, or if our co-promotion agreement with Astellas is amended, terminated or otherwise restructured, we may not be able to generate significant revenue.

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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 product or product candidates, our commercial opportunities may be reduced or eliminated.

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 sole source suppliers for the clinical supply of Zohydro and Relday, and if we experience problems with any of these suppliers, the manufacturing of Sumavel DosePro, Zohydro or Relday could be delayed.

## **Table of Contents**

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

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

Delays in the commencement or completion of clinical testing for Zohydro 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 additional revenues from, such product candidates.

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.

We may encounter unexpected safety, manufacturing, supply, regulatory or other issues relating to Sumavel DosePro, which may limit its commercial sales or regulatory acceptance.

### **Company Information**

We were formed as a Delaware corporation on May 11, 2006 as SJ2 Therapeutics, Inc. We commenced our operations on August 25, 2006 and changed our name to Zogenix, Inc. on August 28, 2006. Our principal executive offices are located at 12671 High Bluff Drive, Suite 200, San Diego, CA 92130, and our telephone number is 1-866-ZOGENIX (1-866-964-3649). We formed a wholly-owned subsidiary, Zogenix Europe Limited, in June 2010, a company organized under the laws of England and Wales and which is located in the United Kingdom, and whose principal operations are to support the manufacture of the DosePro technology. Our website address is [www.zogenix.com](http://www.zogenix.com). The information on, or accessible through, our website is not part of this prospectus.

DosePro<sup>®</sup>, Intraject<sup>®</sup>, Relday, Sumavel<sup>®</sup>, Zogenix and Zohydro are our trademarks. This prospectus also contains trademarks of other companies including Abilify<sup>®</sup>, Amerge<sup>®</sup>, Axert<sup>®</sup>, BOTOX<sup>®</sup>, Cambia, Fanafan<sup>®</sup>, Frova<sup>®</sup>, Geodon<sup>®</sup>, Imigran<sup>®</sup>, Imitrex<sup>®</sup>, Imitrex STATdose System<sup>®</sup>, Invega<sup>®</sup>, Latuda<sup>®</sup>, Lortab<sup>®</sup>, Maxalt<sup>®</sup>, Neurontin<sup>®</sup>, Relpax<sup>®</sup>, Relprevv, Risperdal, Risperdal Consta<sup>®</sup>, SABER, Saphris<sup>®</sup>, Seroquel<sup>®</sup>, SODAS<sup>®</sup>, Sustenna, Treximet<sup>®</sup>, Vicodin<sup>®</sup>, Vicoprofen<sup>®</sup>, Voltaren<sup>®</sup>, Zomig<sup>®</sup> and Zyprexa<sup>®</sup>. Unless otherwise specified, all prescription, prescriber and patient data in this prospectus is from Wolters Kluwer Pharma Solutions, Source<sup>®</sup> Pharmaceutical Audit Suite (PHAST), Institutional/Retail, Source<sup>®</sup> PHAST Retail, Source<sup>®</sup> Prescriber or Source<sup>®</sup> Dynamic Claims.

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**Table of Contents**

**The Offering**

**Common stock offered** 12,000,000 shares of common stock (or 13,800,000 shares if the underwriters' option to purchase additional shares is exercised in full).

**Common stock to be outstanding after this offering** 46,473,278 shares of common stock (or 48,273,278 shares if the underwriters' option to purchase additional shares is exercised in full).

**Use of proceeds** We intend to use the net proceeds from this offering to fund the cost of submitting an NDA to the FDA for U.S. regulatory approval of Zohydro, to fund the initial clinical development of Relday and to fund the ongoing commercialization of Sumavel DosePro and for working capital and other general corporate purposes.

**Risk factors** You should read the Risk Factors section of this prospectus for a discussion of the factors to consider carefully before deciding to purchase any shares of our common stock.

**Nasdaq Global Market symbol** ZGNX

The number of shares of common stock to be outstanding after this offering is based on 34,473,278 shares outstanding as of July 31, 2011, and excludes:

508,271 shares of common stock issuable upon the exercise of warrants outstanding as of July 31, 2011, at a weighted average exercise price of \$9.70 per share;

3,327,795 shares of common stock issuable upon the exercise of options and restricted stock units outstanding as of July 31, 2011, at a weighted average exercise price of \$4.07 per share; and

2,054,292 additional shares of common stock reserved for future issuance under our 2010 equity incentive award plan, or 2010 Plan, and our 2010 employee stock purchase plan, or Purchase Plan, as of July 31, 2011, plus any annual increases in the number of shares of common stock reserved for future issuance under the 2010 Plan and the Purchase Plan pursuant to evergreen provisions and any other shares that may become issuable under the 2010 Plan or the Purchase Plan pursuant to their terms, as more fully described in Compensation Discussion and Analysis Employee Equity Incentive Plans.

Except as otherwise indicated, all information in this prospectus assumes:

no exercise by the underwriters of their option to purchase up to an additional 1,800,000 shares of common stock; and

no exercise of outstanding options or warrants since July 31, 2011.

Cowen Healthcare Royalty Partners II, L.P., a current stockholder, Roger L. Hawley, our Chief Executive Officer, and Ann D. Rhoads, our Executive Vice President and Chief Financial Officer, have indicated an interest in purchasing \$1.5 million, \$100,000 and \$100,000 of shares of our common stock in this offering, respectively. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these parties, or any of these parties may

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determine to purchase more, less or no shares in this offering. The underwriters will not receive an underwriting discount or commission on any sales of shares to these parties.



**Table of Contents****Summary Financial Data**

The following table summarizes certain of our financial data. The summary statement of operations data for the years ended December 31, 2010, 2009 and 2008 are derived from our audited financial statements included elsewhere in this prospectus. The summary statement of operations data for the six months ended June 30, 2011 and 2010 and the historical balance sheet data as of June 30, 2011 have been derived from our unaudited interim financial statements, which are included elsewhere in this prospectus. The unaudited interim financial statements have been prepared on the same basis as the audited financial statements and, in the opinion of management, reflect all adjustments, consisting primarily of normal recurring adjustments, necessary to fairly present our financial position as of June 30, 2011 and results of operations for the six months ended June 30, 2011 and 2010. Our historical results of operations and financial condition are not necessarily indicative of the results or financial condition that may be expected in the future. The summary financial data set forth below should be read together with our financial statements and related notes, Selected Financial Data and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this prospectus.

	June 30,		Year Ended December 31,		
	2011	2010	2010	2009	2008
(In Thousands, Except Per Share Amounts)					
<b>Statement of Operations Data</b>					
<b>Revenue:</b>					
Net product revenue	\$ 16,151	\$ 6,118	\$ 19,069	\$ 0	\$ 0
Contract revenue	3,126	1,461	4,373	0	0
<b>Total revenue</b>	<b>19,277</b>	<b>7,579</b>	<b>23,442</b>	<b>0</b>	<b>0</b>
<b>Operating expenses:</b>					
Cost of sales	8,850	5,302	12,846	0	0
Royalty expense	630	382	843	0	0
Research and development	17,406	11,389	28,643	21,438	33,910
Selling, general and administrative	27,940	25,422	51,270	14,102	11,820
<b>Total operating expenses</b>	<b>54,826</b>	<b>42,495</b>	<b>93,602</b>	<b>35,540</b>	<b>45,730</b>
<b>Loss from operations</b>	<b>(35,549)</b>	<b>(34,916)</b>	<b>(70,160)</b>	<b>(35,540)</b>	<b>(45,730)</b>
<b>Other income (expense):</b>					
Interest income	19	3	5	10	696
Interest expense	(2,515)	(1,511)	(10,013)	(9,188)	(1,718)
Change in fair value of warrant liability	0	(13,020)	6,725	(755)	1,119
Other income (expense)	(103)	139	(111)	(416)	63
<b>Total other income (expense)</b>	<b>(2,599)</b>	<b>(14,389)</b>	<b>(3,394)</b>	<b>(10,349)</b>	<b>160</b>
<b>Net loss before income taxes</b>	<b>(38,148)</b>	<b>(49,305)</b>	<b>(73,554)</b>	<b>(45,889)</b>	<b>(45,570)</b>
Provision for income taxes	(13)	0	(10)	0	0
<b>Net loss</b>	<b>\$ (38,161)</b>	<b>\$ (49,305)</b>	<b>\$ (73,564)</b>	<b>\$ (45,889)</b>	<b>\$ (45,570)</b>
Net loss per share, basic and diluted	\$ (1.12)	\$ (37.44)	\$ (17.63)	\$ (40.97)	\$ (52.68)
Weighted-average shares outstanding, basic and diluted	34,015	1,317	4,173	1,120	865



**Table of Contents**

	As of June 30, 2011		
	Actual	Pro Forma (In Thousands)	Pro Forma As Adjusted
<b>Balance Sheet Data:</b>			
Cash and cash equivalents	\$ 7,672	\$ 37,172	\$ 74,872
Working capital (deficit)	(61)	29,439	67,139
Total assets	51,393	80,893	118,593
Long-term debt, less current portion	19,547	47,547	47,547
Accumulated deficit	(236,263)	(236,263)	(236,263)
Total stockholders' equity (deficit)	(7,142)	(5,642)	32,058

The summary pro forma balance sheet data above gives effect to the borrowing of \$30.0 million in July 2011 under our financing agreement with Cowen Healthcare Royalty Partners II, L.P., or Cowen Royalty, and receipt of \$1.5 million from the sale and issuance of 388,601 shares of common stock to Cowen Royalty in connection with such financing, which in the aggregate resulted in net proceeds of \$29.5 million, as if such transactions had occurred as of June 30, 2011. The summary pro forma as adjusted balance sheet data above additionally gives effect to our proposed sale of 12,000,000 shares of common stock in this offering and our receipt of the estimated net proceeds therefrom, based on the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us, and also assumes that Cowen Royalty, Roger L. Hawley and Ann D. Rhoads purchase all of the \$1.5 million, \$100,000 and \$100,000 of shares of our common stock in this offering, respectively, that they have indicated an interest in purchasing as described above, as if such transactions had occurred as of June 30, 2011.

Each \$1.00 increase or decrease in the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, would increase or decrease, respectively, the pro forma as adjusted amount of cash and cash equivalents, working capital, total assets and total stockholders' equity by approximately \$11.3 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

**Table of Contents**

**RISK FACTORS**

*Investing in our common stock involves a high degree of risk. You should carefully consider the following risk factors, as well as the other information in this prospectus, before deciding whether to invest in shares of our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and prospects. In that case, the trading price of our common stock could decline, and you may lose all or part of your investment.*

**Risks Related to Our Business and Industry**

**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, and borrowings under our loan and financing agreements with Cowen Healthcare Royalty Partners II, L.P. or Cowen Royalty, Oxford Finance LLC, as successor in interest to Oxford Finance Corporation, or Oxford, Silicon Valley Bank, or SVB, and, until June 30, 2011, General Electric Capital Corporation, or GE Capital. We believe, based on our current operating plan, that the net proceeds from this offering, together with our cash and cash equivalents as of June 30, 2011, future product revenues, borrowings available under our \$10.0 million revolving credit facility and the net proceeds from our recently completed equity and royalty financing with Cowen Royalty, will be sufficient to fund our operations into the third quarter of 2012, although there can be no assurance in that regard. We will need to obtain additional funds to finance our operations beyond that point in order to:

maintain and continue to increase our sales and marketing activities for Sumavel DosePro, particularly if our co-promotion agreement with Astellas Pharma US, Inc., or Astellas, is terminated, amended or otherwise restructured;

qualify secondary sources for the manufacturing of Sumavel DosePro;

fund our operations, continue to conduct clinical trials of Zohydro, initiate clinical trials for Relday and fund development of any other product candidate to support potential regulatory approval of marketing applications; and

commercialize any of our product candidates or any products or product candidates that we may develop, in-license or otherwise acquire, if any of these product candidates receive regulatory approval.

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

the commercial success of Sumavel DosePro;

the timing of regulatory approval, if granted, of Zohydro or any other product candidates;

the rate of progress and cost of our clinical trials and other product development programs for Zohydro, Relday and our other product candidates and any other product candidates that we may develop, in-license or acquire;

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the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with Sumavel DosePro, Zohydro, Relday and any of our other product candidates;

the costs and timing of completion of outsourced commercial manufacturing supply arrangements for any product candidate;

**Table of Contents**

the costs of maintaining and expanding our sales and marketing infrastructure or establishing distribution capabilities;

the effect of competing technological and market developments; and

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

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

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

We anticipate that, for at least the next several years, our ability to generate revenues and become profitable will depend in large part on the commercial success of our only marketed product, Sumavel DosePro, which in turn, will depend on several factors, including our ability to:

successfully maintain and increase market demand for, and sales of, Sumavel DosePro through our sales and marketing efforts and those of Astellas, our co-promotion partner (or, in the event that our co-promotion agreement with Astellas is amended, terminated or otherwise restructured, as described under Business Collaboration, Commercial and License Agreements Astellas Co-Promotion Agreement, by expanding our sales force and/or through another co-promotion partner, if available);

obtain greater acceptance of Sumavel DosePro by physicians and patients;

maintain adequate levels of coverage and reimbursement for Sumavel DosePro from commercial health plans and government health programs, which we refer to collectively as third-party payors, particularly in light of the availability of other branded and generic competitive products;

maintain compliance with regulatory requirements;

establish and maintain agreements with wholesalers and distributors on commercially reasonable terms;

maintain commercial manufacturing arrangements with third-party manufacturers as necessary to meet commercial demand for Sumavel DosePro and continue to manufacture commercial quantities at acceptable cost levels; and

successfully maintain intellectual property protection for Sumavel DosePro.



## **Table of Contents**

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 quarterly growth in total prescriptions from the launch of Sumavel DosePro in January 2010 through June 30, 2011, we have at certain times experienced a reduction in total and new prescriptions month over month. In addition, while we have initiated activities to expand our sales force in the United States by approximately 15 sales representatives by the end of the third quarter of 2011 to further promote Sumavel DosePro, there is no guarantee that this expansion will result in increased sales of Sumavel DosePro. If we fail to successfully increase sales of Sumavel DosePro, we may be unable to generate sufficient revenues to grow or sustain our business and we may never become profitable, and our business, financial condition and results of operations will be materially adversely affected.

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

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

We have generated significant net losses and negative cash flow from operations since our inception in 2006. For example, for 2008, 2009, 2010 and the six months ended June 30, 2011, we incurred net losses of \$45.6 million, \$45.9 million, \$73.6 million and \$38.2 million, respectively, our net cash used in operating activities was \$41.3 million, \$32.4 million, \$72.0 million, and \$40.5 million, respectively, and, at June 30, 2011, our accumulated deficit was \$236.3 million. We expect our losses and negative cash flow to continue for at least the next several years as a result of the development expenses in connection with our ongoing clinical development for Zohydro, the initiation of clinical development for Relday and the cost of the sales and marketing expense associated with Sumavel DosePro. Our ability to generate revenues from Sumavel DosePro or any of our product candidates will depend on a number of factors, including, in the case of Sumavel DosePro, the factors described in the following two risk factors and, in the case of our product candidates, our ability to successfully complete clinical trials, obtain necessary regulatory approvals and negotiate arrangements with third parties to help finance the development of, and market and distribute, any product candidates that receive regulatory approval. In addition, we will be subject to the risk that the marketplace will not accept our products.

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

**We may not be successful in executing our sales and marketing strategy for the commercialization of Sumavel DosePro and, as part of this strategy, we are dependent on our collaboration with Astellas to promote Sumavel DosePro primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists. If we are unable to successfully execute such strategy or if our co-promotion agreement with Astellas is amended, terminated or otherwise restructured, we may not be able to generate significant revenue.**

Prior to the launch of Sumavel DosePro in January 2010, we built a commercial sales and marketing organization including sales, marketing, communications, managed markets, trade and distribution functions, which is now focused exclusively on marketing and selling Sumavel DosePro primarily to physicians, nurses and other healthcare professionals in the United States. Our field sales force includes approximately 80 sales representatives who are promoting Sumavel DosePro primarily to neurologists and other prescribers of migraine



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**Table of Contents**

medications, including headache clinics and headache specialists in the United States. We have initiated activities to expand our sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. Although we believe we have adequately sized our sales force in order to reach this audience, we may either increase or decrease the size of our sales force in the future based upon market conditions and actual sales performance. In that regard, if our co-promotion agreement with Astellas is amended, terminated or otherwise restructured, as described below, we would expect to either expand our sales force to promote Sumavel DosePro and/or seek another co-promotion partner, if available. In addition, we could lose sales personnel or the performance of our sales personnel as measured by actual sales may be disappointing. Many of our competitors have significantly larger sales and marketing organizations, and significantly greater experience than we do in selling, marketing and distributing pharmaceuticals, and we may not be able to compete successfully with them with the commercial infrastructure we have developed.

To complement our sales force, we entered into an exclusive co-promotion agreement with Astellas in July 2009 under which Sumavel DosePro is also being promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists, or collectively the Astellas Segment, in the United States by approximately 400 Astellas sales representatives. Although the agreement stipulates annual minimum levels of sales effort, we have limited control over the amount and timing of resources that Astellas dedicates to the promotion of Sumavel DosePro, and we do not hire, train or manage such resources. For example, Astellas could reduce the number of its sales representatives promoting Sumavel DosePro while still complying with these minimum requirements. The ability to generate revenue from our arrangement with Astellas depends on Astellas' efforts in promoting Sumavel DosePro and its ability to achieve broad market acceptance and prescribing of Sumavel DosePro in the Astellas Segment.

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

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

Astellas could terminate the co-promotion agreement for any or no cause upon 180-days written notice at any time, which may negatively impact our ability to generate, or prevent us from generating, sufficient revenue;

Astellas could fail to comply with applicable regulatory guidelines with respect to the promotion of Sumavel DosePro, which could result in administrative or judicially imposed sanctions, including warning letters, civil and criminal penalties, and injunctions; and

disputes regarding the co-promotion agreement that negatively impact or terminate the commercialization efforts of Astellas may negatively impact or prevent the generation of sufficient revenue or result in significant litigation or arbitration.

For the six months ended June 30, 2011, sales to the Astellas Segment represented approximately 40% of our net product revenue. Under the terms of the co-promotion agreement, Astellas may terminate the agreement for any reason or no reason upon 180-days written notice to us. The co-promotion agreement may also be terminated by Astellas or us for a number of other specified reasons, some of which are beyond our control. In the event Astellas terminates the agreement for specified reasons, including a material uncured breach by us of our minimum sales effort obligations and our failure to cure such breach within a specified period, we would be required to pay Astellas only the first of the two annual tail payments described below.

In addition, either party may terminate the agreement based upon, among other things, a failure of the Sumavel DosePro brand to achieve certain minimum sales levels in 2011, as defined in the co-promotion agreement. Based on our net product revenue through June 30, 2011, we do not expect to meet these 2011 minimum sales levels for Sumavel DosePro, and therefore expect that both we and Astellas will have the right to terminate the agreement on this basis. If either party were to exercise this termination right, it must provide

## Table of Contents

90 days written notice to the other party, such notice to be provided within 30 days after the actual net sales of Sumavel DosePro through December 31, 2011 have been provided to Astellas pursuant to the terms of the co-promotion agreement. In the event of such a termination relating to sales levels of Sumavel DosePro, we would be required to make two annual tail payments to Astellas calculated as decreasing fixed percentages (ranging from a mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion. In the event of a termination by us or Astellas, we would expect to either expand our sales force to promote Sumavel DosePro to certain physicians within the Astellas Segment and/or seek another co-promotion partner, if available. We may also seek to amend or restructure our co-promotion agreement with Astellas.

In addition, Astellas may terminate the co-promotion agreement in the event we undergo a change of control, as defined in the co-promotion agreement, if a governmental authority takes action that prevents or makes it unlawful for Astellas to perform its obligations under the agreement, in the event of our inability to supply commercial product, under certain circumstances where a third party asserts that the making or selling of Sumavel DosePro infringes the intellectual property rights of a third party, upon the occurrence of a large scale recall or market withdrawal of Sumavel DosePro, upon a material uncured breach by us or in the event of our insolvency or bankruptcy or other event which affects our ability to perform our obligations under the agreement.

We cannot assure you that Astellas will not terminate the agreement under the circumstances described above. As an alternative to termination, we and Astellas could agree to amend or otherwise restructure the current co-promotion agreement. Such amendment or restructuring could change the financial terms of our agreement, change our respective minimum sales force requirements, or otherwise materially alter our co-promotion relationship. Such an amendment or restructuring could require us to expand our sales force or otherwise invest significant additional financial resources in order to adequately support the successful sales and marketing of Sumavel DosePro.

In addition, our co-promotion agreement with Astellas expires on June 30, 2013, subject to a one-year extension at the option of Astellas. We cannot assure you that Astellas will enter into any extension of the agreement or, if it does so, that it will not condition any such extension upon changes in the agreement that could have a material adverse effect on us. If Astellas were to terminate the agreement or elect not to extend the agreement upon its expiration, we would lose the efforts of their sales force, and we would need to make arrangements with another third party to replace Astellas' sales force, or significantly expand our sales and marketing organization. We may not be able to enter into such arrangements with third parties in a timely manner, on acceptable terms or at all. To the extent that we enter into another co-promotion or other licensing arrangement, our portion of retained product revenues is likely to be lower than if we directly marketed and sold Sumavel DosePro solely on our own, and a portion of those revenues generated will depend upon the efforts of such third parties similar to our dependence on Astellas, and these efforts may not be successful. If our co-promotion agreement with Astellas 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 to cover this segment and any such expansion could, in any event, substantially increase our expenses and capital requirements that we might not be able to fund.

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

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

The commercial success of Sumavel DosePro and, if approved, Zohydro and Relday, or any other product candidates for which we obtain marketing approval from the FDA or other regulatory authorities will depend

**Table of Contents**

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

our ability to provide acceptable evidence of safety and efficacy;

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

the relative convenience and ease of administration;

the prevalence and severity of adverse side effects;

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

the clinical indications for which the product is approved;

in the case of product candidates that are controlled substances, the U.S. Drug Enforcement Agency, or DEA, scheduling classification;

availability and perceived advantages of alternative treatments;

any negative publicity related to our or our competitors' products;

the effectiveness of our or any current or future collaborators' sales, marketing and distribution strategies;

pricing and cost effectiveness;

our ability to obtain sufficient third-party payor coverage or reimbursement; and

the willingness of patients to pay out of pocket in the absence of third-party payor coverage.

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

In addition, products used to treat and manage pain, especially in the case of opioids, are from time to time subject to negative publicity, including illegal use, overdoses, abuse, diversion, serious injury and death. These events have led to heightened regulatory scrutiny. Controlled substances are classified by the DEA as Schedule I through V substances, with Schedule I substances being prohibited for sale in the United

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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 contains *hydrocodone*, and we anticipate it will be regulated as a Schedule II controlled substance, and despite the strict regulations on the marketing, prescribing and dispensing of such substances, illicit use and abuse of *hydrocodone* is well-documented. Thus, the regulatory approval process and the marketing of Zohydro may generate public controversy that may adversely affect regulatory approval and market acceptance of Zohydro.

Our efforts to educate the medical community and third-party payors on the benefits of Sumavel DosePro and Zohydro and Relday, if approved, and 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.

## **Table of Contents**

### **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 recently 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 efforts and significantly increase our costs to recover or reproduce the data. Similarly, we rely on a large number of third parties to supply components for and manufacture our product and product candidates, warehouse and distribute Sumavel DosePro and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the commercialization of Sumavel DosePro and development of Zohydro, 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 organization, conducting product development activities for our product and product candidates, in-licensing rights to Zohydro and Relday, and commercializing Sumavel DosePro. Moreover, Sumavel DosePro is our only product that is approved for sale. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

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

The majority of our sales of Sumavel DosePro are to wholesale pharmaceutical distributors who, in turn, sell the products to pharmacies, hospitals and other customers. Three wholesale pharmaceutical distributors, Cardinal Health, Inc., McKesson Corporation and AmerisourceBergen Corporation, individually comprised 46.2%, 34.8% and 11.1%, respectively, of our total gross sales of Sumavel DosePro for the six months ended June 30, 2011, 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

**Table of Contents**

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

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

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary therapeutics. We face competition from a number of sources, some of which may target the same indications as our product or product candidates, including large pharmaceutical companies, smaller pharmaceutical companies, biotechnology companies, academic institutions, government agencies and private and public research institutions, many of which have greater financial resources, sales and marketing capabilities, including larger, well-established sales forces, manufacturing capabilities, experience in obtaining regulatory approvals for product candidates and other resources than us. Many large, well-capitalized companies offer products in the United States that compete with Sumavel DosePro. Sumavel DosePro currently competes with branded products in the triptan class such as Imitrex and Treximet marketed by GlaxoSmithKline, or GSK, as well as six other branded triptan therapies being sold by AstraZeneca PLC, Endo Pharmaceuticals Holdings Inc., Johnson & Johnson, Merck & Co., Inc., and Pfizer Inc. In addition to those migraine therapeutics there are other marketed non-triptan migraine therapeutics such as Cambia sold by Nautilus Neurosciences, Inc. and Migranal sold by Valeant Pharmaceutical International. We also face competition from generic *sumatriptan* 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 directly substituted for Sumavel DosePro, generic versions of *sumatriptan* injection and alternative autoinjector forms of *sumatriptan* injection may reduce the future adoption of Sumavel DosePro by third-party payors and consumers, as financial pressure to use generic products may encourage the use of a generic product over Sumavel DosePro. Sumavel DosePro is currently more expensive on a per dose basis than most of the competing branded and all of the generic triptan products for migraine, which may also limit the coverage and reimbursement by third-party payors, which could adversely affect adoption by physicians and patients.

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

In addition to already marketed therapeutics, we also face competition from product candidates that are or could be under development by many of the above-mentioned entities and others. For example, there are several

**Table of Contents**

products for the treatment of migraine under development by large pharmaceutical companies such as GSK and Merck & Co., and other smaller companies such as NuPathe, Inc. and MAP Pharmaceuticals, Inc. If approved, Zohydro may also compete with at least 15 opioid product candidates under development, including abuse and diversion resistant formulations of currently available opioids, novel opioids and alternative delivery forms of various opioids under development at other pharmaceutical companies, including single-entity extended-release *hydrocodone* product candidates being developed by Cephalon, Inc., Egalet A/S, Pfizer and Purdue Pharma L.P. Zohydro 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, Intellipharmaceutics International Inc., Pfizer and QRxPharma Ltd.

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

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

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

capital resources;

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;

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**Table of Contents**

manufacturing and distribution resources and experience;

name recognition; and

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

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

**We are dependent on numerous third parties in our supply chain, all of which are currently single source suppliers, for the commercial supply of Sumavel DosePro and for the clinical supply of Zohydro and Relday, and if we experience problems with any of these suppliers, the manufacturing of Sumavel DosePro, Zohydro 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, Relday or any other products or product candidates. Our DosePro device and Sumavel DosePro are manufactured by contract manufacturers, component fabricators and secondary service providers. Final aseptic fill, finish, assembly and packaging of Sumavel DosePro are performed at Patheon UK Limited, Swindon, United Kingdom, a specialist in the aseptic fill/finish of injectables and other sterile pharmaceutical products. In addition, Nypro Limited, located in Bray, Ireland, manufactures the actuator assemblies and injection molded components for our DosePro device and MGlas AG, located in Műnnerstadt, Germany, manufactures the specialized glass capsule that houses the *sumatriptan* active pharmaceutical ingredient, or API, in our DosePro device. Each of these manufacturers and each other company that supplies, fabricates or manufactures any component used in our DosePro device is currently the only qualified source of their respective components. We currently rely on Dr. Reddy's Laboratories as the only supplier of *sumatriptan* API for use in Sumavel DosePro. We also outsource all manufacturing and packaging of the clinical trial materials for Zohydro and Relday to third parties. Although we plan to qualify additional manufacturers and suppliers of some of the components used in Sumavel DosePro, there can be no assurance that we will be able to do so and the current manufacturers and suppliers of these components will likely be single source suppliers to us for a significant period of time. Similarly, under our license agreements, Elan Pharma International Ltd., or Elan, is the exclusive manufacturer of Zohydro and Durect is the exclusive manufacturer of Relday for all clinical trials through Phase 2 clinical trials and has the option to supply Relday for Phase 3 clinical trials and, if approved, commercial distribution. We may never be able to establish additional sources of supply for Zohydro or Relday.

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

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

reliance on the third parties for regulatory compliance and quality assurance;



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**Table of Contents**

the possible breach of the manufacturing agreements by the third parties because of factors beyond our control or the insolvency of any of these third parties or other financial difficulties, labor unrest, natural disasters or other factors adversely affecting their ability to conduct their business; and

the possibility of termination or non-renewal of the agreements by the third parties, at a time that is costly or inconvenient for us, because of our breach of the manufacturing agreement or based on their own business priorities.

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

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

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

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

We have retained third-party service providers to perform a variety of functions related to the sale and distribution of our products, key aspects of which are out of our direct control. For example, we rely on Cardinal Health 105, Inc. (a/k/a Specialty Pharmaceutical Services) to provide key services related to logistics, warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management and call center management, and, as a result, most of our inventory is stored at a single warehouse maintained by the service provider. We place substantial reliance on this provider as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical damage or natural disaster at their facilities, our ability to deliver product to meet commercial demand would be

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**Table of Contents**

significantly impaired. In addition, we utilize third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services. If the quality or accuracy of the data maintained by these service providers is insufficient, our ability to continue to market our products could be jeopardized or we could be subject to regulatory sanctions. We do not currently have the internal capacity to perform these important commercial functions, and we may not be able to maintain commercial arrangements for these services on reasonable terms.

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

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

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

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

We have not yet completed all necessary studies, nor submitted a new drug application, or NDA, or received marketing approval, for Zohydro and we have not yet commenced clinical studies for Relday. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. The FDA also has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. For example:

the FDA may not deem a product candidate safe and effective;

the FDA may not find the data from pre-clinical studies and clinical trials sufficient to support approval;

the FDA may require additional pre-clinical studies or clinical trials;

the FDA may not approve of our third-party manufacturers' processes and facilities; or

the FDA may change its approval policies or adopt new regulations.

Zohydro has undergone Phase 1 pharmacokinetics studies as well as Phase 2 clinical trials. However, these studies and trials were conducted by a third party and, accordingly, we did not directly participate in their design or execution. In addition, we will also need to successfully complete Phase 3 clinical trials to establish its safety and efficacy, additional Phase 1 studies, and additional pre-clinical studies prior to our submission of an NDA to the FDA for approval. We initiated the Phase 3 clinical development program for Zohydro in March 2010 and reported positive top-line results from our pivotal Phase 3 efficacy trial, Study 801, in August 2011 and completed enrollment in our open-label Phase 3 safety trial, Study 802, in November 2010. Zohydro and any of

## **Table of Contents**

our other product candidates may fail to achieve their specified endpoints in clinical trials. Furthermore, product candidates such as Zohydro may not be approved even if they achieve their specified endpoints in clinical trials. The FDA may disagree with our trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials. The FDA may also approve a product candidate for fewer or more limited indications than we request, or may grant approval contingent on the performance of costly post-approval clinical trials. In addition, the FDA may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates. Although we have not yet begun clinical studies for Relday, the development of Relday will be subject to most of the risks described in this paragraph.

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

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

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

In light of widely publicized events concerning the safety risk of certain drug products, particularly opioid drug products, regulatory authorities, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products after approval. In addition, the Federal Food, Drug, and Cosmetic Act, or FDCA, as amended by the Food and Drug Administration Amendments Act of 2007, grants significant expanded authority to the FDA, much of which is aimed at improving the safety of drug products before and after approval. In particular, the FDCA 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 risk evaluation and mitigation strategy, or REMS, for certain drugs, including certain currently approved drugs. It also significantly expands the federal government's clinical trial registry and results databank, which we expect will result in significantly increased government oversight of clinical trials. Under the FDCA, companies that violate these and other provisions of the law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties.

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

With regard to Zohydro, top-line results from our pivotal Phase 3 efficacy clinical trial in patients with chronic lower back pain has shown what we believe is a clinically acceptable efficacy and safety profile which supports submission of an NDA for the treatment of moderate to severe pain in patients requiring around-the-clock opioid therapy. The trial successfully met the primary efficacy endpoint of the study in demonstrating a significant difference ( $p=0.008$ ) between the mean changes in daily pain intensity Numeric Rating Scale (NRS) scores between Zohydro and placebo groups. The two key secondary endpoints were also met, specifically, the proportion of patients with at least 30% improvement in pain intensity and the improvement of overall satisfaction of medication. In the pivotal Phase 3 efficacy trial, the observed adverse events were

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## **Table of Contents**

similar to the side effects we observed in prior Phase 2 trials of Zohydro and consistent with the reported side effects of opioids currently prescribed for chronic pain. The incidence of adverse events was 33.7% and 28.8% in the open-label titration and double blind treatment periods, respectively. Overall, the most commonly reported adverse events (32%) were constipation, nausea, somnolence, vomiting, diarrhea, insomnia, fatigue, headache, dizziness and dry mouth. These results may not be predictive of results obtained in our ongoing Phase 3 safety trial or any other required future trials, and we may be unable to demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals or approvals for commercially viable uses. In addition, the top-line data we have reported and may continue to report from our Zohydro clinical trials is based on preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the applicable clinical trial, and may also change in connection with the continued review of such data as part of our planned submission and the FDA's review of our NDA. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. If Zohydro is not shown to be safe and effective in clinical trials, this program could be delayed or terminated, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

Clinical trials are very expensive, time consuming and difficult to design and implement. Delays in the commencement or completion of clinical testing for Zohydro or pre-clinical or clinical testing for Relday or any of our other product candidates could significantly affect our product development costs and business plan. In March 2010, we initiated a Phase 3 clinical development program for Zohydro, including a pivotal efficacy trial. We reported positive top-line results from our pivotal Phase 3 efficacy trial in August 2011 and are still conducting our fully-enrolled Phase 3 safety trial for Zohydro. Phase 3 clinical efficacy trials, in general, are significantly more complex and time-consuming and involve more patients than the Phase 1 and 2 clinical trials. We do not know whether our ongoing Phase 3 clinical trial of Zohydro will be completed on schedule, if at all. We expect to initiate clinical testing for Relday in patients with schizophrenia in early 2012. In addition, we do not know whether this or any other pre-clinical or clinical trials will begin on time or be 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 pain, migraine or 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.

## **Table of Contents**

We believe that we have planned and designed an adequate Phase 3 clinical trial program for Zohydro, and we presented the trial design for our Phase 3 trials to the FDA at our End of Phase 2 meeting in June 2008. Although we believe the FDA has generally agreed with the design of our Phase 3 clinical trial program, the FDA could still determine that it is not satisfied with our plan, the details of our pivotal clinical trial protocols and designs or the results of our studies. While the FDA has provided us with a written record of our discussions and responses to our questions at our End of Phase 2 meeting, such records and responses do not guarantee that the FDA will deem our trial design to be sufficient for the purpose of obtaining marketing approval for Zohydro. We did not seek a Special Protocol Assessment from the FDA for our pivotal Phase 3 efficacy study for Zohydro (Study 801).

In addition, while we completed enrollment in our open-label Phase 3 trial, Study 802, in November 2010, chronic pain patients have historically been difficult to keep enrolled in clinical trials. If a significant number of patients fail to stay enrolled in any of our current or future clinical trials of Zohydro, 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;

in the case of Zohydro, regulatory concerns with opioid products generally and the potential for abuse and diversion of the drugs; and

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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 Zohydro, 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.

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**Table of Contents**

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

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

Certain of our competitors may file a 505(b)(2) application for extended-release *hydrocodone* either before or shortly after we submit our own NDA for Zohydro. The first approved 505(b)(2) applicant for a particular condition of use, or change to a marketed product, such as a new extended-release formulation for a previously approved product, may be granted three-year Hatch-Waxman exclusivity if one or more clinical studies, other than bioavailability or bioequivalence studies, was essential to the approval of the application and was conducted/sponsored by the applicant. Three-year Hatch-Waxman exclusivity delays the FDA's approval of other 505(b)(2) applicants for the same condition of use or change to the drug product that was granted exclusivity, regardless of the date of submission of each NDA. We believe that several competitors are developing extended-release *hydrocodone* products, and if the FDA approves a competitor's 505(b)(2) application for its extended-release *hydrocodone* product before our application, and granted the competitor three-year exclusivity, the FDA would be precluded from making effective our NDA for Zohydro until after that three-year exclusivity period has run, and such delay would dramatically reduce our expected market potential for Zohydro. Additionally, even if our 505(b)(2) application for extended-release *hydrocodone* is approved first, we may still be subject to competition by other *hydrocodone* products, including approved products or other 505(b)(2) applications for different conditions of use that would not be restricted by the three-year exclusivity.

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

extending patent protection for existing products that would block Section 505(b)(2) approval of the product candidate by pursuing new patents for existing products that may be granted just before the expiration of one patent, which could extend patent protection for a number of years or otherwise delay the launch of generic, 505(b)(2) or other competing products;

submitting Citizen Petitions to request the FDA to take adverse administrative action with respect to approval of a generic, 505(b)(2) or other competing product;

filing patent infringement lawsuits, whether or not meritorious, to trigger up to a 30-month stay in the approval of a generic, 505(b)(2) or other competing product; and

engaging in state-by-state initiatives to enact legislation or regulatory policies that restrict the substitution of some generic, 505(b)(2) or other competing drugs for brand-name drugs.

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



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**Table of Contents**

**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 have agreements with third-party CROs to conduct our Phase 3 trials for Zohydro, and anticipate that we may enter into other such agreements 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 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 development of a REMS for Zohydro could cause significant delays in the approval process for Zohydro and will add additional layers of regulatory requirements, including the requirement for a Medication Guide and educational requirements for prescribers and patients, which could significantly impact our ability to commercialize Zohydro and dramatically reduce its market potential.**

The Food and Drug Administration Amendments Act, or FDAAA, added Section 505-1 to the FDCA. 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 must 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, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. 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

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**Table of Contents**

REMS must include a timetable to assess the strategy at 18 months, three years and seven years after the strategy's approval.

In February 2009, the FDA informed drug manufacturers that it will require a class-wide REMS for all long-acting and sustained-release opioid drug products. The FDA has since initiated efforts to develop a new standardized REMS for these opioid medications to ensure their safe use. In April 2011, FDA announced that it had finalized the elements of a class-wide REMS for these products. The central component of the opioid REMS program is an education program for prescribers and patients. Specifically, the REMS for these products must include a Medication Guide available for distribution to patients who are dispensed the drug, as well as a number of elements to assure safe use. These elements include training for prescribers who prescribe the drug; information provided to prescribers that prescribers can use to educate patients in the safe use, storage, and disposal of opioids; and information provided to prescribers of the existence of the REMS and the need to successfully complete the necessary training. Moreover, the REMS must include a timetable for submission of assessments that shall be no less frequent than 6 months, 12 months, and annually after the REMS is approved to assess the extent to which the elements to assure safe use are meeting the goals of the REMS and whether the goals or elements should be modified. The FDA expects that manufacturers of long-acting and extended-release opioids work together to provide educational materials as part of a class-wide single shared system to reduce the burden of the REMS on the healthcare system.

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

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

In March 2008, we entered into a licensing and distribution agreement with Desitin pursuant to which we granted Desitin the exclusive right under our intellectual property rights related to Sumavel DosePro to develop, use, distribute, sell, offer for sale, and import Sumavel DosePro and any potential modified versions of Sumavel DosePro in the European Union, Norway, Switzerland and Turkey. In that regard, Desitin is not obligated under the agreement to pursue regulatory approval or commercialization of Sumavel DosePro in any of these countries except for Germany. Since we will depend on Desitin to develop, obtain regulatory approval for and, if regulatory approval is granted, commercialize Sumavel DosePro in these countries, we will have limited control over the success of Desitin's development, regulatory approval and commercialization efforts. Desitin submitted a Marketing Authorization Application for Sumavel DosePro to the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)) in Germany, the reference member state, through the Decentralized Procedure in October 2009, following completion of a European pivotal bioequivalence trial comparing needle-free Sumavel DosePro to a traditional needle-based autoinjector, Imigran-Inject, the European brand of Imitrex STATdose. In November 2010, Denmark became the first member of the European Union to approve marketing of Sumavel DosePro in that country. Subsequently, Sumavel DosePro has received marketing approval in Germany, Sweden, Norway and the United Kingdom.

Any additional clinical studies Desitin may be required to conduct as part of the regulatory approval process may not corroborate the results of the clinical studies we have conducted or may have adverse results or effects on our ability to maintain regulatory approvals in the United States or obtain them in other countries. In addition, although we believe that the U.S. market represents the largest commercial opportunity for Sumavel DosePro, Desitin may not develop Sumavel DosePro as fast or generate as large of a market as we would like or as the

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**Table of Contents**

market may expect and Desitin may not seek to develop, obtain approval for or commercialize Sumavel DosePro in countries for which it has exclusive rights, other than in Germany, where Desitin is required to develop, seek approval for and commercialize Sumavel DosePro. Any failure by Desitin to successfully commercialize Sumavel DosePro or to successfully obtain applicable foreign regulatory approval for Sumavel DosePro would limit our opportunity to receive revenue from the territories licensed to Desitin. Furthermore, negative developments occurring in those territories controlled by Desitin could have a negative impact on physician and patient impressions of our product in the United States and elsewhere.

**Our failure to successfully establish new partnerships with pharmaceutical companies or contract sales organizations to co-promote 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 of approximately 80 representatives primarily targeting neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. We have initiated activities to expand our sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. In addition, in July 2009, we entered into an exclusive agreement with Astellas under which Sumavel DosePro is also being marketed by Astellas in the United States and promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists by approximately 400 Astellas sales representatives. In order to expand the market opportunity for any additional product candidates that receive regulatory approval into the broader primary care physician audiences, we will need to continue 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 product candidates, particularly if our co-promotion agreement with Astellas is amended, terminated or otherwise restructured. 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 commercialize any product candidates that may receive regulatory approval, we are likely to receive less revenues than if we commercialized these products ourselves. Further, by entering into strategic partnerships or similar arrangements, we may rely in part on such third parties for financial and commercialization resources. Even if we are able to identify suitable partners to assist in the commercialization of our product candidates, they may fail to devote the resources necessary to realize the full commercial potential of our products. In addition, we may lack the financial and managerial resources to increase the size of our sales and marketing organization to adequately commercialize any product candidates that may be approved, and any increase in our sales force would result in an increase in our expenses, which could be significant before we generate revenues from any newly approved product candidate. If we are unable to expand our sales and marketing infrastructure or enter into a third-party arrangement, we would not be able to successfully commercialize any approved products. Even if we are able to expand our sales and marketing personnel or successfully establish partnership arrangements, such sales force and marketing teams may not be successful in commercializing our products, which would adversely affect our ability to generate revenue for such products, which will have a material adverse effect on our business, results of operations, financial condition and prospects.

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

As part of our growth strategy we intend to seek to expand our product pipeline by exploring acquisition or in-licensing opportunities of proven drugs that can be paired with our DosePro needle-free drug delivery system. However, the current version of our DosePro drug delivery system cannot be used with drug formulation

## Table of Contents

volumes greater than 0.5 mL. Many marketed and development-stage injectable products, including most biologics, have formulation volumes greater than 0.5 mL and would require reformulation, if possible, to accommodate the approved doses in smaller volumes that are compatible with DosePro. Any reformulation may increase the risk of failure during development, extend the development timelines, increase development costs and add complexity to the regulatory approval process and in some cases reformulation may not be possible. If we are not able to identify additional drug compounds that can be delivered via the current version of our DosePro technology, or if we are unable to successfully develop higher dose versions of this technology, our ability to develop additional product candidates and grow our business would be adversely affected. We will also seek opportunities to out-license the DosePro technology to partners seeking to enhance, differentiate, or extend the life-cycle of their injectable products. If we are unable to secure partnerships with companies that have compounds that can be delivered via the current version of our DosePro technology, or if we are unable to successfully develop higher dose versions of this technology, we will not be able to generate revenues from out-licensing our DosePro technology.

We have initiated early stage design and development of a larger volume, second generation version of our DosePro technology to accommodate drug formulation volumes greater than 0.5 mL, which if successfully developed, would allow for a broader range of potential applications for our technology. However, the full development of such technology will require substantial investment and we may consider entering into a third-party collaboration in order to obtain third-party financing to help fully develop such technology. There is no guarantee that we or any potential future third-party collaborator will be able to successfully develop such a device technology, whether for financial or technical reasons or otherwise.

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

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

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including pre-clinical or clinical testing and approval by the FDA and applicable foreign regulatory authorities. We expect to initiate clinical testing for Relday in patients in schizophrenia in early 2012. We may not be able to obtain necessary approvals to initiate such clinical testing in a timely manner or at all. In addition, all product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any products that we develop or approved products that we acquire will be manufactured or sold profitably or achieve market acceptance.

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**Table of Contents**

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

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

We increased our full-time employees from 48 as of October 31, 2009 to 150 as of July 31, 2011. In addition, we have initiated activities to expand our sales force in the United States from approximately 80 sales representatives to approximately 95 sales representatives by the end of the third quarter of 2011 and may need to further increase our sales force, perhaps substantially, if our co-promotion agreement with Astellas is amended, terminated or otherwise restructured. Any such increases in our sales force could substantially increase our expenses. We may need to continue to expand our managerial, operational and other resources in order to grow, manage and fund our existing business. Our management and personnel, systems and facilities currently in place may not be adequate to support this recent and any future growth, and we may be unable to fund the costs and expenses required to increase our necessary headcount and infrastructure. Our need to effectively manage our operations, any future growth and various projects requires that we:

manage our internal and external commercialization efforts for Sumavel DosePro effectively while carrying out our contractual obligations to Astellas and other third parties and complying with all applicable laws, rules and regulations;

manage our internal development efforts for Zohydro, 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, the anticipated increase in our sales force is expected to increase our expenses and any further increase of our sales force if the Astellas co-promotion agreement is amended, terminated or otherwise restructured may further increase our expenses, perhaps substantially. Our future financial performance and our ability to execute on our business plan will depend, in part, on our ability to effectively manage any future growth and our failure to effectively manage any growth could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

Our success depends on our continued ability to attract, retain and motivate highly qualified management and key clinical development, regulatory, sales and marketing and other personnel. We are highly dependent on the development, regulatory, commercial and financial expertise of our senior management team. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the areas in Southern and Northern California, where we currently operate. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercialization objectives, our ability to raise additional capital and our ability to implement our business strategy. The loss of the services of any members of our senior

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**Table of Contents**

management team, especially our Chief Executive Officer, Roger L. Hawley, and President and Chief Operating Officer, Stephen J. Farr, Ph.D., could negatively impact the commercialization of Sumavel DosePro and could delay or prevent the development and commercialization of any other product candidates, including Zohydro or Relday. In addition, under the terms of our amended and restated loan and security agreement with Oxford and SVB, or the amended Oxford/SVB loan agreement, if our Chief Executive Officer, Chief Financial Officer or President resigns, is terminated or is no longer actively involved in his or her current position and is not replaced by a person acceptable to our board of directors within 120 days, an event of default would be triggered under the agreement, and the lenders would be able to demand immediate repayment of all borrowings outstanding under the agreement. Further, if we lose any members of our senior management team, we may not be able to find suitable replacements, and our business may be harmed as a result. In addition to the competition for personnel, our locations in California in particular are characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

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

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

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

exposure to unknown liabilities;

disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;

incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;

higher than expected acquisition and integration costs;

write-downs of assets or goodwill or impairment charges;

increased amortization expenses;

difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;

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impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and

inability to retain key employees of any acquired businesses.

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## **Table of Contents**

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

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

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

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

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

Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third-party coverage and reimbursement for Sumavel DosePro or any of our other product candidates for which we may receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

The commercial use of our product and clinical use of our product and product candidates expose us to the risk of product liability claims. This risk exists even if a product is approved for commercial sale by the FDA and manufactured in facilities licensed and regulated by the FDA, such as the case with Sumavel DosePro, or an applicable foreign regulatory authority. Our product and product candidates are designed to affect important bodily functions and processes. Any side effects, manufacturing defects, misuse or abuse associated with Sumavel DosePro or our product candidates could result in injury to a patient or even death. For example, because our DosePro technology is designed to be self-administered by patients, it is possible that a patient could fail to follow instructions and as a result apply a dose in a manner that results in injury. In addition, Zohydro is an opioid pain reliever that contains *hydrocodone*, which is a regulated controlled substance under the Controlled Substances Act of 1970, or CSA, and could result in harm to patients relating to its potential for abuse. In addition, a liability claim may be brought against us even if our product or product candidates merely appear to have caused an injury. Product liability claims may be brought against us by consumers, health care providers,



**Table of Contents**

pharmaceutical companies or others selling or otherwise coming into contact with our product or product candidates, among others. If we cannot successfully defend ourselves against product liability claims we will incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

the inability to commercialize our product or product candidates;

decreased demand for our product or, if approved, product candidates;

impairment of our business reputation;

product recall or withdrawal from the market;

withdrawal of clinical trial participants;

costs of related litigation;

distraction of management's attention from our primary business;

substantial monetary awards to patients or other claimants; or

loss of revenues.

We have obtained product liability insurance coverage for commercial product sales and clinical trials with a \$10 million per occurrence and a \$10 million annual aggregate coverage limit. Our insurance coverage may not be sufficient to cover all of our product liability related expenses or losses and may not cover us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost, in sufficient amounts or upon adequate terms to protect us against losses due to product liability. If we determine that it is prudent to increase our product liability coverage based on sales of Sumavel DosePro, approval of Zohydro or otherwise, we may be unable to obtain this increased product liability insurance on commercially reasonable terms or at all. Large judgments have been awarded in class action or individual lawsuits based on drugs that had unanticipated side effects, including side effects that are less severe than those of Sumavel DosePro and our product candidates. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and have a material adverse affect our business, results of operations, financial condition and prospects.

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

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

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

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

## **Table of Contents**

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

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

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

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

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

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

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

Payments to our material suppliers and contract manufactures 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 six months ended June 30, 2011, \$5.3 million (based on exchange rates as of June 30, 2011) of our materials, contract manufacturing costs and other manufacturing-related costs were denominated in foreign currencies. As a result, we are exposed to foreign exchange risk, and our results of

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**Table of Contents**

operations may be negatively impacted by fluctuations in the exchange rate between the U.S. dollar and the Euro or U.K. pound sterling. A significant appreciation in the Euro or U.K. pound sterling relative to the U.S. dollar will result in higher expenses and cause increases in our net losses. Likewise, to the extent that we generate any revenues denominated in foreign currencies, or become required to make payments in other foreign currencies, fluctuations in the exchange rate between the U.S. dollar and those foreign currencies could also negatively impact our results of operations. We currently have not entered into any foreign currency hedging contracts to reduce the effect of changes in foreign currency exchange rates, and foreign currency hedging is inherently risky and may result in unanticipated losses.

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

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

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

**Risks Related to Our Financial Position and Capital Requirements**

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

We launched our only approved product, Sumavel DosePro, in January 2010. Without a long history of sales, we may not accurately predict future sales, and we may never be able to significantly increase these sales, especially in light of our reliance on our partnership with Astellas to co-promote Sumavel DosePro. 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, and debt, and have incurred losses and negative cash flow from operations in each year since our inception. Our net loss applicable to common stockholders was \$45.6 million in 2008, \$45.9 million in 2009, \$73.6 million in 2010 and \$38.2 million for the six months ended June 30, 2011, and our cash used in operating activities was \$41.3 million in 2008, \$32.4 million in 2009, \$72.0 million in 2010 and \$40.5 million for the six months ended June 30, 2011. As of June 30, 2011, we had an accumulated deficit of \$236.3 million. These losses and negative cash flow from operations have had a material adverse effect on our stockholders' equity and working capital. Further, despite the revenues from Sumavel DosePro, we expect our losses to continue for at least the next several years as a result of the development expenses incurred in connection with our ongoing clinical development for Zohydro, the initiation of clinical development for Relday and the cost of the sales and marketing expense associated with Sumavel DosePro. In addition, if we obtain regulatory approval for Zohydro or any of our other product candidates, we expect to incur significant sales, marketing and manufacturing expenses as well as continued development expenses. As a result, we are and will remain dependent upon external sources of financing to finance our business and the development and commercialization of our approved product and product candidates. We cannot assure you 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

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**Table of Contents**

in our cash resources could require that we delay or abandon certain development and commercialization activities and could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

**Our independent registered public accounting firm has expressed substantial doubt as to our ability to continue as a going concern.**

In its report accompanying our audited consolidated financial statements for the year ended December 31, 2010, our independent registered public accounting firm included an explanatory paragraph stating that our recurring losses from operations and lack of sufficient working capital raise substantial doubt as to our ability to continue as a going concern. A going concern 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 will depend, 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 may have to liquidate our assets and may receive less than the value at which those assets are carried on our consolidated financial statements, and it is likely that investors will lose all or a part of their investment. In addition, our amended Oxford/SVB loan agreement includes a covenant that the audit reports accompanying our annual consolidated financial statements for fiscal year 2010 and thereafter not include a going concern qualification and any breach of that covenant would permit the lenders to demand immediate repayment of all loans outstanding under the agreement and to seize and sell the collateral pledged to secure these loans. In March 2011, we obtained a waiver from Oxford and SVB for the breach caused by the receipt of the 2010 audit report from our independent registered public accounting firm which included a going concern qualification.

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

As of June 30, 2011, the principal amount of our total indebtedness was approximately \$28.7 million. In July 2011, we completed the royalty financing transaction with Cowen Royalty, which increased our total indebtedness by an additional \$30.0 million. We have and expect to continue to make borrowings under our \$10.0 million revolving credit facility to fund working capital and other cash needs and we may incur substantial additional indebtedness in the future, both under our \$10.0 million revolving credit facility and any other debt facilities we may enter into in the future. Our outstanding debt and related debt service obligations could have important adverse consequences to us, including:

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

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

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

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

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

If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay product development, sales and marketing, capital and other expenditures, sell assets,

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**Table of Contents**

seek additional capital or restructure or refinance our indebtedness. These alternative measures may not be successful and may not permit us to meet our scheduled debt service obligations. This risk is increased by the fact that borrowings under our credit facility with Oxford and SVB bear interest at a variable rates, exposing us to the risk that the amount of cash required to pay interest will increase to the extent that market interest rates increase.

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

Our amended Oxford/SVB loan agreement includes covenants requiring, among other things, that (1) we achieve, as of the last day of each month, measured on a trailing three-month basis, actual revenues of at least a specified percentage of our projected revenue as provided to Oxford and SVB in the event we fail to maintain a liquidity ratio (defined, in general, as the ratio of (a) cash and cash equivalents deposited with SVB plus unused borrowing capacity under that agreement to (b) all debt, capital lease obligations and contingent obligations owed to the lenders) of 1.25 to 1.00, and (2) the audit report accompanying our year-end consolidated financial statements for fiscal year 2010 and thereafter not include a going concern qualification. As discussed above, the audit report from our independent registered public accounting firm accompanying our 2010 consolidated financial statements includes a going concern qualification and, as a result, our results of operations and financial condition will have to improve to a point where our auditors can deliver their audit report without this qualification in order to avoid a future breach of this covenant. In addition to certain other customary restrictive covenants, the amended Oxford/SVB loan agreement prohibits us, subject to certain customary exceptions, from (1) incurring any debt other than, among other things, debt under the amended loan agreement and other debt permitted thereunder, (2) entering into sale and leaseback transactions, (3) having a change in our management such that our Chief Executive Officer, Chief Financial Officer or President resigns, is terminated or is no longer actively involved in our management in his or her current position and is not replaced with a person acceptable to our board of directors within 120 days, (4) entering into mergers with, or acquisitions of all or substantially all the assets of, another entity with a value in excess of \$100,000 or a change in control of our company (as defined in the amended Oxford/SVB loan agreement), (5) permitting liens to exist on our properties and (6) making distributions and investments. The amended Oxford/SVB loan agreement provides that an event of default will occur if, among other customary events of default, (1) there is a material adverse change in our business, operations or condition (financial or otherwise) or material impairment in the prospects of us repaying any portion of our obligations under the agreement, (2) there is a material impairment in the value of the collateral pledged to secure our obligations under the agreement or in the perfection or priority of such collateral, (3) we default in the payment of any amount payable under the agreement when due, or (4) we breach any covenant in the agreement (subject to a grace period in some cases). In 2009, 2010 and 2011, we were required to obtain amendments or waivers under our credit facilities, and we may in the future need to obtain waivers or amendments under our credit facilities or other debt instruments, in order to avoid a breach or default, particularly if our business deteriorates or does not perform in accordance with our expectations. Our amended Oxford/SVB loan agreement is secured by substantially all of our personal property (including, among other things, accounts receivable, equipment, inventory, contract rights or rights to payment of money, license agreements, general intangibles, including all intellectual property, and cash).

In connection with the Cowen Royalty transaction, we paid off all outstanding amounts under our prior loan and security agreement with GE Capital and terminated that agreement.

Pursuant to the terms of our \$30.0 million royalty financing agreement with Cowen Royalty, or the Cowen Royalty financing agreement, we are required to make payments to Cowen Royalty of \$10.0 million on each of January 31, 2015, 2016 and 2017, as well as fixed percentages of amounts received or recorded from our products sales.

Our obligations under the Cowen Royalty financing agreement are secured under a security agreement by a second priority security interest (junior to the security interest of Oxford and SVB under the amended

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**Table of Contents**

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

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

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

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

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

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

Our results of operations and liquidity could be materially negatively affected by economic conditions generally, both in the United States and elsewhere around the world. Domestic and international equity and debt markets have experienced and may continue to experience heightened volatility and turmoil based on domestic and international economic conditions and concerns. In the event these economic conditions and concerns continue or worsen and the markets continue to remain volatile, our results of operations and liquidity could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary, and our stock price may decline. In addition, we maintain significant amounts of cash and cash

## **Table of Contents**

equivalents at one or more financial institutions that are not federally insured. If economic instability continues, we cannot provide assurance that we will not experience losses on these investments.

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

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

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

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

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

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



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## **Table of Contents**

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

### ***Risks Related to Regulation of our Product and Product Candidates***

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

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

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

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

impose restrictions on the marketing or manufacturing of the product, suspend or withdraw product approvals or revoke necessary licenses;

issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;

commence criminal investigations and prosecutions;

impose injunctions, suspensions or revocations of necessary approvals or other licenses;

impose fines or other civil or criminal penalties;



**Table of Contents**

suspend any ongoing clinical trials;

deny or reduce quota allotments for the raw material for commercial production of our controlled substance products;

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

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

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

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

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

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

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

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

regulatory authorities may withdraw their approval of the product;

regulatory authorities may require us to recall product;

regulatory authorities may require the addition of warnings in the product label or narrowing of the indication in the product label;

we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;

we may be required to change the way the product is administered or modify the product in some other way;

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the FDA may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety or efficacy of the product;

we could be sued and held liable for harm caused to patients; and

our reputation may suffer.

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

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## **Table of Contents**

While the adverse reaction profile for Zohydro has not yet been fully characterized, in one completed Phase 3 study and two completed Phase 2 studies of Zohydro, patients experienced mild to moderate adverse events, such as constipation, nausea, urinary tract infection, vomiting, headache, dizziness, sweating and drowsiness, which are similar to the reported effects of opioids currently prescribed for chronic pain. We are continuing to assess the safety of Zohydro in our pending Phase 3 safety trial (Study 802).

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

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

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

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

Zohydro 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, because it is a single-entity *hydrocodone* product, is expected to be regulated by the DEA as a Schedule II controlled substance under the CSA. All Schedule II substance prescriptions, such as prescriptions for Zohydro, must be in writing and signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription.

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

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**Table of Contents**

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

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

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

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

**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 clinical development of Zohydro as well as the production or sale of Zohydro even if we obtain FDA approval.**

The DEA limits the availability and production of all Schedule II substances through a quota system which includes a national aggregate quota and individual quotas. Because *hydrocodone* is subject to the DEA's production and procurement quota scheme, the DEA establishes annually an aggregate quota for how much *hydrocodone* may be produced in total in the United States based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. This limited aggregate amount of *hydrocodone* that the DEA allows to be produced in the United States each year is allocated among individual companies, who must submit applications annually to the DEA for individual production and procurement quotas. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments. Elan, which has licensed us the right to sell Zohydro in the United States, if approved, was allocated a sufficient quantity of *hydrocodone* to meet our planned clinical and pre-clinical needs during 2011. However, in future years, we may need greater amounts of *hydrocodone* to sustain and complete our development program for Zohydro, and we will need significantly greater amounts of *hydrocodone* to implement our commercialization plans if the FDA approves Zohydro.

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

**Table of Contents**

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

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

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

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

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

Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed in these Risk Factors and elsewhere in this prospectus regarding

## **Table of Contents**

FDA approval in the United States. As described above, such effects include the risks that our product and product candidates may not be approved at all or for all requested indications, which could limit the uses of our product and product candidates and have an adverse effect on their commercial potential or require costly, post-marketing studies. In addition, we, Desitin, or any potential partner may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution if we fail to comply with applicable foreign regulatory requirements.

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

In the United States, there have been a number of legislative and regulatory changes to the healthcare system in ways that could affect our future results of operations and the future results of operations of our potential customers. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established 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 or any of our product candidates that are approved by the FDA are not widely included on the formularies of these plans, our ability to market our products to the Medicare population could suffer.

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

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

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

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

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

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

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

new requirements to report certain financial arrangements with physicians and others, including reporting any transfer of value made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their



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immediate family members during each calendar year beginning in 2012, with reporting starting in 2013;

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**Table of Contents**

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

a licensure framework for follow-on biologic products;

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

creation of the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and

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

Many of the details regarding the implementation of the PPACA are yet to be determined, and at this time, it remains unclear the full effect that the PPACA would have on our business.

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

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

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

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

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**Table of Contents**

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

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

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

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

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

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

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

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

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

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

## **Table of Contents**

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

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

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

### **Risks Related to Intellectual Property**

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

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

We in-license certain intellectual property for Zohydro from Elan, 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 Elan and Durect, we cannot be certain that such activities by Elan 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. Elan 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 Elan 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 Elan. 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 Elan 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.

## **Table of Contents**

Most of our patents related to DosePro were acquired from Aradigm, who acquired those patents from a predecessor owner. Our patents related to Zohydro are licensed from Elan. 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 licensor 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 Elan 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:

others may be able to make or use compounds that are similar to the pharmaceutical compounds used in Sumavel DosePro and our product candidates but that are not covered by the claims of our patents;

the APIs in Sumavel DosePro and our current product candidates are, or will soon become, commercially available in generic drug products, and no patent protection will be available without regard to formulation or method of use;

we or our licensors, as the case may be, may not be able to detect infringement against our in-licensed patents, which may be especially difficult for manufacturing processes or formulation patents;

we or our licensors, as the case may be, might not have been the first to make the inventions covered by our owned or in-licensed issued patents or pending patent applications;

we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;

others may independently develop similar or alternative technologies or duplicate any of our technologies;

it is possible that our pending patent applications will not result in issued patents;



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**Table of Contents**

it is possible that there are dominating patents to Sumavel DosePro or our product candidates of which we are not aware;

it is possible that there are prior public disclosures that could invalidate our or our licensors' inventions, as the case may be, or parts of our or their inventions of which we or they are not aware;

it is possible that others may circumvent our owned or in-licensed patents;

it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;

the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;

the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our device or product candidates;

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

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

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

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

If any of our owned or in-licensed patents are found to be invalid or unenforceable, or if we are otherwise unable to adequately protect our rights, it could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Likewise, our patents covering certain technology used in our DosePro device are expected to expire on various dates from 2014 through 2026 and the patents licensed to us by Elan are expected to expire in 2019. As of August 16, 2011, our patent portfolio included eight issued U.S. patents, three pending U.S. patent applications, 38 issued foreign patents and three pending foreign patent applications relating to various aspects of Sumavel DosePro and our DosePro technology. Five 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 and 7,901,385, are expected to expire in 2014, 2016, 2017, 2026 and 2026, 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 Number 7,776,007 covers the cap and latch mechanism; and U.S. Patent No. 7,901,385 covers a casing for enclosing the injection devices. Upon the expiration of these patents, we will lose the right to exclude others from practicing these inventions. Additionally, since these five patents are the only patents currently listed in the FDA Orange Book for Sumavel DosePro, their expiration will mean that we lose certain advantages that come with Orange Book listing of patents. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects. Moreover, if Elan 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

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right to initiate proceedings after receiving their notice. Such proceedings will require the assistance of Elan or Durect, as applicable, and we have limited control over the amount or timing of resources Elan or Durect devotes on our behalf or the priority they place on enforcing these patent rights.



## **Table of Contents**

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

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

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

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

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

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

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**Table of Contents**

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

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

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

## **Table of Contents**

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.

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

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

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

Periodic maintenance fees on our owned and in-licensed patents are due to be paid to the PTO in several stages over the lifetime of the patents. Future maintenance fees will also need to be paid on other patents which may be issued to us. We have systems in place to remind us to pay these fees, and we employ outside firms to remind us or our in-licensor to pay annuity fees due to foreign patent agencies on our pending foreign patent applications. The PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business. For the patents and patent applications related to Zohydro, Elan is obligated to maintain our in-licensed patents in the United States under our license agreement. Should Elan fail to pursue maintenance of our licensed patents and patent applications, Elan 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



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**Table of Contents**

commercially reasonable efforts, under our license agreement. Should Durect fail to pursue maintenance of certain of those licensed patents and patent applications, Durect is obligated to notify us and, at that time, we will be granted an opportunity to maintain the prosecution and avoid withdrawal, cancellation, expiration or abandonment of those licensed patents and applications.

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

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

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

**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 from time to time 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 this quarter ended June 30, 2011, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price of \$3.54 to a high sale price of \$5.14. 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 Astellas commercial progress in promoting and selling Sumavel DosePro, including sales and revenue trends, and any amendment, termination or restructuring of our agreement with Astellas;

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

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

**Table of Contents**

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

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

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

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

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

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

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

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

actual and anticipated fluctuations in our quarterly operating results;

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

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

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

additions or departures of key personnel;

third-party payor coverage and reimbursement policies;

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

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

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

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

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

changes in accounting principles; and

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

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 elsewhere in this prospectus could have a dramatic and material adverse impact on the market price of our common stock.

## **Table of Contents**

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

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

### **If you purchase shares of our common stock sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares.**

The offering price of our common stock in this offering is considerably more than the net tangible book value (deficit) per share of our outstanding common stock. Investors purchasing shares of common stock in this offering will pay a price that substantially exceeds the value of our tangible assets after subtracting liabilities. Assuming a public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, and giving pro forma effect to the borrowing of \$30.0 million in July 2011 under our financing agreement with Cowen Royalty and receipt of \$1.5 million from the sale and issuance of 388,601 shares of common stock to Cowen Royalty in connection with such financing as if they had occurred as of June 30, 2011, these investors will incur immediate pro forma as adjusted dilution of \$2.70 per share.

For additional information on how the foregoing amounts were calculated, see Dilution. To the extent outstanding stock options or warrants are exercised, there may be further dilution to new investors.

Because we may need to raise additional capital to fund our commercialization efforts and clinical development programs, among other things, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock. These future issuances of common stock or common stock-related securities, together with the exercise of outstanding options and warrants and any additional shares issued in connection with acquisitions, if any, may result in further dilution to investors. See the Dilution section in this prospectus.

### **We may invest or spend our cash, including the net proceeds of this offering, in ways with which you may not agree or in ways which may not yield a significant return.**

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

### **Our quarterly operating results may fluctuate significantly.**

Our quarterly operating results are difficult to predict and may fluctuate significantly from period to period, particularly because the commercial success of, and demand for, Sumavel DosePro, as well as the success and costs of our Zohydro, 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 our distributors' inventory management practices and buying patterns and the performance of Astellas or, if applicable, the amendment, termination or restructuring of our co-promotion agreement with Astellas;



**Table of Contents**

the level of underlying demand for Sumavel DosePro or any of our other product candidates that may receive regulatory approval;

our ability to control production spending and underutilization of production capacity;

variations in the level of development expenses related to Zohydro, Relday or other development programs;

results of clinical trials for Zohydro and Relday;

any intellectual property infringement lawsuit in which we may become involved;

regulatory developments and legislative changes, including healthcare reform, affecting our product and product candidates or those of our competitors; and

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

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

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

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations as well as a broad range of other factors, including the realization of any of the risks described in these Risk Factors, may cause the market price of our common stock to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies generally experience significant stock price volatility. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business. Any adverse determination in any such litigation or any amounts paid to settle any such actual or threatened litigation could require that we make significant payments.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. As of July 31, 2011, we had research coverage by only four securities analysts. If these securities analysts cease coverage of our company, the trading price for our stock would be negatively impacted. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

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

Immediately following this offering and assuming that Roger L. Hawley, our Chief Executive Officer, and Ann D. Rhoads, our Chief Financial Officer, each purchase all of the \$100,000 of shares of our common stock in this offering that they have indicated an interest in purchasing as described elsewhere in this prospectus, our executive officers and directors and their affiliates will together control approximately 44.7% of our outstanding common stock. Four of our non-employee directors are, or are representatives designated by, significant stockholders and two of our directors are executive officers. As a result, these stockholders will collectively be able to significantly influence and may be able to control all

matters requiring approval of our stockholders, including the election of directors and approval of significant corporate

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**Table of Contents**

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 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 July 31, 2011, we had 34,473,278 shares of common stock outstanding. Of these shares, approximately 14,520,875 were freely tradable, without restriction, in the public market.

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

Certain holders of shares of our common stock, warrants to purchase our common stock and the shares of common stock issuable upon exercise of those warrants are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by our affiliates. In addition, our directors and executive officers may establish programmed selling plans under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for the purpose of effecting sales of our common stock. Any sales of securities by these stockholders, or the perception that those sales may occur, including the entry into such programmed selling plans, could have a material adverse effect on the trading price of our common stock.

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

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

a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;

a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;

**Table of Contents**

a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by a majority of the total number of authorized directors;

advance notice requirements for stockholder proposals and nominations for election to our board of directors;

a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than 66 <sup>2</sup>/<sub>3</sub>% of all outstanding shares of our voting stock then entitled to vote in the election of directors;

a requirement of approval of not less than 66 <sup>2</sup>/<sub>3</sub>% of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and

the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

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

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

The continued operation and expansion of our business will require substantial funding. Investors seeking cash dividends in the foreseeable future should not purchase our common stock. We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our available cash to fund the development and growth of our business. Any determination to pay dividends in the future will be at the discretion of our board of directors and will depend upon results of operations, financial condition, contractual restrictions, restrictions imposed by applicable law and other factors our board of directors deems relevant. In addition, our ability to pay cash dividends is currently prohibited by the terms of our loan and security agreements. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any return to stockholders, including investors who purchase shares in this offering, will therefore be limited to the appreciation in the market price of their stock, which may never occur.

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

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the Nasdaq Stock Market, or Nasdaq, that impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and financial condition. In addition, on

**Table of Contents**

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

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

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**Table of Contents**

**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND MARKET DATA**

This prospectus contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in the sections entitled Prospectus Summary, Risk Factors, Management's Discussion and Analysis of Financial Condition and Results of Operations and Business. In some cases, you can identify forward-looking statements by the following words: may, will, could, would, should, expect, intend, plan, anticipate, believe, estimate, predict, project, potential, negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. These forward-looking statements include, but are not limited to, statements about:

our ability to maintain and increase market demand for, and sales of, Sumavel DosePro;

our and Astellas Pharma US, Inc.'s ability to successfully execute our sales and marketing strategy for the commercialization of Sumavel DosePro;

the progress and timing of clinical trials for Zohydro and our other product candidates;

the potential for, and timing of, an NDA submission to the FDA for Zohydro;

the timing of submissions to, and decisions made by, the FDA and other regulatory agencies, including foreign regulatory agencies, and demonstrating the safety and efficacy of Zohydro or any other product candidates to the satisfaction of the FDA and such other agencies;

adverse side effects or inadequate therapeutic efficacy of Sumavel DosePro that could result in product recalls, market withdrawals or product liability claims;

the safety and efficacy of our Zohydro and our product candidates;

the market potential for migraine treatments, and our ability to compete within that market;

the goals of our development activities and estimates of the potential markets for our product candidates;

estimates of the capacity of manufacturing and other facilities to support our product and product candidates;

the net proceeds from this offering, together with our cash and cash equivalents as of June 30, 2011, future product revenues, borrowings available under our \$10.0 million revolving credit facility and the net proceeds from our recently completed equity and royalty financing with Cowen Royalty Healthcare Partners II, L.P. will be sufficient to fund our operations into the third quarter of 2012 and to enable us to complete our submission of the NDA for Zohydro and complete our submission of the IND for Relday with the FDA;

our ability to ensure adequate and continued supply of Sumavel DosePro to successfully meet anticipated market demand;

the amount of our estimated third party research and development costs for Zohydro remaining through our NDA filing with the FDA;

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

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

**Table of Contents**

the impact of healthcare reform legislation; and

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

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual results may differ materially from what we expect as expressed or implied by our forward-looking statements. In light of the significant risks and uncertainties to which our forward-looking statements are subject, you should not place undue reliance on or regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all. We discuss many of these risks and uncertainties in greater detail under the section entitled **Risk Factors** in this prospectus. These forward-looking statements represent our estimates and assumptions only as of the date of this prospectus regardless of the time of delivery of this prospectus or any sale of our common stock and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this prospectus. 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.

This prospectus also contains estimates, projections and other information concerning our industry, our business, and the markets for Sumavel DosePro, Zohydro, Relday and other drugs, including data regarding the estimated size of those markets, their projected growth rates, the incidence of certain medical conditions, statements that certain drugs, classes of drugs or dosages are the most widely prescribed in the United States or other markets, the perceptions and preferences of patients and physicians regarding certain therapies and other prescription, prescriber and patient data, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. In particular, unless otherwise specified, all prescription, prescriber and patient data in this prospectus is from Wolters Kluwer Pharma Solutions, Source<sup>®</sup> Pharmaceutical Audit Suite (PHAST) Institution/Retail, Source<sup>®</sup> PHAST Retail, Source<sup>®</sup> Prescriber or Source<sup>®</sup> Dynamic Claims. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.



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**Table of Contents**

**USE OF PROCEEDS**

We estimate that we will receive net proceeds of approximately \$37.7 million (or approximately \$43.4 million if the underwriters' option to purchase additional shares is exercised in full) from the sale of the shares of common stock offered by us in this offering, based on the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us and assuming that Cowen Healthcare Royalty Partners II, L.P., or Cowen Royalty, Roger L. Hawley, our Chief Executive Officer, and Ann D. Rhoads, our Executive Vice President and Chief Financial Officer, purchase all of the \$1.5 million, \$100,000 and \$100,000 of shares of our common stock in this offering, respectively, that they have indicated an interest in purchasing as described elsewhere in this prospectus. Each \$1.00 increase or decrease in the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, would increase or decrease, respectively, the estimated net proceeds from this offering by approximately \$11.3 million (or approximately \$13.0 million if the underwriters' option to purchase additional shares is exercised in full).

The principal purpose of this offering is to obtain additional capital to support our operations. We intend to use approximately \$17.0 million of the net proceeds from this offering to fund the cost of submitting an NDA to the FDA for U.S. regulatory approval of Zohydro, approximately \$6.0 million to fund the initial clinical development of Relday and the remainder to fund the ongoing commercialization of Sumavel DosePro and for working capital and other general corporate purposes. Although it is difficult to predict future liquidity requirements, we believe, based on our current operating plan, that the net proceeds from this offering, together with our cash and cash equivalents as of June 30, 2011, future product revenues, borrowings available under our \$10.0 million revolving credit facility and the net proceeds from the recently completed equity and royalty financing with Cowen Royalty will be sufficient to fund our operations into the third quarter of 2012 and will enable us to complete our submission of the NDA for Zohydro to the FDA and complete our submission of the IND for Relday with the FDA, although we cannot assure you that this will occur. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses or products; however, we have no current commitments or obligations to do so.

The amounts and timing of our actual expenditures will depend on numerous factors, including the commercial success of Sumavel DosePro and the progress of our clinical trials and other development and commercialization efforts, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

**Table of Contents****PRICE RANGE OF COMMON STOCK**

Our common stock has been traded on the Nasdaq Global Market under the symbol ZGNX since November 23, 2010. The following table sets forth for the period indicated the high and low sale price of our common stock, as reported by the Nasdaq Global Market.

	<b>Market Price Range</b>	
	<b>High</b>	<b>Low</b>
Quarter Ending September 30, 2011 (through September 2, 2011)	\$ 5.11	\$ 3.10
Quarter Ended June 30, 2011	\$ 5.14	\$ 3.54
Quarter Ended March 31, 2011	\$ 6.90	\$ 3.50
Quarter Ended December 31, 2010 (beginning November 23, 2010)	\$ 6.50	\$ 3.80

On September 2, 2011, the last reported sale price of our common stock on the Nasdaq Global Market was \$3.39. As of July 31, 2011, there were 48 holders of record of our common stock.

**DIVIDEND POLICY**

We have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. We expect to retain available cash to finance ongoing operations and the potential growth of our business. Any future determination to pay dividends on our common stock will be at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant. In addition, unless waived, the terms of our amended and restated loan and security agreement with Oxford Finance LLC and Silicon Valley Bank prohibit us from paying cash dividends and, subject to limited exceptions, other dividends on our common stock.

**Table of Contents****CAPITALIZATION**

The following table sets forth our cash and cash equivalents and capitalization as of June 30, 2011:

on an actual basis;

on a pro forma basis to give effect to the borrowing of \$30.0 million in July 2011 under our financing agreement with Cowen Healthcare Royalty Partners II, L.P., or Cowen Royalty, and receipt of \$1.5 million from the sale and issuance of 388,601 shares of common stock to Cowen Royalty in connection with such financing, resulting in aggregate net proceeds of \$29.5 million, as if such transactions had occurred as of June 30, 2011; and

on a pro forma as adjusted basis to give effect to the transactions described in the immediately preceding bullet point and our proposed sale of 12,000,000 shares of common stock in this offering and our receipt of the estimated net proceeds therefrom, based on the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us, and assuming that Cowen Royalty, Roger L. Hawley, our Chief Executive Officer, and Ann D. Rhoads, our Executive Vice President and Chief Financial Officer, purchase all of the \$1.5 million, \$100,000 and \$100,000 of shares of our common stock in this offering, respectively, that they have indicated an interest in purchasing as described elsewhere in this prospectus, as if such transactions had occurred as of June 30, 2011.

You should read this table together with Management's Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and the related notes appearing elsewhere in this prospectus.

	As of June 30, 2011		Pro Forma As Adjusted
	Actual	Pro Forma (In Thousands Except Per Share Amounts)	
Cash and cash equivalents	\$ 7,672	\$ 37,172	\$ 74,872
Long-term debt, less current portion	19,547	47,547	47,547
Stockholders' equity (deficit)			
Preferred stock, \$0.001 par value; actual, pro forma and pro forma as adjusted 10,000 shares authorized, no shares issued or outstanding	0	0	0
Common stock, \$0.001 par value; actual 100,000 shares authorized, 34,022 shares issued and outstanding; pro forma 100,000 shares authorized, 34,410 shares issued and outstanding; pro forma as adjusted 100,000 shares authorized, 46,410 shares issued and outstanding	34	34	46
Additional paid-in capital	229,087	230,587	268,275
Accumulated deficit	(236,263)	(236,263)	(236,263)
Total stockholders' equity (deficit)	(7,142)	(5,642)	32,058
Total capitalization	\$ 12,405	\$ 41,905	\$ 79,605

(1)

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Each \$1.00 increase or decrease in the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, would increase or decrease, respectively, the amount of pro forma as adjusted cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately \$11.3 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

**Table of Contents**

The number of shares of common stock shown as issued and outstanding in the prior table excludes:

283,271 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2011, at a weighted average exercise price of \$10.26 per share;

225,000 shares of common stock issuable upon the exercise of warrants issued after June 30, 2011, at a weighted average exercise price of \$9.00 per share;

3,388,992 shares of common stock issuable upon the exercise of options and restricted stock units outstanding as of June 30, 2011, at a weighted average exercise price of \$4.01 per share; and

2,056,065 additional shares of common stock reserved for future issuance under our 2010 equity incentive award plan, or 2010 Plan, and our 2010 employee stock purchase plan, or Purchase Plan, as of June 30, 2011, plus any annual increases in the number of shares of common stock reserved for future issuance under the 2010 Plan and the Purchase Plan pursuant to evergreen provisions and any other shares that may become issuable under the 2010 Plan or the Purchase Plan pursuant to their terms, as more fully described in Compensation Discussion and Analysis Employee Equity Incentive Plans.

**Table of Contents****DILUTION**

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock upon the completion of this offering.

As of June 30, 2011, our historical net tangible book value (deficit) of our common stock was approximately \$(7.1) million, or approximately \$(0.21) per share, based on 34,021,708 shares of our common stock outstanding at June 30, 2011. Our historical net tangible book value (deficit) per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of shares of our common stock outstanding as of June 30, 2011.

On a pro forma basis as of June 30, 2011, after giving effect to the borrowing of \$30.0 million in July 2011 under our financing agreement with Cowen Healthcare Royalty Partners II, L.P., or Cowen Royalty, and receipt of \$1.5 million from the sale and issuance of 388,601 shares of common stock to Cowen Royalty in connection with such financing, resulting in aggregate net proceeds of \$29.5 million, the pro forma net tangible book value (deficit) of our common stock would have been approximately \$(5.6) million, or approximately \$(0.16) per share of our pro forma outstanding common stock.

Investors participating in this offering will incur immediate, substantial dilution. After giving effect to (1) the sale of 12,000,000 shares of common stock in this offering at the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us and assuming that Cowen Royalty, Roger L. Hawley, our Chief Executive Officer, and Ann D. Rhoads, our Executive Vice President and Chief Financial Officer, purchase all of the \$1.5 million, \$100,000 and \$100,000 of shares of our common stock in this offering, respectively, that they have indicated an interest in purchasing as described elsewhere in this prospectus, and (2) the pro forma transactions described in the preceding paragraph, our pro forma as adjusted net tangible book value of our common stock as of June 30, 2011 would have been approximately \$32.1 million, or approximately \$0.69 per share of our pro forma as adjusted outstanding common stock. This represents an immediate increase in pro forma as adjusted net tangible book value of \$0.85 per share to our existing stockholders and an immediate dilution in the pro forma as adjusted net tangible book value of \$2.70 per share to investors participating in this offering. The following table illustrates this per share dilution:

Public offering price per share	\$ 3.39
Historical net tangible book value (deficit) per share as of June 30, 2011	\$ (0.21)
Pro forma increase (decrease) in net tangible book value per share attributable to pro forma transactions described above	0.05
Pro forma net tangible book value (deficit) per share before this offering	(0.16)
Increase in pro forma net tangible book value per share attributable to investors participating in this offering	0.85
Pro forma as adjusted net tangible book value per share after this offering	\$ 0.69
Pro forma as adjusted dilution per share to investors in this offering	\$ 2.70

Each \$1.00 increase or decrease in the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, would increase or decrease,

**Table of Contents**

respectively, our pro forma as adjusted net tangible book value after this offering by approximately \$11.3 million, our pro forma as adjusted net tangible book value per share after this offering by approximately \$0.24 per share, the increase in pro forma as adjusted net tangible book value per share to our existing stockholders by approximately \$0.18 per share and the pro forma as adjusted dilution to investors in this offering by approximately \$0.06 per share, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

If the underwriters fully exercise their option to purchase 1,800,000 additional shares of common stock in the offering, our pro forma as adjusted net tangible book value after this offering, calculated in the manner set forth above, would be approximately \$37.8 million, our pro forma as adjusted net tangible book value per share after this offering would be \$0.78 per share, the increase in our pro forma as adjusted net tangible book value per share attributable to investors participating in this offering would be \$0.94 per share and the pro forma as adjusted dilution per share to new investors in this offering would be \$2.61 per share.

The following table summarizes, on the pro forma as adjusted basis described above, as of June 30, 2011, the differences between the number of shares of common stock purchased from us, the total effective cash consideration paid to us and the average price per share paid to us by our existing stockholders and by investors participating in this offering based on the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, before deducting estimated underwriting discounts and commissions and estimated offering costs payable by us, as if those transactions had occurred as of June 30, 2011:

	Shares Purchased		Total Consideration		Average Price
	Number	Percent	Amount	Percent	Per Share
Existing stockholders before this offering	34,410,309	74.1%	\$ 224,820,857	84.7%	\$ 6.53
Investors participating in this offering	12,000,000	25.9	40,680,000	15.3	3.39
<b>Total</b>	<b>46,410,309</b>	<b>100.0%</b>	<b>\$ 265,500,857</b>	<b>100.0%</b>	<b>5.72</b>

Each \$1.00 increase or decrease in the assumed public offering price of \$3.39 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 2, 2011, would increase or decrease, respectively, the total consideration paid by investors participating in this offering by \$12,000,000.

If the underwriters fully exercise their option to purchase 1,800,000 additional shares of common stock in this offering, our existing stockholders would own 71.4% and our new investors would own 28.6% of the total number of shares of our common stock outstanding upon completion of this offering, calculated in the manner set forth above, and our existing stockholders would have paid \$224,820,857 and our new investors would have paid \$46,782,000 of the total consideration paid for shares of our common stock outstanding upon completion of this offering.

For purposes of all of the data in this section, the number of shares of common stock to be outstanding after this offering excludes:

283,271 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2011, at a weighted average exercise price of \$10.26 per share;

225,000 shares of common stock issuable upon the exercise of warrants issued after June 30, 2011, at a weighted average exercise price of \$9.00 per share;

3,388,992 shares of common stock issuable upon the exercise of options and restricted stock units outstanding as of June 30, 2011, at a weighted average exercise price of \$4.01 per share; and

2,056,065 additional shares of common stock reserved for future issuance under our 2010 equity incentive award plan, or 2010 Plan, and our 2010 employee stock purchase plan, or Purchase Plan, as





**Table of Contents**

of June 30, 2011, plus any annual increases in the number of shares of common stock reserved for future issuance under the 2010 Plan and the Purchase Plan pursuant to evergreen provisions and any other shares that may become issuable under the 2010 Plan or the Purchase Plan pursuant to their terms, as more fully described in Compensation Discussion and Analysis Employee Equity Incentive Plans.

To the extent that outstanding exercisable options or warrants are exercised, you may experience further dilution. If all in-the-money outstanding exercisable options and warrants were exercised, our pro forma as adjusted net tangible book value (deficit) as of June 30, 2011 (calculated on the basis of the assumptions set forth above) would have been approximately \$33.0 million, or approximately \$0.70 per share, causing immediate pro forma as adjusted dilution of \$2.69 per share to investors participating in this offering.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital by issuing equity securities or convertible debt, your ownership will be further diluted.

**Table of Contents****SELECTED FINANCIAL DATA**

The following table summarizes certain of our selected financial data. The selected financial data for the years ended December 31, 2010, 2009, 2008 and 2007 and the period from inception (August 25, 2006) through December 31, 2006 have been derived from our audited financial statements, of which the 2010, 2009 and 2008 financial statements are included elsewhere in this prospectus. The selected financial data for the six months ended June 30, 2011 and 2010 and the balance sheet data as of June 30, 2011 have been derived from our unaudited interim financial statements which are included elsewhere in this prospectus. The unaudited interim financial statements have been prepared on the same basis as the audited financial statements and reflect all adjustments, consisting primarily of normal recurring adjustments, that, in the opinion of our management, are necessary to fairly present our financial position as of June 30, 2011 and results of operations for the six months ended June 30, 2011 and 2010. Our historical results and financial condition are not necessarily indicative of the results or financial condition that may be expected in the future. The selected financial data set forth below should be read together with our financial statements and related notes and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this prospectus.

	Six Months Ended June 30,		Year Ended December 31,				Inception (August 25, 2006) through December 31, 2006
	2011	2010	2010	2009	2008	2007	
(In Thousands, Except Per Share Amounts)							
<b>Statement of Operations Data</b>							
<b>Revenue:</b>							
Net product revenue	\$ 16,151	\$ 6,118	\$ 19,069	\$ 0	\$ 0	\$ 0	\$ 0
Contract revenue	3,126	1,461	4,373	0	0	0	0
<b>Total revenue</b>	<b>19,277</b>	<b>7,579</b>	<b>23,442</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>Operating expenses:</b>							
Cost of sales	8,850	5,302	12,846	0	0	0	0
Royalty expense	630	382	843	0	0	0	0
Research and development	17,406	11,389	28,643	21,438	33,910	24,329	4,902
Selling, general and administrative	27,940	25,422	51,270	14,102	11,820	4,725	1,474
<b>Total operating expenses</b>	<b>54,826</b>	<b>42,495</b>	<b>93,602</b>	<b>35,540</b>	<b>45,730</b>	<b>29,054</b>	<b>6,376</b>
<b>Loss from operations</b>	<b>(35,549)</b>	<b>(34,916)</b>	<b>(70,160)</b>	<b>(35,540)</b>	<b>(45,730)</b>	<b>(29,054)</b>	<b>(6,376)</b>
<b>Other income (expense):</b>							
Interest income	19	3	5	10	696	927	395
Interest expense	(2,515)	(1,511)	(10,013)	(9,188)	(1,718)	(377)	0
Change in fair value of warrant liability	0	(13,020)	6,725	(755)	1,119	(107)	0
Other financing income	0	0	0	0	0	906	582
Other income (expense)	(103)	139	(111)	(416)	63	25	0
<b>Total other income (expense)</b>	<b>(2,599)</b>	<b>(14,389)</b>	<b>(3,394)</b>	<b>(10,349)</b>	<b>160</b>	<b>1,374</b>	<b>977</b>
<b>Net loss before income taxes</b>	<b>(38,148)</b>	<b>(49,305)</b>	<b>(73,554)</b>	<b>(45,889)</b>	<b>(45,570)</b>	<b>(27,680)</b>	<b>(5,399)</b>
Provision for income taxes	(13)	0	(10)	0	0	0	0
<b>Net loss</b>	<b>\$ (38,161)</b>	<b>\$ (49,305)</b>	<b>\$ (73,564)</b>	<b>\$ (45,889)</b>	<b>\$ (45,570)</b>	<b>\$ (27,680)</b>	<b>\$ (5,399)</b>
<b>Deemed dividend for the beneficial conversion on Series A-1 and Series A-2 convertible preferred stock</b>							
	0	0	0	0	0	(18,360)	0

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<b>Net loss attributable to common stockholders</b>	\$ (38,161)	\$ (49,305)	\$ (73,564)	\$ (45,889)	\$ (45,570)	\$ (46,040)	\$ (5,399)
Net loss per share, basic and diluted	\$ (1.12)	\$ (37.44)	\$ (17.63)	\$ (40.97)	\$ (52.68)	\$ (80.77)	\$ (13.60)
Weighted-average shares outstanding, basic and diluted	34,015	1,317	4,173	1,120	865	570	397

**Table of Contents**

	As of June 30, 2011	2010	As of December 31, 2009      2008      2007      2006 (In Thousands)			
<b>Balance Sheet Data:</b>						
Cash and cash equivalents and investment securities, available for sale	\$ 7,672	\$ 49,172	\$ 44,911	\$ 14,225	\$ 43,255	\$ 22,103
Working capital (deficit)	(61)	38,626	42,102	3,032	38,836	20,035
Total assets	51,393	94,268	74,568	27,625	53,007	26,942
Long-term debt, less current portion	19,547	19,934	8,778	15,336	2,870	0
Convertible preferred stock warrant liability	0	0	5,041	467	259	0
Convertible preferred stock	0	0	149,312	76,955	76,955	27,110
Accumulated deficit	(236,263)	(198,102)	(124,538)	(78,649)	(33,079)	(5,399)
Total stockholders' equity (deficit)	(7,142)	28,734	(122,300)	(77,534)	(32,926)	(5,385)

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**Table of Contents**

**MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL  
CONDITION AND RESULTS OF OPERATIONS**

*The following discussion and analysis of our financial condition and results of operations should be read in conjunction with Selected Financial Data and our financial statements and related notes appearing elsewhere in this prospectus. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including, but not limited, to those set forth under Risk Factors and elsewhere in this prospectus.*

**Overview**

*Background*

We are a pharmaceutical company commercializing and developing products for the treatment of central nervous system disorders and pain. Our first commercial product, Sumavel DosePro (*sumatriptan* injection) Needle-free Delivery System, 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. 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. Our sales and marketing organization is comprised of approximately 100 professionals. Our field sales force of approximately 80 representatives is promoting Sumavel DosePro primarily to neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. To build upon our success in growing Sumavel DosePro prescriptions, we have initiated activities to expand our sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. Our promotional efforts are complemented by our collaboration with Astellas and approximately 400 of its sales representatives, who are promoting Sumavel DosePro primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists in the United States, or the Astellas Segment. Our lead product candidate, Zohydro (formerly ZX002), is a novel, oral, single-entity extended-release formulation of *hydrocodone* currently in Phase 3 development for the treatment of moderate to severe chronic pain in patients requiring around-the-clock opioid therapy. We reported positive top-line results from our pivotal Phase 3 efficacy trial for Zohydro in August 2011 and expect to submit a New Drug Application, or NDA, with the U.S. Food and Drug Administration, or FDA, by early 2012. We in-licensed exclusive U.S. rights to Zohydro from Elan Pharma International Limited, or Elan, in 2007.

In July 2011, we entered into a development and license agreement with Durect Corporation, or the Relday license agreement, pursuant to which we will be responsible for the clinical development and commercialization of Relday, a proprietary, long-acting injectable formulation of risperidone using Durect's SABER controlled-release formulation technology in combination with our DosePro needle-free, subcutaneous drug delivery system. Risperidone is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. Relday will be developed to address unmet clinical needs in this patient population and is being developed to be a once-monthly, subcutaneous antipsychotic product. We expect to initiate clinical studies for this new product candidate in patients with schizophrenia in early 2012 following filing of an investigational new drug application.

We have experienced net losses and negative cash flow from operating activities since inception, and as of June 30, 2011, had an accumulated deficit of \$236.3 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next several years primarily as a result of the development expenses in connection with clinical trials and pre-clinical studies for Zohydro, the costs of clinical development of Relday and the cost of the sales and marketing expenses associated with Sumavel DosePro. As of June 30, 2011, we had cash and cash equivalents of \$7.7 million. In addition, we amended certain terms of our loan agreement with Oxford Finance LLC, as successor in interest to Oxford Finance Corporation, or Oxford, and Silicon Valley Bank, or SVB, including the deferral of principal repayment to February 1, 2012. In July 2011, we entered into an equity and royalty financing agreement with Cowen Healthcare Royalty Partners II,

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**Table of Contents**

L.P., or Cowen Royalty, resulting in net proceeds of \$29.5 million to us. Although it is difficult to predict future liquidity requirements, based on our current operating plan we believe that the net proceeds from this offering, together with our cash and cash equivalents as of June 30, 2011, future product revenues, borrowings available under our \$10.0 million revolving credit facility and the net proceeds from the recently completed equity and royalty financing with Cowen Royalty, will be sufficient to fund our operations into the third quarter of 2012. We will need to obtain additional capital to finance our operations beyond that point. We intend to raise additional capital through debt or equity financings or through collaborations or partnerships with other companies. If we are not able to raise additional capital on terms acceptable to us, or at all, as and when needed, we may be required to reduce or curtail our operations and costs, and we may be unable to continue as a going concern. In its report on our consolidated financial statements for the year ended December 31, 2010, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern.

*Co-Promotion Agreement*

Under our co-promotion agreement with Astellas that we entered into in July 2009, or the co-promotion agreement, Astellas primarily promotes Sumavel DosePro to the Astellas Segment in the United States. Our sales force promotes Sumavel DosePro primarily to neurologists and other prescribers of migraine medications, including headache clinics and headache specialists in the United States. We jointly share in the cost of advertising, marketing and other promotional activities related to the Sumavel DosePro brand and are required to provide minimum levels of sales effort to promote Sumavel DosePro. Under the co-promotion agreement, we are responsible for the manufacture, supply and distribution of all Sumavel DosePro commercial product and are principally responsible for entering into any contracts and other arrangements with third parties regarding the sale of Sumavel DosePro.

At the inception of the 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 agreed to make an additional \$18.0 million of payments to us upon the achievement of a series of milestones. As of June 30, 2011, we had received a total of \$20.0 million from Astellas. These proceeds are reflected as deferred revenues on our consolidated balance sheet at June 30, 2011. Beginning with the launch of Sumavel DosePro in January 2010, we began recognizing these proceeds as contract revenues on a ratable basis over the remaining term of the agreement, which remains in effect through June 30, 2013, subject to extension by one year at Astellas' option, contingent upon payment of a predetermined option fee. As of June 30, 2011, the remaining balance of these proceeds in deferred revenue was \$12.5 million.

In consideration for Astellas' performance of its commercial efforts, we are 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. In addition, upon completion of the co-promotion term, Astellas generally will be eligible to receive two additional annual tail payments calculated as decreasing fixed percentages (ranging from a mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion. Astellas pays us the lesser of our direct out-of-pocket costs or a fixed fee for all sample units they order 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. For the six months ended June 30, 2011 and 2010, we incurred \$3.2 million and \$1.1 million, respectively, in service fee expenses. For the six months ended June 30, 2011 and 2010, we recognized shared marketing expense of \$1.2 million and \$2.8 million, respectively.

We record the revenues related to all products sales, including sales generated by the Astellas sales force. Consequently, we record cost of sales for all product sales.

We rely on Astellas and its sales force to promote Sumavel DosePro to the Astellas Segment and any inability of its sales force to effectively sell the product or any termination, amendment or restructuring of the co-promotion agreement could adversely affect our consolidated results of operations and financial condition.

## **Table of Contents**

For the six months ended June 30, 2011, the Astellas Segment represented approximately 40% of our net product revenue before consideration of the cost of the service fee payable to Astellas for its sales efforts as described above.

Under the terms of the co-promotion agreement, Astellas may terminate the agreement for any reason or no reason upon 180-days written notice to us. The co-promotion agreement may also be terminated by Astellas or us for a number of other specified reasons, some of which are beyond our control. In the event Astellas terminates the agreement for specified reasons, including a material uncured breach by us of our minimum sales effort obligations and our failure to cure such breach within a specified period, we would be required to pay Astellas only the first of the two annual tail payments described above.

In addition, either party may terminate the agreement based upon a failure of the Sumavel DosePro brand to achieve certain minimum sales levels in 2011, as defined in the co-promotion agreement. Based on our net product revenue through June 30, 2011, we do not expect to meet these 2011 minimum sales levels for Sumavel DosePro, and therefore expect that both we and Astellas will have the right to terminate the agreement on this basis. If either party were to exercise this termination right, it must provide 90 days written notice to the other party, such notice to be provided within 30 days after the actual net sales of Sumavel DosePro through December 31, 2011 have been provided to Astellas pursuant to the terms of the co-promotion agreement. In the event of such a termination relating to sales levels of Sumavel DosePro, we would be required to make the two annual tail payments to Astellas described above.

In the event of a termination by us or Astellas, we would expect to expand our sales force to promote Sumavel DosePro to certain physicians within the Astellas Segment and/or seek another co-promotion partner, if available, in order to support the future sales and marketing of Sumavel DosePro. We may also seek to amend or restructure our co-promotion agreement with Astellas. As noted above, we have initiated activities to expand our sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011.

### *Direct License Agreement*

In July 2011, we paid a non-refundable upfront fee to Durect of \$2.25 million under the Relday license agreement. We are obligated to pay Durect up to \$103.0 million in total future milestone payments with respect to Relday subject to and upon the achievement of various development, regulatory and sales milestones. We are also required to pay a mid single-digit to low double-digit percentage patent royalty on annual net sales of the product determined on a jurisdiction-by-jurisdiction basis. The patent royalty term in any jurisdiction is equal to the later of the expiration of all Durect technology patents or joint patent rights in a particular jurisdiction, the expiration of marketing exclusivity rights in such jurisdiction, or 15 years from first commercial sale in such jurisdiction. After the patent royalty term, we will continue to pay royalties on annual net sales of the product at a reduced rate for so long as we continue to sell the product in the jurisdiction. We are also required to pay to Durect a tiered percentage of fees received in connection with any sublicense of the licensed rights.

### *Revenues*

During the year ended December 31, 2010, we began recognizing product revenues from sales of Sumavel DosePro made by us and Astellas under our co-promotion agreement and through sales by us to Desitin Arzneimittel GmbH, or Desitin, under our licensing and distribution agreement. During this same period, we began recognizing contract revenues from license and milestone payments received under the Astellas co-promotion agreement. For the six months ended June 30, 2011 and 2010 we recognized \$16.2 million and \$6.1 million, respectively, in net product revenues. For the six months ended June 30, 2011 and 2010 we recognized \$3.1 million and \$1.5 million, respectively, in contract revenues associated with license and milestone payments made to us by Astellas under the co-promotion agreement.

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## **Table of Contents**

We sell Sumavel DosePro product in a package of six pre-filled, single-dose units to wholesale pharmaceutical distributors, and on a limited basis to retail pharmacies, or, collectively, our customers, at a wholesale acquisition cost, or gross sales price, of \$522 per package as of June 30, 2011. Sales to our customers are subject to specified rights of return. We currently defer recognition of revenue on product shipments of Sumavel DosePro to our customers until the right of return no longer exists, which occurs at the earlier of the time Sumavel DosePro units are dispensed through patient prescriptions or expiration of the right of return. We do not have significant history estimating the number of patient prescriptions dispensed. If we underestimate or overestimate patient prescriptions dispensed for a given period, adjustments to net product revenue may be necessary in future periods.

As a result of this policy, we had a deferred revenue balance of \$0.7 million at June 30, 2011 for Sumavel DosePro product shipments, which is net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs. We will continue to recognize revenue upon the earlier to occur of prescription units dispensed or expiration of the right of return until we can reliably estimate product returns, at which time we will record a one-time increase in net revenue related to the recognition of revenue previously deferred.

In November 2010, Desitin received regulatory approval to market Sumavel DosePro in Denmark and subsequently received approvals in Germany, Sweden, Norway and the United Kingdom. As a result, we started to sell Sumavel DosePro to Desitin under our licensing and distribution agreement in December 2010. We sell our product to Desitin at a specified transfer price with the right of return available for damaged goods upon receipt by Desitin or in the event of a recall. Desitin retains all risk for retail and wholesaler fees and discounts, collectability of customer receivables, customer returns and expiration of the product. We will also receive a low single-digit royalty from Desitin on net sales of Sumavel DosePro in Europe and other licensed territories, as a pass through of royalties payable to Aradigm. As such, we recognize revenues for product sales to Desitin upon acceptance of product by Desitin (generally at point of shipment). For the six months ended June 30, 2011 and 2010 we recognized no revenue for sales to Desitin. We recognized an immaterial amount of royalty revenues related to the Desitin agreement for the six months ended June 30, 2011.

### *Cost of Sales*

Cost of sales consist primarily of materials, third-party manufacturing costs, freight and indirect personnel and other overhead costs associated with sales of Sumavel DosePro based on units dispensed through patient prescriptions, as well as reserves for excess, dated or obsolete commercial inventories and production manufacturing variances. Our cost of sales for the six months ended June 30, 2011 and 2010 was \$8.9 million and \$5.3 million, respectively. Our product gross margin for the six months ended June 30, 2011 and 2010 was 45% and 13%, respectively. The cost of sales associated with the deferred product revenues are recorded as deferred costs, which are included in inventory, until such time the deferred revenue is recognized. Deferred cost of sales totaled \$0.2 million and \$1.1 million at June 30, 2011 and December 31, 2010, respectively.

### *Royalty Expense*

Royalty expense consists of the amortization of the \$4.0 million milestone payment paid by us to Aradigm Corporation upon the first commercial sale of Sumavel DosePro in the United States (which occurred in January 2010) and royalties payable to Aradigm based on net sales of Sumavel DosePro by us or one of our licensees. We are not required to make any further milestone payments to Aradigm. Our ongoing royalty obligation payable to Aradigm is set forth in the asset purchase agreement we entered into with Aradigm in August 2006 pursuant to which we acquired the rights to the DosePro technology. During the six months ended June 30, 2011 and 2010, we incurred \$0.6 million and \$0.4 million, respectively, in royalty expense on net product sales and the amortization of milestone payments paid to Aradigm.

The royalty payments payable to Cowen Royalty in future periods in connection with the \$30.0 million in borrowings will be reflected as interest expense and not be reflected as royalty expense.



**Table of Contents***Research and Development Expenses*

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

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

expenses associated with regulatory submissions, preclinical development and clinical trials;

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

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

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

facility, maintenance, depreciation and other related expenses.

We expense all research and development costs as incurred.

In March 2010, we initiated our Phase 3 clinical development program for Zohydro. We utilize CROs, contract laboratories and independent contractors for the conduct of pre-clinical studies and clinical trials. In 2010, we began tracking third party costs by type of study being conducted. We recognize the expenses associated with the services provided by CROs based on the percentage of each study completed at the end of each reporting period. We coordinate clinical trials through a number of contracted investigational sites and recognize the associated expense based on a number of factors, including actual and estimated subject enrollment and visits, direct pass-through costs and other clinical site fees. For the six months ended June 30, 2011, we incurred \$12.9 million in third party research and development costs related to Zohydro.

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. However, we estimate that the majority of our research and development expenses incurred to date are attributable to our Sumavel DosePro and Zohydro programs. The following table illustrates, for each period presented, our research and development costs broken down by major categories of the cost:

	Six Months Ended June 30,		Year Ended December 31,		
	2011	2010	2010	2009	2008
	(In Thousands)				
<b>Research and development expenses:</b>					
Manufacturing development expenses	\$ 0	\$ 0	\$ 0	\$ 13,772	\$ 22,381
Clinical/regulatory expenses	17,406	11,389	28,643	7,666	11,529
Total	\$ 17,406	\$ 11,389	\$ 28,643	\$ 21,438	\$ 33,910

We expect our research and development costs for 2011 to increase over amounts incurred in 2010 as we progress through the Phase 3 clinical program of Zohydro and with the addition of our Relday program. We expect third party research and development costs for Zohydro remaining through NDA filing with the FDA to range from \$17 million to \$19 million. These expenditures are subject to numerous uncertainties regarding,

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among other things, timing and cost to completion. Completion of our Phase 3 clinical trials may take longer than currently estimated. The cost of clinical trials may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others:

the number of sites included in the trials;

**Table of Contents**

the length of time required to enroll suitable subjects;

the duration of subject follow-ups;

the length of time required to collect, analyze and report trial results;

the cost, timing and outcome of regulatory review; and

potential changes by the FDA in clinical trial and NDA filing requirements for a specific therapeutic area.

In addition, in August 2011 we paid Elan, from whom we in-licensed exclusive rights to Zohydro in November 2007, a milestone payment in the amount of \$750,000 in connection with the completion of the treatment phase of our pivotal efficacy Phase 3 clinical trial, Study 801. We may be obligated to pay Elan up to \$3.75 million in total future milestone payments with respect to Zohydro depending upon the achievement of various development and regulatory events. If Zohydro is approved, we are also required to pay a mid single-digit percentage royalty on its net sales for a specified period of time and continue to pay royalties on net sales of the product thereafter at a reduced low single-digit percentage rate in accordance with the terms of the license agreement.

If our Phase 3 clinical trials are successful, we expect to submit an NDA for Zohydro with the FDA by early 2012. However, the successful development and commercialization of Zohydro is highly uncertain. We also expect to incur customary regulatory costs associated with the NDA, if and when submitted, which will be significant. If Zohydro is approved, we also expect to incur significant expenses related to manufacturing and marketing activities. However, at this time, we cannot reasonably estimate or know the nature, specific timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of Zohydro after submission of our NDA filing, if or when Zohydro will receive regulatory approval and, if approved, if and when material net cash inflows may commence from Zohydro or the amount of any such inflows. This is due to the numerous risks and uncertainties associated with developing and commercializing drugs, including the uncertainty of:

the costs, timing and outcome of our clinical trials and pre-clinical studies of Zohydro;

the costs, timing and outcome of regulatory review of Zohydro;

the costs of commercialization activities, including product marketing, sales and distribution;

the potential for future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development and commercialization plans and capital requirements;

the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;

the emergence of competing technologies and products and other adverse marketing developments;

the effect on our product development activities of actions taken by the FDA or other regulatory authorities; and

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our degree of success in commercializing Zohydro, if approved.

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

We also expect to incur costs associated with pre-clinical studies and formulation work for our early-stage product candidates. However, at this time, due to the inherently unpredictable nature of pre-clinical development and given the early stage of such product candidates, we are unable to estimate with any certainty the costs we will incur for such pre-clinical work.

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**Table of Contents**

*Selling, General and Administrative Expenses*

Our selling expenses, which include sales and marketing costs, consisted primarily of salaries, benefits, consulting fees, costs of obtaining prescription and market data and market research studies related to Sumavel DosePro and Zohydro, including shared marketing and advertising costs under our co-promotion agreement with Astellas, service fees to Astellas and sample costs. Through the fiscal year ended December 31, 2009, our selling expenses consisted primarily of salaries, benefits, consulting fees and market research studies related to preparations for the launch of Sumavel DosePro, including shared marketing and advertising costs under our co-promotion agreement with Astellas. We have initiated activities to expand our field sales force in the United States from approximately 80 sales representatives to approximately 95 sales representatives by the end of the third quarter of 2011 and expect our selling expenses to increase as a result of this expansion. In addition, our selling expenses may further increase in the event our co-promotion agreement with Astellas is terminated and we further expand our sales force and/or seek another co-promotion partner.

Our general and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, accounting, business development and internal support functions. In addition, general and administrative expenses include facility costs and professional fees for legal, consulting and accounting services. We expect general and administrative expense to increase as a result of the costs we incur operating as a public company. These increases likely will include salaries and related expenses, legal and consultant fees, accounting fees, director fees, increased directors and officers insurance premiums, fees for investor relations services and enhanced business and accounting systems.

*Interest Income*

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

*Interest Expense*

Interest expense consists of interest incurred in connection with the \$4.5 million borrowed under our loan and security agreement with General Electric Capital Corporation, or GE Capital, which was recently terminated, our \$25.0 million loan and security agreement and revolving credit facility with Oxford and SVB and non-cash interest expense associated with amortization of debt discount and debt issuance costs.

On June 30, 2011, we amended and restated the existing loan and security agreement with Oxford and SVB, or the amended Oxford/SVB loan agreement, to provide for, among other things, the addition of intellectual property to the collateral securing the obligations thereunder and deferral of principal repayment to February 1, 2012. In connection with entering into the amended Oxford/SVB loan agreement, we issued to Oxford and SVB warrants exercisable into an aggregate of 26,455 shares of our common stock. The warrants are exercisable at \$3.78 per share of common stock and have a term of 7 years. The amended Oxford/SVB loan agreement consists of a \$25.0 million term loan and a \$10.0 million revolving credit facility. As of June 30, 2011, we had borrowed \$3.7 million under the revolving credit facility. Concurrently with the amended Oxford/SVB loan agreement in 2010, we issued \$15.0 million in new convertible promissory notes, or the 2010 Notes, to certain of our stockholders. The 2010 Notes were subsequently converted into 3,873,756 shares of common stock in connection with our initial public offering in November 2010. As a result of additional borrowings under the amended Oxford loan agreement, and the deferral of principal payments resulting from the amended Oxford/SVB loan agreement in June 2011 and the \$30.0 million royalty financing entered into in July 2011, interest expense related to debt service will increase over 2010 levels. This increase will be primarily driven by the cost of royalty obligations to be incurred under the royalty financing with Cowen Royalty.

## **Table of Contents**

### *Change in Fair Value of Warrant Liability*

Change in fair value of warrant liability for the six months ended June 30, 2010 represents non-cash (expense) income associated with changes in the fair value of the warrants to purchase preferred stock.

In connection with our initial public offering in November 2010, the liability reflected on our consolidated balance sheet for convertible preferred stock warrants was reclassified to stockholders' equity (deficit) and we will no longer recognize the change in fair value of these warrants in the consolidated statement of operations.

### *Other Income (Expense)*

Other income (expense) consists of foreign currency transaction gains and losses. All of our revenues are currently generated in U.S. dollars while a majority of our manufacturing expenses are payable in foreign currencies, primarily U.K. pound sterling and the Euro.

### *Provision for Income Taxes*

We incurred \$13,000 and \$0 in income tax expense for the six months ended June 30, 2011 and 2010, respectively, related to taxable income generated by our wholly-owned subsidiary, Zogenix Europe Limited.

### *Net Operating Loss and Tax Credit Carryforward*

As of December 31, 2010, we had federal and state net operating loss carryforwards of approximately \$159.6 million and \$136.2 million, respectively. If not utilized, the net operating loss carryforwards will begin expiring in 2026 for federal tax purposes and 2016 for state tax purposes. As of December 31, 2010, we had federal and state research and development tax credit carryforwards of approximately \$1.8 million and \$1.3 million, respectively. The federal research and development income tax credit carryforwards will begin to expire in 2026 unless previously utilized. The California research and development income tax credit carryforwards will carry forward indefinitely until utilized.

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the IRC, substantial changes in our ownership may limit the amount of net operating loss and research and development income tax credit carryforwards (collectively, tax attributes) that could be utilized annually in the future to offset taxable income, if any. Specifically, this limitation may arise in the event of a cumulative change in ownership of our company of more than 50% within a three-year period as determined under the IRC, which we refer to as an ownership change. Any such annual limitation may significantly reduce the utilization of these tax attributes before they expire. Prior to our initial public offering in November 2010, we performed an IRC Section 382 and 383 analysis and determined that we had one ownership change, which occurred in August 2006 upon the issuance of convertible preferred stock. As a result of this ownership change, our ability to use our then existing tax attributes was limited. We expect the issuance of common stock in this offering, together with the issuance of common stock in our initial public offering and certain other transactions involving our common stock, will result in an additional ownership change, which will further limit the amount of the tax attributes we may use to offset future taxable income, if any. In addition, any future equity financing transactions, private placements and other transactions that occur within the specified three-year period may trigger additional ownership changes, which could further limit our use of such tax attributes. Any such limitations, whether as the result of this offering, prior or future offerings of our common stock or sales of common stock by our existing stockholders, could have an adverse effect on our consolidated results of operations in future years. In each period since our inception, we have recorded a valuation allowance for the full amount of our deferred tax asset, as the realization of the deferred tax asset is uncertain. As a result, we have not recorded any federal or state income tax benefit in our consolidated statement of operations.

## **Table of Contents**

### *Internal Control Over Financial Reporting*

Assessing our staffing and training procedures to improve our internal control over financial reporting is an ongoing process. For the year ending December 31, 2011, pursuant to Section 404 of the Sarbanes-Oxley Act, management will be required to deliver a report that assesses the effectiveness of our internal control over financial reporting. Pursuant to Section 404(c) of the Sarbanes-Oxley Act, our independent registered public accounting firm will not be required to deliver an attestation report on the effectiveness of our internal control over financial reporting for the year ending December 31, 2011.

### *Cowen Royalty Financing Agreement*

In July 2011 we completed an equity and royalty financing with Cowen Royalty pursuant to which we borrowed \$30.0 million and issued warrants to purchase 225,000 shares of our common stock to Cowen Royalty. Although we have not completed our assessment of the accounting treatment for this transaction, we believe certain elements of the royalty financing may include derivatives that would be reflected on our balance sheet on a fair value basis with periodic changes in value recorded in other income and expense on our statement of operations.

### **Critical Accounting Policies and Estimates**

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in conformity with generally accepted accounting principles in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and related disclosures. Actual results could differ from those estimates.

While our significant accounting policies are more fully described in Note 2 to our consolidated financial statements appearing elsewhere in this prospectus, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our consolidated financial statements.

#### *Revenue Recognition*

We recognize revenues from the sale of Sumavel DosePro and from license fees and milestones earned on collaborative arrangements. Revenue is recognized when there is persuasive evidence that an arrangement exists, delivery has occurred and title has passed, the price is fixed or determinable and we are reasonably assured of collecting the resulting receivable.

#### *Product Revenue*

Sales of Sumavel DosePro to our customers are subject to rights of return within a period beginning six months prior to, and ending 12 months following, product expiration. Given the limited sales history of Sumavel DosePro, we currently cannot reliably estimate expected returns of the product at the time of shipment. Accordingly, we defer recognition of revenue on product shipments of Sumavel DosePro until the right of return no longer exists, which occurs at the earlier of the time Sumavel DosePro units are dispensed through patient prescriptions or expiration of the right of return. Units dispensed are not generally subject to return. We estimate patient prescriptions dispensed using an analysis of third-party information, including third-party market research data, information obtained from certain wholesalers with respect to inventory levels and inventory movement and retail pharmacy re-stocking activity. Sumavel DosePro was launched in January 2010 and, accordingly, we do not have significant history estimating the number of patient prescriptions dispensed. If we underestimate or overestimate patient prescriptions dispensed for a given period, adjustments to revenue may be necessary in future periods.

As a result of this policy, we recognized \$16.2 million in product revenue from U.S. sales of Sumavel DosePro for the six months ended June 30, 2011, which is net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs. We

## **Table of Contents**

had a deferred revenue balance of \$0.7 million at June 30, 2011 for Sumavel DosePro product shipments, which is net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs. We will continue to recognize revenue upon the earlier to occur of prescription units dispensed or expiration of the right of return until we can reliably estimate product returns. We expect a change in revenue recognition may not result in a material impact to revenues upon the initial change in methodology as we would contemporaneously recognize an accrual for potential returns on units of Sumavel DosePro sold to wholesalers that remain unconsumed by patients. In addition, the costs of manufacturing Sumavel DosePro associated with the deferred revenue are recorded as deferred costs, which are included in inventory, until such time the deferred revenue is recognized.

Under our licensing and distribution agreement with Desitin, we sell Sumavel DosePro to Desitin at a specified transfer price with the right of return available for damaged goods upon receipt by Desitin or in the event of a recall. Desitin retains all risk for retail and wholesaler fees and discounts, collectability of customer receivables, customer returns and expiration of the product. We will also receive royalties from Desitin on net sales of Sumavel DosePro in Europe and other licensed territories at a predetermined rate. As such, we recognize revenues for product sales to Desitin upon acceptance of product by Desitin (generally at point of receipt of shipment). For the six months ended June 30, 2011, we recognized no revenue for sales to Desitin. We recognized an immaterial amount of royalty revenues related to the Desitin agreement for the six months ended June 30, 2011.

### *Product Sales Allowances*

We recognize products sales allowances as a reduction of product sales in the same period the related revenue is recognized. Product sales allowances are based on amounts owed or to be claimed on the related sales. These estimates take into consideration the terms of our agreements with customers and third-party payors and the levels of inventory within the distribution and retail channels that may result in future rebates or discounts taken. In certain cases, such as patient support programs, we recognize the cost of patient discounts as a reduction of revenue based on estimated utilization. If actual future results vary, we may need to adjust these estimates, which could have an effect on product revenue in the period of adjustment. Our product sales allowances include:

*Wholesaler and Retail Pharmacy Discounts.* We offer discounts to certain wholesale distributors and retail pharmacies based on contractually determined rates. We accrue the discount on shipment to the respective wholesale distributors and retail pharmacies and recognize the discount as a reduction of revenue in the same period the related revenue is recognized.

*Prompt Pay Discounts.* We offer cash discounts to our customers, generally 2% of the sales price, as an incentive for prompt payment. We account for cash discounts by reducing accounts receivable by the full amount and recognizing the discount as a reduction of revenue in the same period the related revenue is recognized.

*Chargebacks.* We provide discounts to authorized users of the Federal Supply Schedule, or FSS, of the General Services Administration under an FSS contract negotiated by the Department of Veterans Affairs and various organizations under Medicaid contracts and regulations. These entities purchase products from the wholesale distributors at a discounted price, and the wholesale distributors then charge back to us the difference between the current retail price and the price the federal entity paid for the product. We estimate and accrue chargebacks based on estimated wholesaler inventory levels, current contract prices and historical chargeback activity. Chargebacks are recognized as a reduction of revenue in the period the related revenue is recognized.

*Rebates.* We participate in certain rebate programs, which provide discounted prescriptions to qualified insured patients. Under these rebate programs, we pay a rebate to the third-party administrator of the program, generally two to three months after the quarter in which prescriptions subject to the rebate are filled. We estimate and accrue these rebates based on current contract prices, historical and estimated future percentages of product sold to qualified patients and estimated levels of inventory in the distribution channel. Rebates are recognized as a reduction of revenue in the period the related revenue is recognized.



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**Table of Contents**

*Patient Discount Programs.* We offer discount card and automatic electronic pharmacy discount programs to patients for Sumavel DosePro in which patients receive discounts on their prescriptions that are reimbursed by us. We estimate the total amount that will be redeemed based on levels of inventory in the distribution and retail channels and recognize the discount as a reduction of revenue in the same period the related revenue is recognized.

*Stocking Allowances.* We may offer discounts and extended payment terms, generally in the month of the initial commercial launch of a new product, on the first order made by certain wholesale distributors and retail pharmacies based on contractually determined rates. We accrue the discount on shipment to the respective wholesale distributors and retail pharmacies and recognize the discount as a reduction of revenue in the same period the related revenue is recognized.

In the first quarter of 2010, we provided stocking allowances on initial orders placed by our customers in connection with the launch of Sumavel DosePro. In accordance with our accounting policy for stocking allowances as disclosed, the allowance provided was accrued at the time of shipment to our customers and recognized as a reduction to revenue in the same period the related revenue was recognized. There have been no additional orders placed with stocking allowances. The amounts accrued for wholesaler and retail pharmacy discounts and prompt pay discounts were \$0.4 million at June 30, 2011, \$0.4 million at December 31, 2010 and none at December 31, 2009. We recognized \$1.4 million in reductions to product revenues related to these discounts for each of the six months ended June 30, 2011 and the year ended December 31, 2010. Contractually agreed upon discounts with our wholesale and retail customers are typically paid to our customers on a quarterly basis one to two months after the quarter in which product was shipped to the customer. Based on our experience, our customers generally comply with our payment terms to earn prompt pay discounts. These discounts are measureable at the time of shipment of product to our customers and generally do not vary materially from our estimates.

The amounts accrued for rebates, chargebacks and other incentive programs were \$0.5 million at June 30, 2011, \$0.5 million at December 31, 2010 and none at December 31, 2009. We recognized \$1.6 million in reductions to product revenues related to these sales allowances for the six months ended June 30, 2011. Our procedures for estimating amounts accrued for rebates, chargebacks and other incentive programs at the end of any period are based on available quantitative data and are supplemented by management's judgment with respect to many factors, including but not limited to, current market dynamics, changes in contract terms, impact of new contractual arrangements and changes in sales trends. Quantitatively, we use historical sales, inventory movement through commercial channels, product utilization and rebate data and apply forecasting techniques in order to estimate our liability amounts. Qualitatively, management's judgment is applied to these items to modify, if appropriate, the estimated liability amounts. There are inherent risks in this process. For example, patients may not achieve assumed utilization levels; third parties may misreport their utilization to us; and discounts determined under federal guidelines, which affect our rebate programs with U.S. federal government agencies, may differ from those estimated. On a quarterly basis, we analyze our estimates against actual rebate, chargeback and incentive program activity and adjust our estimates as necessary. Given our limited history with the commercialization of Sumavel DosePro, we may experience variability in our provisions for these sales allowances as we continue to initiate new sales initiatives and/or managed care programs in connection with the commercialization of our product. An adjustment to our estimated liabilities for rebates, chargebacks and other incentive programs of 5% of net product sales on a quarterly basis, based on operating results for the three months ended June 30, 2011, would have resulted in an increase or decrease to net sales for that period of approximately \$0.4 million to \$0.5 million. The sensitivity of our estimates can vary by program and type of customer. Additionally, there is a time lag between the date we determine the estimated liability and when we actually pay the liability. Due to this time lag, we may record adjustments to our estimated liabilities over several reporting periods, which can result in a net increase to net revenues or a net decrease to net revenues in those periods. Material differences may result in the amount of revenue we recognize from product sales if the actual amount of rebates, chargebacks and incentives differ materially from the amounts estimated by management. To date, there have been no material differences between the amount recorded in a period and actual charges incurred.

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## **Table of Contents**

We also sell our product to third party distributors under license and distribution agreements where we do not participate in the commercialization efforts of the product in the licensed territories. Our product is sold at a specified transfer price with the right of return to us for damaged goods or in the event of a recall. The distributor retains all risk for retail and wholesaler fees and discounts, collectability of customer receivables, customer returns and expiration of the product. We recognize revenues for product sales under these license arrangements upon acceptance of the product by the licensee (generally at point of shipment).

### *Contract Revenue*

We recognize revenues related to license fees and milestone payments received under our co-promotion agreement with Astellas. Revenue arrangements with multiple deliverables are divided into separate units of accounting if criteria are met, including whether the deliverable has stand-alone value to the customer and the customer has a general right of return relative to the delivered item and delivery or performance of the undelivered item is probable and substantially within the vendor's control. Arrangement consideration is allocated at the inception of the arrangement to all deliverables on the basis of their relative selling price.

In connection with the co-promotion agreement, Astellas made a non-refundable up-front payment of \$2.0 million and agreed to make an additional \$18.0 million of payments to us upon the achievement of a series of milestones. As of June 30, 2011, we have received a total of \$20.0 million from Astellas.

We identified the deliverables in the co-promotion agreement and divided them into separate units of accounting as follows: (1) co-exclusive right to promote Sumavel DosePro combined with the manufacturing and supply of commercial and sample product; and (2) sales support of Sumavel DosePro. We concluded both units of accounting require recognition ratably through the term of the co-promotion agreement, which began with the date of the launch of Sumavel DosePro (January 2010) and ends June 30, 2013, subject to a one-year extension at Astellas' option upon Astellas' payment of a pre-determined fee to us, and therefore, the allocation of the upfront and milestone financial consideration is not necessary. Consequently, we recorded the \$20.0 million in upfront and milestone payments received from Astellas as deferred revenue in the consolidated balance sheets at June 30, 2011 and December 31, 2010 and 2009. Beginning with the launch of Sumavel DosePro in January 2010, we began amortizing the license fees and milestone payments as contract revenue in the consolidated statement of operations over the remaining term of the agreement, which remains in effect through June 30, 2013, subject to extension by one year at Astellas' option, contingent upon payment of a predetermined option fee.

In consideration for Astellas' performance of its commercial efforts, we are 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. In addition, upon completion of the co-promotion term, Astellas generally will be eligible to receive two additional annual tail payments calculated as decreasing fixed percentages (ranging from a mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion. Astellas pays us the lesser of our direct out-of-pocket costs or a fixed fee for all sample units they order for distribution to their sales force. Amounts received from Astellas for shared marketing costs 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.

### *Inventories and Related Reserves*

Inventories are stated at the lower of cost (FIFO) or market and consist of finished goods, work in progress and raw materials used in the manufacture of Sumavel DosePro. We have significant lead times for the procurement and manufacture of our finished goods and we therefore order goods from our suppliers and manufacturers based on our forecasts of future demand. To the extent we procure component materials or produce finished goods in excess of actual future demand, we may be required to provide reserves for potentially excess or dated inventories. We provide such reserves based on an analysis of inventory on hand and on firm purchase commitments compared to forecasts of future sales.

**Table of Contents***Clinical Trial Expenses*

Our expense accruals for clinical trials are based on estimates of the services received from clinical trial investigational sites and CROs. Payments under some of the contracts we have with such parties depend on factors such as the milestones accomplished, successful enrollment of certain numbers of patients, site initiation and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If possible, we obtain information regarding unbilled services directly from these service providers. However, we may be required to estimate these services based on information available to our product development or administrative staff. If we underestimate or overestimate the activity associated with a study or service at a given point in time, adjustments to research and development expenses may be necessary in future periods. Historically, our estimated accrued liabilities have approximated actual expense incurred. Subsequent changes in estimates may result in a material change in our accruals.

*Stock-Based Compensation*

Stock-based compensation expense is measured at the grant date, based on the estimated fair value of the award, and is recognized as expense over the employee's requisite service period, or vesting period, on a straight-line basis. Equity awards issued to non-employees are recorded at their fair value on the grant date and are periodically re-measured as the underlying awards vest unless the instruments are fully vested, immediately exercisable and nonforfeitable on the date of grant. Expense recognized for consultant stock options was immaterial for the six months ended June 30, 2011 and the years ended December 31, 2010, 2009 and 2008.

We utilize 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 are as follows:

	Six Months Ended		2010	Year Ended December 31,	
	2011	June 30, 2010		2009	2008
<b>Stock Options</b>					
Risk free interest rate	1.8% to 2.6%	2.0% to 2.3%	1.7 % to 2.3%	2.3% to 2.8%	2.7% to 3.2%
Expected term	5.0 to 6.1 years	5.0 to 5.9 years	5.0 to 6.1 years	5.0 to 6.1 years	5.0 to 6.1 years
Expected volatility	72.3% to 89.7%	94.6% to 95.7%	90.8% to 96.0%	105.6% to 107.6%	80.6% to 86.0%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%	0.0%
Fair value of underlying stock	\$3.87 to \$5.04	\$1.35	\$5.73 to \$13.50	\$3.20 to \$3.60	\$3.50 to \$19.10
<b>Employee Stock Purchase Plan</b>					
Risk free interest rate	0.1%				
Expected term	0.5 years				
Expected volatility	75.2%				
Expected dividend yield	0.0%				
Fair value of underlying stock	\$4.15				

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 our 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 our limited historical experience. In addition, due to our limited historical data, the estimated volatility was calculated based upon the historical volatility of comparable companies whose share prices have been publicly available for a sufficient period of time.

**Table of Contents****Results of Operations***Comparison of the six months ended June 30, 2011 and 2010*

**Revenue.** Revenue for the six months ended June 30, 2011 was \$19.3 million and \$7.6 million for the six months ended June 30, 2010. Product revenue for the six months ended June 30, 2011 and 2010 consists of \$16.2 million and \$6.1 million, respectively, of Sumavel DosePro dispensed to patients, which is net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs. The \$10.1 million increase in product revenue is primarily due to an increase in prescription volume from the initial launch of the Sumavel DosePro in late January 2010. Contract revenue for the six months ended June 30, 2011 and 2010 consists of \$3.1 million and \$1.5 million, respectively. Contract revenue represents amortization of license fee payments and milestone payments we received in connection with the co-promotion agreement we entered into with Astellas in July 2009 and which we began recognizing upon the commencement of sales of Sumavel DosePro in January 2010. The contract revenue in the first six months of 2010 reflects a pro-rata amount of amortization of license fees and milestones as compared to the contract revenues in the first six months of 2011, which reflects the full amortization of all license fees and milestone payments.

**Cost of Sales.** Cost of sales for the six months ended June 30, 2011 was \$8.9 million and \$5.3 million for the six months ended June 30, 2010. Product gross margin for the six months ended June 30, 2011 was 45% compared to 13% for the six months ended June 30, 2010. Cost of sales, for the six months ended June 30, 2011 represents the cost of Sumavel DosePro units dispensed to patients and the impact of underutilized production capacity and other manufacturing variances. We developed production capacity to support higher levels of Sumavel DosePro production than initial sample and prescription demand required to ensure adequate stock levels and to maintain the ability to support increased demand, as necessary. Until our prescription and sample demands are at a level where we can fully utilize the capacity committed to our contract manufacturing facilities, we will continue to experience underutilization of our production capacity. In addition, as we adjust production levels in certain periods to manage our inventory levels, we may incur additional charges for excess capacity which will negatively impact our gross margins.

**Royalty Expense.** Royalty expense increased to \$0.6 million for the six months ended June 30, 2011 from \$0.4 million for the six months ended June 30, 2010. Royalty expense represents the amortization of a \$4.0 million milestone payment we made in connection with the asset purchase agreement with Aradigm payable on the first commercial sale of Sumavel DosePro, which occurred in January 2010, as well as royalties payable to Aradigm from net sales of Sumavel DosePro during the period. The \$0.2 million increase in royalty expense is primarily due to the increase in sales.

**Research and Development Expenses.** Research and development expenses increased to \$17.4 million for the six months ended June 30, 2011 compared to \$11.4 million for the six months ended June 30, 2010. This increase of \$6.0 million primarily was due to:

an increase of \$7.1 million in research and development costs as a result of the ongoing Phase 3 clinical trials for Zohydro, which were initiated in March 2010; offset by

a decrease of \$1.1 million in research and development costs incurred for the Phase 4 study conducted for Sumavel DosePro as it was completed in the second quarter of 2010 and other costs related to product development.

**Selling, General and Administrative Expenses.** Selling, general and administrative expenses increased to \$28.0 million for the six months ended June 30, 2011 compared to \$25.4 million for the six months ended June 30, 2010. Selling expenses were \$21.4 million for the six months ended June 30, 2011 compared to \$21.6 million for the six months ended June 30, 2010. General and administrative expenses were \$6.5 million for the six months ended June 30, 2011 compared to \$3.8 million for the six months ended June 30, 2010. The increase of \$2.6 million in selling, general and administrative expenses primarily was due to:

an increase of \$2.7 million of general and administrative expenses as a result of the costs we incurred for operating as a public company. These costs include salaries and related expenses, stock-based

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**Table of Contents**

compensation charges, legal and consultant fees, accounting fees, director fees, increased directors and officers insurance premiums and fees for investor relations services; offset by

a decrease of \$0.1 million in sales and marketing expense primarily as a result of a decrease in sampling efforts and other advertising and promotion activities relative to the levels of activity during the initial launch of Sumavel DosePro in the first half of 2010 partially offset by increased services fees payable to our co-promotion partner from higher net product revenues over the prior quarter

*Interest Income.* Interest income increased to \$19,000 for the six months ended June 30, 2011 compared to \$3,000 for the six months ended June 30, 2010. This increase of \$16,000 was due primarily to the increase in average cash and cash equivalent balances.

*Interest Expense.* Interest expense increased to \$2.5 million for the six months ended June 30, 2011 compared to \$1.5 million for the six months ended June 30, 2010. This increase of \$1.0 million was primarily due to higher debt balances in connection with the amended Oxford/SVB loan agreement.

*Change in Fair Value of Warrant Liability.* During the six months ended June 30, 2011 there was no warrant liability outstanding due to the termination or conversion of the preferred stock warrants to warrants to purchase common stock in connection with our initial public offering in November 2010. The change in fair value of warrant liability during the six months ended June 30, 2010 of \$13.0 million is due to the increase in fair value of convertible preferred stock during the period.

*Other Income (Expense).* Other income (expense) decreased to \$0.1 million of expense for the six months ended June 30, 2011 compared to \$0.1 million of income for the six months ended June 30, 2010. This decrease was due to foreign currency transaction losses which primarily related to the settlement of our liabilities payable in Euro and U.K. pound sterling.

**Comparison of year ended December 31, 2010 and 2009**

*Revenue.* Revenue for the year ended December 31, 2010 was \$23.4 million and zero for the year ended December 31, 2009. Revenue for the year ended December 31, 2010 consists of \$19.1 million of product revenue and \$4.4 million of contract revenue. Product revenue for the year ended December 31, 2010 consists of \$18.7 million of Sumavel DosePro dispensed to patients, which is net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs. Product revenue also includes \$0.4 million in product sales to our distribution partner, Desitin, for the commercial launch of Sumavel DosePro in Denmark, Germany, Sweden, Norway and the United Kingdom. We began selling Sumavel DosePro in January 2010 and therefore had no product revenue prior to that time. Contract revenue represents amortization of license fee payments and milestone payments we received in connection with the co-promotion agreement we entered into with Astellas in July 2009 and which we began recognizing upon the commencement of sales of Sumavel DosePro in January 2010.

*Cost of Sales.* Cost of sales for the year ended December 31, 2010 was \$12.8 million and zero for the year ended December 31, 2009. Cost of sales for the year ended December 31, 2010 represents the cost of Sumavel DosePro units dispensed to patients and sold to Desitin, and the impact of underutilized production capacity and other manufacturing variances. We developed production capacity to support higher levels of Sumavel DosePro production than initial unit requirements to ensure adequate safety stock levels and to maintain the ability to support increased demand, as necessary. We began selling Sumavel DosePro in January 2010 and therefore had no cost of sales prior to that time. Prior to regulatory approval of Sumavel DosePro, costs of prototypes, testing and process refinement were charged to research and development. Beginning in the second half of 2009, we began capitalizing manufacturing cost of inventories.

In the fourth quarter of 2010, we reclassified certain manufacturing variances incurred in the production of sample product to selling, general and administrative expenses. These expenses were previously recorded under

## **Table of Contents**

cost of sales. Accordingly, cost of sales has been decreased by \$1.6 million. This reclassification does not have any effect on net loss for 2010, nor does it have any effect on prior years.

*Royalty Expense.* Royalty expense was \$0.8 million for the year ended December 31, 2010 and zero for the year ended December 31, 2009. Royalty expense for the year ended December 31, 2010 represents the amortization of a \$4.0 million milestone payment we made in connection with the asset purchase agreement with Aradigm payable on the first commercial sale of Sumavel DosePro, which occurred in January 2010, as well as royalties payable to Aradigm from net sales of Sumavel DosePro during the period.

*Research and Development Expenses.* Research and development expenses increased to \$28.6 million for the year ended December 31, 2010 compared to \$21.4 million for the year ended December 31, 2009. This increase of \$7.2 million primarily was due to:

an increase of \$20.0 million in research and development costs primarily as a result of the initiation of our Phase 3 clinical trials for Zohydro and our Phase 4 clinical trial for Sumavel DosePro, which was initiated in late 2009; offset by,

a decrease of \$12.8 million due to the capitalization of third-party direct labor, materials and internal overhead costs related to the manufacturing of Sumavel DosePro commercial product, inclusive of related salaries and personnel costs, subsequent to the FDA approval of Sumavel DosePro in July 2009. Prior to FDA approval, these costs were recognized as research and development expenses.

*Selling, General and Administrative Expenses.* Selling, general and administrative expenses increased to \$51.3 million for the year ended December 31, 2010 compared to \$14.1 million for the year ended December 31, 2009. Selling expenses were \$42.3 million for the year ended December 31, 2010 compared to \$7.3 million for the year ended December 31, 2009. General and administrative expenses were \$9.0 million for the year ended December 31, 2010 compared to \$6.8 million for the year ended December 31, 2009. The increase of \$37.2 million in selling, general and administrative expenses primarily was due to:

an increase of \$35.1 million in sales and marketing expense as a result of the expansion of our commercial infrastructure, which included the hiring of approximately 80 sales representatives, marketing and advertising costs, the cost of prescription and other market data, sample product, service fees to Astellas and other commercial tactical efforts associated with the commercial launch of Sumavel DosePro; and

an increase of \$2.1 million of general and administrative expenses due to an increase in salaries and related benefits.

*Interest Income.* Interest income decreased to \$5,000 for the year ended December 31, 2010 compared to \$10,000 for the year ended December 31, 2009. This decrease of \$5,000 was due primarily to the decrease in average cash and investment balances.

*Interest Expense.* Interest expense increased to \$10.0 million for the year ended December 31, 2010 compared to \$9.2 million for the year ended December 31, 2009. This increase of \$0.8 million was primarily due to:

an increase of \$4.7 million in amortization of debt discount costs in connection with the \$15.0 million borrowed under promissory notes we issued in 2010, or the 2010 Notes, which notes were converted to common stock upon completion of our initial public offering;

an increase of \$1.3 million in the amortization of debt issuance and debt discount costs in connection with the \$18.0 million loan and security agreement with Oxford and CIT Healthcare LLC, or CIT, entered into in June 2008 and amended in July and October 2010;

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an increase of \$0.5 million in interest expense due to higher debt balances in connection with the loan and security agreement with Oxford and SVB, which was further amended and restated in July and October 2010; and

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**Table of Contents**

an increase of \$0.3 million in interest expense in connection with (1) the early settlement of our outstanding principal balance on our \$18.0 million loan and security agreement with Oxford and CIT entered into in June 2008 and amended in July and October 2010 and (2) the 2010 Notes; offset by

a decrease of \$3.0 million in debt discount costs in connection with the \$14.8 million borrowed under the promissory notes we issued in 2009, or the 2009 Notes, which notes were converted in September 2009, resulting in an acceleration of the recognition of the debt discount upon conversion; and

a decrease of \$3.0 million associated with the recognition in fair value of the right to convert the outstanding principal and interest under the 2009 Notes to convertible preferred stock.

*Change in Fair Value of Warrant Liability.* Change in the fair value of warrant liability changed to \$6.7 million in income for the year ended December 31, 2010 compared to \$0.8 million in expense for the year ended December 31, 2009 due to the decrease in fair value of our Series A-1, Series A-2 and Series B convertible preferred stock. This decrease in the fair value of the warrants is a result of the re-valuation of the warrants upon their conversion to warrants to purchase common stock in connection with our initial public offering in November 2010. Upon conversion they were re-valued based on our public offering price of \$4.00 per share of common stock.

*Other Income (Expense).* Other income (expense) decreased to \$0.1 million of expense for the year ended December 31, 2010 compared to \$0.4 million of expense for the year ended December 31, 2009. This decrease was due to foreign currency transaction gains which primarily related to the settlement of our liabilities payable in Euro and U.K. pound sterling.

**Comparison of year ended December 31, 2009 and 2008**

*Research and Development Expenses.* Research and development expenses decreased to \$21.4 million for the year ended December 31, 2009 compared to \$33.9 million for the year ended December 31, 2008. This decrease of \$12.5 million primarily was due to:

a decrease of approximately \$13.2 million due to the capitalization of third-party direct labor, materials and internal overhead costs related to the manufacturing of Sumavel DosePro commercial product, inclusive of related salaries and personnel costs;

a decrease of approximately \$2.0 million in expenses associated with consulting services, \$0.4 million in travel-related expenses, and \$0.4 million of salaries and personnel related costs;

a decrease of \$1.6 million for Zohydro clinical trial expenses, as the Phase 3 clinical trials for this program were temporarily delayed, and a \$0.2 million reduction in clinical trial expenses for Sumavel DosePro; offset by

an increase of \$5.3 million in manufacturing costs related to services and supplies in the testing and manufacturing development of Sumavel DosePro prior to the production of commercial inventories.

*Selling, General and Administrative Expenses.* Selling, general and administrative expenses increased to \$14.1 million for the year ended December 31, 2009 compared to \$11.8 million for the year ended December 31, 2008. This increase of \$2.3 million primarily was due to:

an increase of \$2.7 million in salaries and personnel costs as we expanded our commercial and administrative infrastructure, including the hiring of approximately 20 sales representatives, in preparation for the January 2010 commercial launch of Sumavel DosePro, \$0.2 million in travel related expenses and \$0.2 million in facilities costs; offset by

a decrease of \$0.8 million of expenses associated with consulting and professional services.





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**Table of Contents**

*Interest Income.* Interest income decreased to \$10,000 for the year ended December 31, 2009 compared to \$696,000 for the year ended December 31, 2008. This decrease of \$686,000 was due primarily to the decrease in average cash and investment balances as a result of investing the proceeds received from our Series B preferred stock financing and Astellas in lower yielding instruments.

*Interest Expense.* Interest expense increased to \$9.2 million for the year ended December 31, 2009 compared to \$1.7 million for the year ended December 31, 2008. This increase of \$7.5 million was primarily due to:

an increase of \$1.0 million in the amortization of debt issuance cost, debt discount costs and interest expense in connection with the loan and security agreement with GE Capital entered into in March 2007 and the \$18.0 million loan and security agreement with Oxford and CIT entered into in June 2008;

an increase of \$3.5 million in interest and the amortization of debt discount costs in connection with the \$14.8 million borrowed under the 2009 Notes; and

recognition of \$3.0 million in fair value of the right to convert the outstanding principal and interest under the 2009 Notes to convertible preferred stock.

*Change in Fair Value of Warrant Liability.* Change in the fair value of warrant liability changed to \$0.8 million in expense for the year ended December 31, 2009 compared to \$1.1 million in income for the year ending December 31, 2008 due to the increase in fair value of our Series A-1, Series A-2 and Series B convertible preferred stock.

*Other Income (Expense).* Other expense was \$0.4 million for the year ended December 31, 2009 compared to other income of \$0.1 million for the year ended December 31, 2008. This \$0.5 million increase in expense was due to foreign currency transaction losses which primarily related to the settlement of our liabilities payable in Euro and U.K. pound sterling.

**Liquidity and Capital Resources**

We have experienced net losses and negative cash flow from operations since inception, and as of June 30, 2011, had an accumulated deficit of \$236.3 million, and expect to continue to incur net losses and negative cash flow from operations for at least the next several years primarily as a result of, among other things, the development expenses in connection with our clinical trials and pre-clinical studies for Zohydro and Relday and the cost of the sales and marketing expenses associated with Sumavel DosePro.

As of June 30, 2011, we had cash and cash equivalents of \$7.7 million. In addition, on June 30, 2011, we amended certain terms of our loan agreement with Oxford and SVB including the deferral of principal repayment to commence on February 1, 2012. In July 2011, we entered into equity and royalty financing agreements with Cowen Royalty, pursuant to which we borrowed \$30.0 million from Cowen Royalty and sold \$1.5 million of our common stock to Cowen Royalty resulting in \$29.5 million in net proceeds to us. Although it is difficult to predict future liquidity requirements, based on our current operating plan we believe that the net proceeds from this offering, together with our cash and cash equivalents as of June 30, 2011, future product revenues, borrowings available under our \$10.0 million revolving credit facility with Oxford and SVB and the net proceeds from our recently completed equity and royalty financing with Cowen Royalty, will be sufficient to fund our operations into the third quarter of 2012, although there can be no assurance in this regard. We will need to obtain additional capital to finance our operations beyond that point or possibly earlier. We intend to raise additional capital through debt or equity financings or through collaborations or partnerships with other companies. If we are not able to raise additional capital on terms acceptable to us, or at all, as and when needed, we may be required to reduce or curtail our operations and costs, and we may be unable to continue as a going concern.

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**Table of Contents**

In its report on our consolidated financial statements for the year ended December 31, 2010, 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, as well as the continued availability of borrowings under our amended Oxford/SVB loan agreement. 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 co-promotion agreement. Through June 30, 2011, we received aggregate net cash proceeds of approximately \$215.1 million from the sale of shares of our preferred and common stock as follows:

from August 25, 2006 (inception) to December 31, 2009, we issued and sold a total of 1,444,468 shares of common stock for aggregate net cash proceeds of \$0.2 million;

in August 2006, we issued and sold a total of 30,775,000 shares of Series A-1 convertible preferred stock for aggregate net cash proceeds of \$30.5 million;

in September 2007 and December 2007, we issued and sold an additional 38,025,000 shares of Series A-1 convertible preferred stock for aggregate net cash proceeds of \$38.0 million; in December 2007, we issued and sold a total of 9,090,909 shares of Series A-2 convertible preferred stock for aggregate net cash proceeds of \$9.9 million;

in September 2009, we issued and sold 32,689,062 shares of Series B convertible preferred stock for aggregate net cash proceeds of \$34.8 million (inclusive of \$14.8 million of outstanding principal of convertible notes held by certain investors that we issued earlier in 2009 and that were converted into Series B convertible preferred stock in connection with the financing) and warrants to purchase up to 3,363,619 shares of Series B convertible preferred stock ;

in December 2009, we issued and sold an additional 31,818,171 shares of Series B convertible preferred stock and warrants to purchase up to 9,545,447 shares of Series B convertible preferred stock for aggregate net cash proceeds of \$34.9 million;

in July 2010, we issued unsecured convertible promissory notes in an aggregate amount of \$15.0 million under which all the outstanding principal and interest automatically converted to 3,873,756 shares of common stock upon the completion of our initial public offering; and

in November 2010 and December 2010, we issued and sold a total of 14,436,493 shares of common stock in our initial public offering, including shares issued upon the exercise of the underwriters' over-allotment option, for aggregate net proceeds of \$51.7 million.

In March 2007, we entered into a loan and security agreement with GE Capital for the purpose of financing our capital equipment costs. Under the agreement, we were allowed to borrow up to \$10.0 million based on purchases of property and equipment at a fixed interest rate determined at the time of borrowing. Pursuant to the loan and security agreement, we borrowed approximately \$4.5 million under two promissory notes during the year ended December 31, 2007. We had the option to repay outstanding borrowings under the GE Capital agreement, subject to prepayment fees. The outstanding principal balance of the GE Agreement as of December 31, 2010 was \$675,000 and was repaid in full on June 30, 2011.



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**Table of Contents**

In June 2008, we entered into and borrowed \$18.0 million under the loan and security agreement with Oxford and CIT, or the Oxford loan agreement. The borrowings under the Oxford loan agreement bore an interest rate of 9.76%. Payments consisted of interest-only payments for the first 10 months followed by principal and interest payments for the subsequent 36 months. The agreement required a final payment of \$1.0 million, in addition to principal repayments, at final maturity, which was May 1, 2012. As described below, we amended and restated the Oxford loan agreement in July and again in October 2010, and entered into an amendment to the Oxford loan agreement in June 2011.

In July 2009, we entered into the co-promotion agreement with Astellas. In connection with this co-promotion agreement, Astellas made a non-refundable up-front payment to us of \$2.0 million and agreed to make an additional \$18.0 million of payments to us upon the achievement of a series of milestones. As of June 30, 2011, we received the entire \$20.0 million in milestone payments from Astellas.

In July and October 2010, we amended and restated the Oxford loan agreement and Oxford and SVB became parties to such amended Oxford loan agreement. The amended Oxford loan agreement consists of a \$25.0 million term loan and a \$10.0 million revolving credit facility. The obligations under the amended Oxford loan agreement are secured by substantially all of our personal property (including, among other things, cash, accounts receivable, equipment, inventory, contract rights or rights to payment of money, license agreements, and general intangibles, excluding all intellectual property).

On June 30, 2011, we amended the existing loan agreement with Oxford and SVB to provide for, among other things, the addition of intellectual property to the collateral securing the Oxford/SVB loan and deferral of principal repayment to commence on February 1, 2012. In connection with entering into the amended Oxford/SVB loan agreement, we issued to Oxford and SVB warrants exercisable into an aggregate of 26,455 shares of our common stock. The warrants are exercisable at \$3.78 per share of common stock and have a term of 7 years.

The amended Oxford/SVB loan agreement includes financial covenants requiring that we achieve, as of the last day of each month measured on a trailing three-month basis, actual revenue of at least a specified percentage of our projected revenue as provided to Oxford and SVB in the event we fail to maintain a liquidity ratio (defined, in general, as the ratio of (a) cash and cash equivalents deposited with SVB plus unused borrowing capacity under that agreement to (b) all debt, capital lease obligations and contingent obligations owed to the lenders) of 1.25 to 1.00. The agreement also includes a covenant that the audit report accompanying our year-end consolidated financial statements for fiscal year 2010 and thereafter not include a going concern qualification. In March 2011, we obtained a waiver from Oxford and SVB for the breach caused by the receipt of the 2010 audit report from our independent registered public accounting firm, which includes a modification of their standard report for the going concern uncertainty. In addition, the amended Oxford/SVB loan agreement prohibits us, subject to certain customary exceptions, from (1) incurring any debt other than, among other things, debt under the amended Oxford/SVB loan agreement, and other debt permitted thereunder, and (2) entering into mergers with, or acquisitions of all or substantially all the assets of, another entity with a value in excess of \$100,000, and also prohibits the occurrence of a change in control of our company, as defined in the amended Oxford/SVB loan agreement. The agreement provides that an event of default will occur if, among other customary events of default, (1) there is a material adverse change in our business, operations or condition (financial or otherwise) or material impairment in the prospects of us repaying any portion of our obligations under the agreement (2) there is a material impairment in the value of the collateral pledged to secure our obligations under the agreement or in the perfection or priority of such collateral, (3) we default in the payment of any amount payable under the agreement when due, or (4) we breach any covenant in the agreement (subject to a grace period in some cases). The \$25.0 million term loan bears an interest rate of 12.06% per annum. Payments consist of monthly interest only payments through January 2012, followed by principal and interest payments for the subsequent 24 months. The term loan requires a final payment of \$1.2 million, in addition to the repayment of unpaid principal, at the loan maturity date, which is on the earliest of January 1, 2014, the occurrence of an event of default resulting in our obligations becoming due and payable in accordance with the amended Oxford/SVB loan agreement or the date of any prepayment of all outstanding obligations under the

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**Table of Contents**

amended Oxford/SVB loan agreement. We have the option to prepay the outstanding balance of the term loan in full subject to a prepayment fee of either 2% or 3% of the principal amount being prepaid depending upon when the prepayment occurs as well as the \$1.2 million final payment. Under the terms of the revolving credit facility, we may borrow up to \$10.0 million, but not more than a specified percentage of our eligible accounts receivable and inventory balances (as defined in the agreement). Amounts outstanding under the revolving credit facility accrue 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 pay a monthly fee equal to 0.5% per annum of the average unused portion of the revolving credit facility. If the revolving credit facility is terminated, a final payment is required in the amount of \$0.1 million, \$0.2 million or \$0.3 million depending upon when the termination occurs. The amended Oxford/SVB loan agreement matures on the earliest of January 1, 2014, the occurrence of an event of default resulting in our obligations becoming due and payable in accordance with the amended Oxford/SVB loan agreement or the date of any prepayment of all outstanding obligations under the amended Oxford/SVB loan agreement, at which time a final payment of \$0.1 million, plus all unpaid principal, must be paid in full. As of June 30, 2011, we had borrowed \$3.7 million under the revolving credit facility. For additional information about the amended Oxford/SVB loan agreement, see Note 6 to our consolidated financial statements appearing elsewhere in this prospectus.

On July 18, 2011, we closed the royalty financing agreement with Cowen Royalty, or the financing agreement. Under the terms of the financing agreement, we borrowed \$30.0 million and we are obligated to repay such borrowed amount together with a specified return to Cowen Royalty, through the payment of tiered royalties ranging from .5% to 5% of our direct product sales, co-promotion revenues and out-license revenues (collectively, revenue interest) that we record or receive as a result of worldwide commercialization of our products including Sumavel DosePro, Zohydro and other future products. Pursuant to the terms of the financing agreement, in the event our co-promotion agreement with Astellas is terminated prior to June 30, 2013, our royalty rate will increase to 5.75%, with a reversion back to 5% possible if certain net sales of Sumavel DosePro are achieved or if Zohydro is commercialized in the four calendar quarters immediately following the effective date of termination.

We are also obligated to make three fixed payments to Cowen Royalty of \$10.0 million on (or before at our option) each of January 31, 2015, January 31, 2016 and January 31, 2017. Pursuant to a subordination and intercreditor agreement executed between us, Oxford, SVB and Cowen Royalty, prepayment of the financing agreement requires the consent of the lenders under the amended Oxford/SVB loan agreement while balances remain outstanding under that facility.

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

Cowen Royalty also has the option to terminate the financing agreement at its election in connection with a change of control of our company, as defined in the financing agreement, the sale of all or substantially all of our assets (which includes the sale, transfer, assignment or licensing of our rights in the United States to either Sumavel DosePro or Zohydro), a bankruptcy event with respect to our company or an event of default, as defined in the financing agreement. Upon such a termination by Cowen Royalty, we are obligated to make a payment of a base amount of \$45 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 fixed payments received by Cowen Royalty up to the date of prepayment.

Unless terminated earlier as discussed above, the financing agreement terminates on March 31, 2018. For additional information about the financing agreement, see Note 11 to our consolidated financial statements appearing elsewhere in this prospectus.

**Table of Contents**

In connection with the financing agreement, in July 2011 we issued and sold 388,601 shares of our common stock to Cowen Royalty for gross proceeds of \$1.5 million and issued to Cowen Royalty warrants to purchase 225,000 shares of our common stock at an exercise price of \$9.00 per share. We also granted Cowen Royalty the right to purchase \$1.5 million of shares of our common stock in the first bona fide equity financing following the date of the financing agreement that would result in gross proceeds to us of at least \$15.0 million, at a price equal to the price paid by other investors participating in such equity financing. Cowen Royalty has indicated an interest in purchasing such shares in this offering.

We received total net proceeds, after expenses, of \$29.5 million from the borrowings under the financing agreement and the sale of common stock to Cowen Royalty.

We depend in part upon borrowings available under the revolving credit facility provided under the amended Oxford/SVB loan agreement, the term loan obtained under the Oxford/SVB loan agreement and the borrowed amount under the Cowen Royalty financing agreement to finance our ongoing operations. Accordingly, any termination of those agreements, or any requirement that we repay any of our outstanding term loans or the borrowed amount under the 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 \$7.7 million and \$49.2 million at June 30, 2011 and December 31, 2010, respectively.

The following table summarizes our cash flows used in operating, investing and financing activities for the six months ended June 30, 2011 and 2010 and the years ended December 31, 2010, 2009, and 2008:

	Six Months Ended June 30,		Year Ended December 31,		
	2011	2010	2010	2009	2008
	(In Thousands)				
<b>Statement of Cash Flows Data:</b>					
Total cash provided by (used in):					
Operating activities	\$ (40,507)	\$ (35,821)	\$ (71,952)	\$ (32,361)	\$ (41,288)
Investing activities	(366)	(1,162)	(3,442)	(2,057)	(2,793)
Financing activities	(627)	(3,435)	79,655	65,104	16,798
Increase (decrease) in cash and cash equivalents	\$ (41,500)	\$ (40,418)	\$ 4,261	\$ 30,686	\$ (27,283)

*Operating Activities.* Net cash used in operating activities was \$40.5 million and \$35.8 million for the six months ended June 30, 2011 and 2010, respectively. Net cash used for the six months ended June 30, 2011 and 2010 primarily reflects the use of \$34.4 million and \$34.0 million, respectively for operations (excluding non-cash items), investments of \$0.3 million and \$2.2 million, respectively, in commercial inventory of Sumavel DosePro, and cash used of \$5.8 million and cash provided of \$0.4 million, respectively, for other working capital uses.

Net cash used in operating activities was \$72.0 million, \$32.4 million and \$41.3 million for the years ended December 31, 2010, 2009 and 2008, respectively. Net cash used for the year ended December 31, 2010 primarily reflects the use of \$71.3 million for operations (excluding non-cash items), payment of a \$4.0 million milestone obligation to Aradigm as a result of the first commercial sale of Sumavel DosePro, and investments of \$3.9 million in commercial inventory of Sumavel DosePro, partially offset by \$7.2 million provided by other working capital sources. Net cash used for the year ended December 31, 2009 primarily reflects expenditures related to testing and manufacturing development of Sumavel DosePro, personnel-related costs, third-party supplier expenses and professional fees. Net cash used for the year ended December 31, 2008 primarily reflects expenditures related to external research and product development, clinical trial costs, personnel related costs, third-party supplier expenses and professional fees.

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**Table of Contents**

*Investing Activities.* Net cash used in investing activities was \$0.4 million and \$1.2 million for the six months ended June 30, 2011 and 2010, respectively. These amounts are the result of the purchase of property and equipment primarily for use in manufacturing Sumavel DosePro.

Net cash used in investing activities was \$3.4 million, \$2.1 million and \$2.8 million for the years ended December 31, 2010, 2009 and 2008, respectively. These amounts are the result of the purchase of property and equipment and in 2008 inclusive of the net purchases, sales and maturities of investment securities.

We expect to incur capital expenditures of approximately \$0.4 million to \$0.9 million in the last six months of 2011. These planned capital expenditures primarily relate to further investments in our manufacturing operations intended to enhance our existing manufacturing technology and equipment.

*Financing Activities.* Net cash used in financing activities was \$0.6 million and \$3.4 million for six months ended June 30, 2011 and 2010, respectively. Net cash used in financing activities for the six months ended June 30, 2011 relates to the repayment of the GE Capital equipment financing of \$0.6 million, payment of fees to Oxford in connection with the amended Oxford/SVB loan agreement of \$0.1 million and net proceeds from borrowings under our revolving credit facility of \$0.1 million. Net cash used in financing activities for the six months ended June 30, 2010 relates to payments on borrowings of debt.

Net cash provided by financing activities was \$79.7 million, \$65.1 million and \$16.8 million for the years ended December 31, 2010, 2009 and 2008, respectively. Net cash provided by financing activities for the year ended December 31, 2010 relates to \$51.7 million in net proceeds received in connection with our initial public offering, \$31.1 million in net proceeds received in connection with the amended Oxford loan agreement, \$15.0 million in proceeds received in connection with the 2010 Notes, offset by principal repayments made of \$18.2 million on our outstanding debt facilities. Net cash provided by financing activities for the year ended December 31, 2009 relates to \$14.8 million in proceeds received in connection with the 2009 Notes and \$54.9 million in net proceeds received in connection with our Series B convertible preferred stock financing offset by \$4.7 million in principal repayments on our outstanding debt facilities. Net cash provided by financing activities for the year ended December 31, 2008 relates to \$17.8 million in net proceeds received in connection with the amended Oxford loan agreement, offset by principal repayments made of \$1.0 million on our outstanding debt facilities.

Our sources of liquidity include our cash balances, cash receipts from the sale of Sumavel DosePro, our debt facilities, and the proceeds from the recently completed equity and royalty financing with Cowen Royalty. As of June 30, 2011, we had \$7.7 million in cash and cash equivalents and in July 2011, we received an additional \$29.5 million in cash under our equity and royalty financing with Cowen Royalty. Other potential sources of near-term liquidity include (i) entering into a commercialization agreement for Zohydro or a licensing arrangement on our DosePro technology, (ii) equity, debt or other financing or (iii) leveraging our sales force capacity to promote a new product.

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 co-promotion agreement. Through June 30, 2011, we received aggregate net cash proceeds of approximately \$263.9 million from the sale of shares of our preferred and common stock, the issuance of notes and payments from collaborators. Although we will continue to be opportunistic in our efforts to obtain cash, there is no guarantee that additional funding will be available or that, if available, such funding will be adequate or available on terms that we or our stockholders view as favorable. In addition, as a result of our outstanding loans with Oxford and SVB and Cowen Royalty, our ability to engage in debt financing transactions is subject to certain limitations and certain debt financing transactions, if consummated, may accelerate our repayment obligations to Oxford and SVB and Cowen Royalty.

Our ability to continue our efforts to commercialize our product and develop our product candidates 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



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**Table of Contents**

marketing and general and administrative expenditures and may adjust such expenditures based upon a variety of factors, such as our available cash, our ability to obtain additional cash, the results and progress of our Sumavel DosePro commercialization efforts, results and progress in our clinical programs, the time and costs related to clinical trials and regulatory decisions, as well as the U.S. economic environment.

As described above, under our amended Oxford/SVB loan agreement, we are subject to financial covenants that require us to achieve certain revenue targets in the event we fail to maintain a liquidity ratio (defined, in general, as the ratio of (a) cash and cash equivalents deposited with SVB plus unused borrowing capacity under that agreement to (b) all debt, capital lease obligations and contingent obligations owed to the lenders) of 1.25 to 1.00 and we are also subject to other covenants and obligations under that agreement. Likewise, the amended Oxford/SVB loan agreement permits the lenders to demand the immediate repayment of all borrowings and other amounts outstanding thereunder if, among other customary events of default, the lender determines, in its sole discretion that a material adverse change with respect to us has occurred. As noted above, we have agreed to specified positive and negative covenants under the financing agreement with Cowen Royalty and upon a termination by Cowen 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 Cowen 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 either the amended Oxford/SVB loan agreement or the financing agreement with Cowen Royalty when due, if we breach our other covenants or obligations under either of these agreements or if other events of default under either of these agreements occur, the applicable lenders 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 2009, 2010 and 2011 we were required to obtain amendments or waivers under our credit facilities.

We cannot be certain if, when and to what extent we will generate positive cash flow from operations from the commercialization of our product and, if approved, product candidates. We expect our development and commercialization expenses to be substantial and to increase over the next few years as we continue to grow the Sumavel DosePro brand, continue to advance our Zohydro product through Phase 3 clinical trials and potentially through commercialization and initiate clinical development of Relday.

Although it is difficult to predict future liquidity requirements, we believe, based on our current operating plan, that the net proceeds from this offering, together with our cash and cash equivalents as of June 30, 2011, future product revenues, borrowings available under our \$10.0 million revolving credit facility with Oxford and SVB and the net proceeds from our recently completed equity and royalty financing with Cowen Royalty, will be sufficient to fund our operations into the third quarter of 2012, although there can be no assurance in that regard. We will need to obtain additional capital to finance our operations beyond that point through public or private equity or debt financings. Although we are currently not a party to any agreement or letter of intent with respect to potential investments in, or acquisitions of, businesses, services or technologies, we may enter into these types of arrangements in the future, which could also require us to seek additional equity or debt financing. There can be no assurance that we will be able to raise additional funds from any of these sources on terms we deem acceptable, or at all. In addition, future issuance of equity, convertible or other equity-linked securities could materially dilute the ownership interests of holders of our common stock and additional debt financing could result in a material increase in the amount of cash necessary to fund debt service payments and also could require that we comply with financial and other covenants that limit our flexibility and operations. In addition, the fact

**Table of Contents**

that we have pledged substantially all of our assets to secure our existing loan facilities will likely increase the cost, perhaps substantially, of any additional debt financing we may obtain or prevent us from obtaining additional debt financing altogether.

**Contractual Obligations and Commitments**

The following table describes our long-term contractual obligations and commitments as of June 30, 2011 (unaudited):

	Total	Payments Due by Period			After 5 Years
		Less than 1 Year	1-3 Years (In Thousands)	4-5 Years	
Debt obligations <sup>(1)</sup>	\$ 28,714	\$ 8,439	\$ 20,275	0	0
Debt interest <sup>(2)</sup>	6,220	2,921	3,299	0	0
Operating lease obligations <sup>(3)</sup>	3,743	1,522	2,083	138	0
Co-Promotion marketing & promotional expenses <sup>(4)</sup>	1,162	1,162	0	0	0
Purchase obligations <sup>(5)</sup>	18,809	10,218	8,591	0	0
Total	\$ 58,648	\$ 24,262	\$ 34,248	\$ 138	0

- (1) Represents principal payments due in each period on our loan and security agreement with Oxford Finance Corporation and Silicon Valley Bank and outstanding balances under our revolving credit facility with Oxford Finance Corporation and Silicon Valley Bank.
- (2) Includes the interest on regular scheduled debt payments to Oxford Finance Corporation and Silicon Valley Bank at an annual rate of 12.06%.
- (3) Includes the minimum rental payments for our San Diego, California office pursuant to a lease entered into in October 2009 and expiring, as extended, in 2012. Also includes the minimum rental payments for our Emeryville, California office pursuant to a lease entered into in July 2007 and expiring, as extended, in September 2015. Also includes the rental payments for a fleet of up to 95 vehicles pursuant to a lease entered into in August 2009. Each vehicle has a lease term of 36 months.
- (4) Represents our portion of the shared marketing and promotional costs as agreed between us and Astellas for 2011 joint promotional efforts for Sumavel DosePro. These obligations are determined on an annual basis through the term of the agreement.
- (5) Primarily represents non-cancellable purchase orders for the production of key components of Sumavel DosePro and a minimum manufacturing fee payable to Patheon UK Limited, our contract manufacturing organization.

Under our co-promotion agreement with Astellas, we are 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. Under our asset purchase agreement with Aradigm, we are required to pay a 3% royalty on global net sales of Sumavel DosePro by us or one of our licensees and, in the event that we or one of our future licensees, if any, commercializes a non-sumatriptan product in the DosePro delivery system, we are required to pay Aradigm, at our election, either a 3% royalty on net sales of each non-sumatriptan product commercialized or a fixed low-twenties percentage of royalty revenue received by us from the licensee. In addition, under our license agreement with Elan we paid a milestone payment in the amount of \$750,000 in connection with the completion of the treatment phase of our pivotal efficacy phase 3 clinical trial, Study 801, and we may be required to pay up to \$3.75 million in total future milestone payments with respect to Zohydro depending upon the achievement of various development and regulatory events. In addition, if Zohydro is approved, we will be required to pay a mid single-digit percentage royalty on its net sales for a specified period of time and continue to pay royalties on net sales of the product thereafter at a reduced low single-digit percentage rate in accordance with the terms of the license agreement. We also maintain agreements with third parties to manufacture our product, conduct our clinical trials and perform data collection and analysis. Our payment obligations under these

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## **Table of Contents**

agreements will likely depend upon the progress of our development programs, sales of our product and commercialization efforts. Therefore, we are unable at this time to estimate with certainty the future costs we will incur under these agreements.

### **Recent Accounting Pronouncements**

In October 2009, the Financial Accounting Standards Board, or the FASB, issued an Accounting Standard Update which replaced the concept of allocating revenue consideration amongst deliverables in a multiple-element revenue arrangement according to fair value with an allocation based on selling price. The amended guidance also establishes a hierarchy for determining the selling price of revenue deliverables sold in multiple element revenue arrangements. The selling price used for each deliverable will be based on vendor-specific objective evidence, or VSOE, if available, third-party evidence if VSOE is not available, or management's estimate of an element's stand-alone selling price if neither VSOE nor third-party evidence is available. The amendments in this update also require an allocation of selling price amongst deliverables be performed based upon each deliverable's relative selling price to total revenue consideration, rather than on the residual method previously permitted. The updated guidance is effective for the first annual reporting period beginning on or after June 15, 2010, and may be applied retrospectively for all periods presented or prospectively to arrangements entered into or materially modified after the adoption date. We prospectively adopted the updated guidance on January 1, 2011 and will apply the amended guidance to revenue arrangements containing multiple deliverables that are entered into or significantly modified on or after January 1, 2011. We will now allocate revenue consideration, excluding contingent consideration, based on the relative selling prices of the separate units of accounting contained within an arrangement containing multiple deliverables. Selling prices are determined using fair value, when available, or our estimate of selling price when fair value is not available for a given unit of accounting. As we did not enter into any new collaborations or materially modify any existing collaborations, adoption of this guidance had no impact on our results of operations for the six months ended June 30, 2011.

In January 2010, the FASB issued a new accounting standard which amends guidance on fair value measurements and disclosures. The new guidance requires disclosure of transfers into and out of Level 1 and Level 2 fair value measurements, and also requires more detailed disclosure about the activity within Level 3 fair value measurements. This standard is effective for annual and interim reporting periods beginning after December 15, 2009, except for the requirements related to Level 3 disclosures, which are effective for annual and interim reporting periods beginning after December 15, 2010. We adopted the relevant provisions of this guidance, and the adoption did not have a material impact on our consolidated financial statements.

In February 2010, the FASB issued a new accounting standard which amends guidance on subsequent events. The new guidance requires evaluation of subsequent events through the date the financial consolidated statements are issued for Securities and Exchange Commission, or SEC, filers, amends the definition of an SEC filer, and changes required disclosures. This standard is effective on February 24, 2010 and did not have a material impact on our consolidated financial statements upon adoption.

In March 2010, the FASB Emerging Issues Task Force, or the EITF, ratified a new accounting standard which amends guidance on the milestone method of revenue recognition. The EITF concluded that the milestone method is a valid application of the proportional performance model when applied to research or development arrangements. Milestones, as defined per the revised guidance, are (1) events that can only be achieved in whole or in part on either the entity's performance or on the occurrence of a specific outcome resulting in the entity's performance (2) for which there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and (3) that would result in additional payments being due to us. We evaluate events under this guidance at the inception of an arrangement to determine the existence of milestones and if they are substantive. This standard allows an entity to make an accounting policy election to recognize a payment that is contingent upon the achievement of a substantive milestone in its entirety in the period in which the milestone is achieved. This standard is effective for fiscal years beginning on or after June 15, 2010 with early adoption permitted. The guidance may be applied prospectively for milestones achieved after the adoption date or

## **Table of Contents**

retrospectively for all periods presented. We adopted this guidance on January 1, 2011 on a prospective basis. Adoption of this guidance did not have a material impact on our results of operations.

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

## **Off-Balance Sheet Arrangements**

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

## **Quantitative and Qualitative Disclosures About Market Risk**

### *Interest Rate Risk*

Our cash and cash equivalents as of June 30, 2011 consisted primarily 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 while at the same time maximizing the income we receive without significantly increasing risk. 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.

Our \$10.0 million revolving credit facility with Oxford and SVB bears interest at the greater of 3.29% above SVB's prime rate or 7.29%. As of June 30, 2011, we had \$3.6 million outstanding on this revolving credit facility.

### *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 manufactures are denominated in the Euro and U.K. pound 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 six months ended June 30, 2011, approximately \$12.1 million (based on exchange rates as of June 30, 2011) of our materials and contract manufacturing costs were denominated in foreign currencies. We do not currently hedge our foreign currency exchange rate risk. As a result, we are exposed to gains and/or losses as the exchange rate of certain foreign currencies fluctuates. A 10% increase or decrease in the average rate of the Euro or the U.K. pound sterling during the six months ended June 30, 2011 would have resulted in approximately \$0.5 to \$0.6 million or \$0.6 to \$0.7 million in gains or losses, respectively. We intend to evaluate various options to mitigate the risk of financial exposure from transacting in foreign currencies in the future.

**Table of Contents****BUSINESS****Overview**

We are a pharmaceutical company commercializing and developing products for the treatment of central nervous system disorders and pain. Our first commercial product, Sumavel<sup>®</sup> DosePro<sup>®</sup> (*sumatriptan* injection) Needle-free Delivery System, was launched in January 2010. Sumavel DosePro offers fast-acting, easy-to-use, needle-free subcutaneous administration of *sumatriptan* for the acute treatment of migraine and cluster headache in a pre-filled, single-use delivery system. Sumavel DosePro is the first drug product approved by the U.S. Food and Drug Administration, or FDA, that allows for the needle-free, subcutaneous delivery of medication. Sumavel DosePro may serve as a treatment alternative to oral and nasal triptans and may offer simple, convenient administration when compared to traditional, needle-based *sumatriptan* injection. As a result, we believe that Sumavel DosePro has the potential to be prescribed by a broad physician audience, especially for difficult to treat migraine episodes. For the six months ended June 30, 2011, we recognized \$16.2 million in net product revenue from sales of Sumavel DosePro, represented by more than 32,000 aggregate dispensed prescriptions.

Migraine is a syndrome that affects approximately 30 million people in the United States, according to a 2010 National Headache Foundation, or NHF, press release. Triptans are the class of drugs most often prescribed for treating migraines. In the United States in the 12 months ended December 2010, triptans generated sales of approximately \$3.5 billion and *sumatriptan*, including branded and generic forms, represented the largest market share of the seven approved triptans, with sales of approximately \$2.1 billion, according to Wolters Kluwer Pharma Solutions (Source<sup>®</sup> PHAST Institution/Retail).

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. Our sales and marketing organization is comprised of approximately 100 professionals. Our field sales force of approximately 80 representatives promotes Sumavel DosePro primarily to neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. To build upon our success in growing Sumavel DosePro prescriptions, we have initiated activities to expand our field sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. Our promotional efforts are complemented by our collaboration with Astellas and approximately 400 of its sales representatives, who are promoting Sumavel DosePro primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists in the United States. We also have entered into a partnership for Sumavel DosePro with Desitin Arzneimittel GmbH, or Desitin, to accelerate development and regulatory approvals in Europe and further enhance the global commercial potential of Sumavel DosePro.

Sumavel DosePro continues to add new and repeat prescribers in both the neurology and primary care settings. The product is also gaining use from a range of patient segments, including new triptan users, patients being converted to the product from other migraine drugs and patients who have been prescribed Sumavel DosePro and also have other triptan prescriptions. Through our ongoing efforts with the largest commercial health plans, Sumavel DosePro is achieving broad coverage in the United States, with a reimbursement claims approval rate of approximately 80% since launch through June 2011 (Source<sup>®</sup> Dynamic Claims January 2010 – June 2011).

Our lead product candidate, Zohydro, is a novel, oral, single-entity extended-release formulation of *hydrocodone* currently in Phase 3 development for the treatment of moderate to severe chronic pain in patients requiring around-the-clock opioid therapy. Zohydro utilizes Elan Pharma International Limited's, or Elan's, proprietary Spheroidal Oral Drug Absorption System, or SODAS<sup>®</sup> technology, which serves to enhance the release profile of *hydrocodone* to provide consistent 12-hour pain relief relative to existing immediate-release combination formulations. Most marketed *hydrocodone* products contain the analgesic combination ingredient *acetaminophen*, which if taken in high quantities over time can cause liver toxicity. Zohydro, if approved, may represent the first available extended-release version of *hydrocodone* and also the first *hydrocodone* product that is not combined with another analgesic. As a result, we believe Zohydro could generate sales from both patients who are using immediate-release opioid products on a chronic basis and patients already using extended-release opioids. We initiated the Phase 3 clinical development program for Zohydro in March 2010 and reported positive top-line results

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## **Table of Contents**

for our pivotal Phase 3 efficacy trial in August 2011. The trial successfully met its primary efficacy endpoint in demonstrating a significant difference ( $p=0.008$ ) between the mean changes in daily pain intensity Numeric Rating Scale (NRS) scores between Zohydro and placebo groups. We expect to submit a new drug application, or NDA, with the FDA by early 2012. We in-licensed exclusive U.S. rights to Zohydro from Elan in 2007.

The American Pain Society estimated in 1999 that 9% of the U.S. adult population suffers from moderate to severe non-cancer related chronic pain. Chronic pain can be treated with both immediate-release and extended-release opioids. We define our target market for Zohydro as prescription, non-injectable *codeine*-based and extended-release *morphine*-based pain products. This market generated U.S. sales of approximately \$13.5 billion for the year ended December 2010, based on average wholesale price, on approximately 206 million prescriptions. During the same period, existing *hydrocodone* products, the most commonly prescribed pharmaceutical products in the United States, generated \$3.2 billion in sales on approximately 128 million prescriptions. (Source<sup>®</sup> PHAST Retail). We believe Zohydro has the potential to be an important therapeutic alternative to existing *hydrocodone* products, including the branded product Vicodin and its generic equivalents.

We are also developing Relday, a proprietary, long-acting injectable formulation of *risperidone* using Durect's SABER controlled-release formulation technology in combination with our DosePro needle-free, subcutaneous drug delivery system through a July 2011 development and license agreement with Durect Corporation. *Risperidone* is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. If successfully developed and approved, we believe Relday may be the first once-monthly, subcutaneous antipsychotic product available in a needle-free delivery system. The existing long-acting injectable *risperidone* product achieved global net sales of \$1.5 billion in 2010, according to industry reports, and requires twice monthly, 2 mL intramuscular injections with a 21 gauge or larger needle. We believe the combination of our DosePro technology with Durect's SABER controlled-release technology will allow Relday to be delivered subcutaneously without a needle on a once-monthly basis with a simplified dosing regimen, improved pharmacokinetic profile and significant reduction in injection volume versus currently marketed long-acting injectable antipsychotics. Based upon these characteristics, Relday may provide an important alternative to currently marketed long-acting injectable antipsychotics as well as a new long-acting treatment option for patients that currently use daily oral antipsychotic products. We intend to initiate clinical studies for Relday in patients with schizophrenia in early 2012 following the filing of an investigational new drug, or IND, application. We completed a pre-IND meeting with the FDA in December 2009.

Our DosePro technology is a novel, patent-protected, needle-free drug delivery system designed for self-administration of a pre-filled, single dose of liquid drug. We believe the FDA's approval of Sumavel DosePro represents an important validation of the technology. Results from our pre-clinical and clinical studies demonstrate that DosePro can be used successfully with small molecules and biological products, including protein therapeutics and monoclonal antibodies. We are building our internal product pipeline by investigating proven drugs that can be paired with DosePro to enhance their benefits and commercial attractiveness, such as with Relday. In addition to Relday, we are also evaluating the market potential, formulation requirements and clinical development pathway of an additional central nervous system, or CNS, compound that could be paired with DosePro to enhance its commercial attractiveness. We are also seeking to capitalize on our DosePro technology by out-licensing it to potential partners enabling them to enhance, differentiate or extend the life cycle of their proprietary injectable products. We acquired the DosePro technology and related intellectual property from Aradigm Corporation in August 2006.

### **Investment Highlights**

We believe we are differentiated by the unique characteristics of our marketed product, Sumavel DosePro, and our late stage product candidate, Zohydro, each of which addresses large market opportunities, as well as our established commercial infrastructure, our innovative technology and the depth of experience of our management team. The following represents the key attributes that help differentiate our company:

*Fully-integrated pharmaceutical company with established commercial infrastructure.* We have a sophisticated and robust commercial infrastructure relative to many companies of similar size and stage

**Table of Contents**

of development in the pharmaceuticals industry. Our sales and marketing organization is comprised of approximately 100 professionals, including a field sales force of approximately 80 representatives who are focused exclusively on the promotion of Sumavel DosePro. We have initiated activities to expand our sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. Our field sales representatives have an average of 12 years of prior experience promoting pharmaceutical products and most have prior experience in the neurology and/or migraine space. In addition, our sales managers have on average 19 years of pharmaceutical industry experience, including an average of eight years of sales management experience.

*Sumavel DosePro, a differentiated entrant in the migraine market that has demonstrated significant quarterly growth in total prescriptions since its launch.* Our first commercial product, Sumavel DosePro, was launched in January 2010. We believe it represents a valuable migraine treatment option that addresses the significant unmet medical needs of patients and physicians. Through our own sales force and our collaboration with Astellas, we have a combined network of more than 475 sales representatives detailing both primary care physicians and specialists who are prescribers of migraine therapeutics. To date, we have seen consistent growth in adoption of Sumavel DosePro by physicians and patients alike, with more than 11,000 prescribing physicians through June 2011, of whom a growing proportion are now repeat-prescribers. (Source<sup>®</sup> Wolters Kluwer Pharma Solutions Source<sup>®</sup> Prescriber January 2010 – June 2011). Monthly prescriptions of Sumavel DosePro have grown from less than 250 in January 2010 to more than 6,300 in June 2011. (Source<sup>®</sup> PHAST Retail January 2010 – June 2011). Sumavel DosePro's acceptance by third-party payors has also been encouraging, with approximately 80% of reimbursement claims submitted for Sumavel DosePro being approved since its launch (Source<sup>®</sup> Dynamic Claims January 2010 – June 2011).

*Zohydro, a novel, extended-release chronic pain therapy with positive top-line pivotal Phase 3 efficacy trial results and anticipated NDA submission by early 2012.* Zohydro has the potential to be the first approved single-entity, extended-release formulation of hydrocodone, the most widely prescribed pharmaceutical product in the United States. Zohydro utilizes Elan's proprietary SODAS delivery system, which serves to enhance the release profile of hydrocodone to provide consistent 12-hour pain relief relative to existing immediate-release formulations. In March 2010, we initiated our Phase 3 development program for Zohydro, and we reported positive top-line results from our pivotal Phase 3 efficacy trial in August 2011. We expect to submit an NDA with the FDA for Zohydro by early 2012.

*Validated, proprietary DosePro technology with broad range of potential applications, including our newest product candidate, Relday, a proprietary, long-acting injectable formulation of risperidone.* Sumavel DosePro, which utilizes our DosePro technology, is the first drug product approved by the FDA which allows for the needle-free, subcutaneous delivery of medication. We believe that DosePro has the potential to become a preferred delivery option for patients and physicians for many medications beyond sumatriptan, including small molecules and biologics. In July 2011, we entered into a development and license agreement with Durect pursuant to which we will develop Relday, a proprietary, long-acting injectable formulation of risperidone paired with our DosePro technology for the treatment of the symptoms of schizophrenia. We are also evaluating further internal development candidates and technology out-licensing opportunities. We and the predecessor owners of the DosePro technology have invested significant resources over a 10 year period in evaluating potential applications of DosePro and optimizing the design, manufacturing and versatility of this technology. As of August 16, 2011, our patent portfolio included eight issued U.S. patents, three pending U.S. patent applications, 38 issued foreign patents and three pending foreign patent applications relating to various aspects of Sumavel DosePro and our DosePro technology. The eight issued U.S. patents are expected to expire on various dates from 2014 through 2026.

*Experienced management team with unique commercial and development expertise, including CNS sales and marketing experience.* Our management team has a proven clinical, regulatory, business development and commercialization track record at Zogenix and prior organizations, as well as significant expertise in CNS disorders and pain. Our executive officers and key employees have an

**Table of Contents**

average of 20 years of experience in the pharmaceutical, financial and commercial sectors. Prior to Zogenix, members of our management team had success in developing, achieving regulatory approval for and commercializing multiple product candidates at their former employers. In particular, our Chief Executive Officer and our Vice President of Sales and Managed Markets participated in the successful launch and market defense of GlaxoSmithKline's, or GSK's, Imitrex, the first triptan to be commercialized in the United States. At Zogenix, our team has successfully acquired, developed, obtained regulatory approval for and launched the commercial sale of Sumavel DosePro and completed a significant primary care co-promotion agreement in the United States for the product. It also initiated and has significantly advanced our Phase 3 development program for our Zohydro product candidate.

**Our Strategy**

Our core strategy is to commercialize and develop differentiated CNS and pain therapeutics that can address significant unmet medical needs and overcome limitations of existing products. Key elements of our strategy include:

*Increasing sales and continuing to drive patient and physician adoption of Sumavel DosePro in the United States.* Total U.S. net product revenue from sales of Sumavel DosePro for the six months ended June 30, 2011 were \$16.2 million, as compared to \$6.1 million for the same period in 2010. We continue to leverage our established commercial infrastructure, our collaboration with Astellas and our investment in sales and marketing programs to help increase awareness and adoption of, and access to, Sumavel DosePro with prescribers, patients, third-party payors, pharmacists and employers.

*Developing and commercializing Zohydro for the treatment of moderate to severe chronic pain.* Our ongoing Phase 3 clinical program for Zohydro is focused on establishing safety and efficacy of extended-release single-entity *hydrocodone* to treat moderate to severe chronic pain in patients requiring around-the-clock opioid therapy. We reported positive top-line results from our pivotal Phase 3 efficacy trial in August 2011 and expect to submit an NDA with the FDA by early 2012. If we receive FDA approval, we intend to expand our sales and marketing infrastructure, including expanding our field sales force to 250 or more representatives, to allow us to reach a broad range of opioid prescribers in our target market.

*Expanding our product pipeline in CNS disorders and/or pain, including through the development of our newest product candidate, Relday.* We are utilizing our proprietary DosePro technology to add to our internal product pipeline. We plan to initiate clinical development of Relday in early 2012 and are also evaluating the market potential, formulation requirements and clinical development pathway of an additional CNS compound that could be paired with DosePro to enhance its commercial attractiveness.

*Obtaining regulatory approvals for Sumavel DosePro outside of the United States.* We have a partnership for Sumavel DosePro with Desitin in order to accelerate development and regulatory approvals in Europe and enhance the global commercial potential of Sumavel DosePro. Desitin received marketing approval from Denmark in November 2010 followed by approvals in Germany, Sweden, Norway and the United Kingdom. We also continue to evaluate potential partnerships to commercialize Sumavel DosePro in additional markets outside of Europe and the United States.

*Out-licensing our proprietary DosePro technology.* We are evaluating opportunities to out-license the DosePro needle-free drug delivery technology to partners seeking to enhance, differentiate or extend the life-cycle of their injectable products. These opportunities include biologics and small molecules that are both currently marketed products and development stage product candidates.

*Securing rights to complementary products and product candidates that address CNS disorders and/or pain.* To strategically leverage our commercial resources and generate additional revenue, we are seeking third-party co-promotion opportunities. In the future, we will also consider in-licensing or acquisition opportunities with a focus on product candidates that utilize novel technologies to improve the profile of existing compounds for CNS disorders and/or pain.



**Table of Contents****Our Product and Product Candidates*****Sumavel DosePro for the Acute Treatment of Migraine and Cluster Headache***

We launched the commercial sale of Sumavel DosePro in the United States in January 2010 with our co-promotion partner, Astellas. Our Sumavel DosePro (*sumatriptan* injection) Needle-free Delivery System offers fast-acting, easy-to-use subcutaneous administration of *sumatriptan* for the acute treatment of migraine and cluster headache. Sumavel DosePro utilizes our proprietary DosePro system which enables patients to self-administer subcutaneous *sumatriptan* in three easy steps. Sumavel DosePro may serve as a treatment alternative to oral and nasal triptans and may offer simple, convenient administration when compared to traditional, needle-based *sumatriptan* injection. As a result, we believe that Sumavel DosePro has the potential to be prescribed by a broad physician audience, especially for difficult to treat migraine episodes.

***Migraine Market***

Migraine is a chronic neurovascular disorder characterized by episodic attacks. According to a 2007 press release from the NHF, approximately 30 million people in the United States suffer from migraines, with women three times more likely to suffer migraines than men. Migraine attacks typically manifest themselves as moderate to severe headache pain, with symptoms that often include nausea and/or vomiting and abnormal sensitivity to light and sound. Migraines can severely limit the normal daily functioning of patients, who may seek dark, quiet surroundings until the episode has passed. According to the International Headache Society, the duration of untreated or unsuccessfully treated migraine episodes ranges from four to 72 hours. According to data published in the March 2002 issue of *Neurology*, 63% of patients suffer one or more attacks per month, 25% of patients have one or more attacks per week and the median duration of an untreated migraine is approximately 24 hours. Overall, the cost burden of migraine in the United States was estimated by Thomson Medstat in June 2006 to approach \$25 billion annually, including \$12.7 billion in direct medical costs and \$12 billion in indirect costs related to employee absenteeism, short-term disability and workers compensation costs to employers.

Cluster headaches are characterized by groups or clusters of debilitating headaches lasting weeks or months, then disappearing for months or years. This type of headache affects an estimated one million sufferers in the United States, and approximately 90% of these sufferers are male, according to the NHF website. Due to the severe nature of cluster headache, patients are commonly treated with prescription medication.

Acute therapies dominate the prescription migraine and cluster headache market and are used during intermittent attacks. The goals of acute therapy are to stop the attack quickly and consistently, minimize the use of backup and rescue medications, enhance self-care and restore the patient's ability to function, use the least amount of medication and limit adverse side effects.

A major advancement in the acute treatment of migraine began in 1993 with the launch of the first triptan, *sumatriptan* injection (Imitrex), in the United States. All triptans are selective agonists for the 5-HT<sub>1B</sub> and 5-HT<sub>1D</sub> receptors. Triptans presumably exert their antimigrainous effect through binding to vascular 5-HT<sub>1</sub> receptors, which have been shown to be present on both the human basilar artery, one of the major arteries that supplies blood to the brain, and the outermost membrane covering the brain. Triptans activate these receptors to cause vasoconstriction, an action in humans correlated with the relief of migraine and cluster headache. *Sumatriptan* was subsequently joined by other drugs in the triptan class. By the year 2003, there were seven approved triptans in the United States with a focus on oral delivery forms to offer convenience of dosing for migraine patients. *Sumatriptan* is the only triptan available in oral, nasal and subcutaneous forms, each of which has different pharmacokinetic properties.

Triptans remain the drugs of choice and the most often prescribed therapy for the acute treatment of migraine and cluster headache. The following table provides a breakdown of the U.S. triptan market, including sales and doses prescribed for oral (tablets and melts), nasal and injectable forms of triptan for the 12 months ended December 2010.

**Table of Contents****U.S. Triptan Market****(12 months ended December 2010)**

<b>Triptan Form</b>	<b>Sales (millions)</b>	<b>\$ Share</b>	<b>Doses (millions)</b>	<b>Dose Share</b>
Oral Tablet	\$ 2,734	77.7%	112.6	85.0%
Oral Melt	354	10.0	13.4	10.2
Nasal	113	3.2	3.0	2.2
Injectable	318	9.1	3.5	2.6
<b>Total</b>	<b>\$ 3,519</b>	<b>100%</b>	<b>132.5</b>	<b>100%</b>

Source<sup>®</sup> PHAST Institution/Retail.

As indicated in the prior table, the triptan market is dominated by oral dosage forms (tablets and melts), with approximately 95% of U.S. triptan doses taken as oral formulations and the remaining 5% split between injectable and nasal formulations. Branded and generic *sumatriptan*, in all dosage forms, remains the most prescribed triptan molecule with sales of approximately \$2.08 billion (59% dollar share of the triptan market). Of that amount, the injectable forms of *sumatriptan* accounted for \$319 million. By comparison, ergotamine agents, another class of drugs used for the acute treatment of migraine, including injectable DHE and Migranal, accounted for \$55.3 million in sales in the United States during the same 12-month period. (Source<sup>®</sup> PHAST Institution/Retail). *Sumatriptan* is the only triptan available to patients in the injectable form and, with the exception of Sumavel DosePro, all other forms of injectable *sumatriptan* make use of needle-based injections for their administration.

In five major European countries (France, Germany, Italy, Spain and the United Kingdom), triptans generated total sales of approximately \$550 million for the 12 months ended June 2007, according to average wholesale price data published by IMS Health MIDAS. Of that \$550 million, the European equivalent of Imitrex, Imigran, represented sales of approximately \$148 million, of which the injectable form accounted for approximately \$35 million.

***Migraine Market Dynamics***

The type of migraine treatment utilized by patients often depends on the frequency and severity of the headache, its speed of onset and previous response to medication. In published studies, migraine sufferers most often cite faster onset of pain relief as a key therapeutic attribute they would like from their migraine medication.

Patients with more frequent or severe migraines or those who do not respond to simple analgesics may seek medical attention with a primary care physician initially and then with a headache clinic or neurology specialist if needed. Once a physician makes a diagnosis of migraine, oral triptans are generally prescribed as first-line therapy.

If a patient does not respond to one triptan product, the physician may switch to another triptan or dosage form or add another triptan or dosage form to a patient's treatment armamentarium. Market research conducted on our behalf by Boston Healthcare Associates, Inc. indicates that it is common for a migraine patient to be offered several different oral triptan options before being offered a nasal or injectable product. In addition, the same market research indicates that approximately 25% of migraine patients had two or more active prescriptions for different brands and/or forms of triptan therapy. We believe these patients maintain multiple prescriptions because they have found that certain medications or dosage forms work better for certain types of migraines and choose which medication to use based on the type of migraine episode they are experiencing.

Clinical research has substantiated that the nature of migraine episodes varies widely. In some episodes, patients can sense a migraine coming and take their medication accordingly. In other episodes, patients may

**Table of Contents**

wake up with a migraine already in progress or the migraine may come on suddenly. An estimated 48% of migraines occur between the hours of 4:00 a.m. and 9:00 a.m., according to an article published in the June 1998 issue of *Headache*. Migraines may also be associated with nausea and/or vomiting. Twenty-nine percent of patients reported vomiting as a symptom of migraine attacks, according to the American Migraine Study II, and epidemiological studies in migraine reveal that over 90% of patients have experienced nausea during a migraine attack and more than 50% have nausea with the majority of attacks, according to an article published in *Drugs* in 2003 (Volume 63, Issue 21). Depending on the type of migraine episode, a treatment may be more or less effective. For example, oral treatments may be of little value in a patient who is vomiting or who is experiencing migraine-associated gastric stasis. There is also clinical evidence that oral agents may be less effective when taken at a later stage of a migraine attack, rather than at an earlier stage. Consequently, rapid onset migraine and waking with a migraine attack may reduce the benefits to patients of oral triptans, because both represent fully-developed attacks.

The following table compares the time to maximum drug concentration in blood, or Tmax, and pain relief of oral forms, including melts and tablets, and nasal forms of marketed triptans to *sumatriptan* injection. The data are derived from Prescribing Information for the different formulations of these marketed triptans:

**Triptan Prescribing Information Data**

Form/Product (API)	Tmax	Relief at 1 hour <sup>(1)(2)</sup>	Relief at 2 hours <sup>(2)</sup>
<b>Subcutaneous</b>			
Sumavel DosePro ( <i>sumatriptan</i> injection)	12 minutes	70%	81-82%
<b>Nasal</b>			
Imitrex ( <i>sumatriptan</i> )	Not provided	38-46%	43-64%
Zomig ( <i>zolmitriptan</i> )	3.0 hrs	60%	69-70%
<b>Oral Melt</b>			
Zomig-ZMT ( <i>zolmitriptan</i> )	3.0 hrs	33-43%	63%
Maxalt-MLT ( <i>rizatriptan</i> )	1.6-2.5 hrs	38-43%	59-74%
<b>Oral Tablets</b>			
Imitrex ( <i>sumatriptan</i> )	2.0-2.5 hrs	28-36%	50-62%
Treximet ( <i>sumatriptan/naproxen sodium</i> )	1.0 hrs	28%	57-65%
Zomig ( <i>zolmitriptan</i> )	1.5 hrs	35-45%	59-67%
Maxalt ( <i>rizatriptan</i> )	1.0-1.5 hrs	38-43%	60-77%
Amerge ( <i>naratriptan</i> )	2.0-3.0 hrs	19-21%	50-66% <sup>(3)</sup>
Axert ( <i>almotriptan</i> )	1.0-3.0 hrs	32-36%	55-65%
Frova ( <i>frovatriptan</i> )	2.0-4.0 hrs	12%	37-46%
Relpax ( <i>eletriptan</i> )	1.5 hrs	20-30%	47-77%

- (1) Other than Sumavel DosePro (*sumatriptan* injection), we have estimated one-hour pain relief data for all forms/products based on Kaplan-Meier plots included in each product's Prescribing Information of the probability over time of obtaining headache response following treatment.
- (2) Range reflects headache relief data obtained in placebo controlled clinical studies, which include different doses of the same triptan.
- (3) Represents pain relief at four hours.

Tmax closely correlates to speed of onset of pain relief, and has also been shown to be correlated with completeness of pain relief and pain freedom over time. Relief at two hours is the standard endpoint used in migraine studies and represents the percentage of patients reporting a reduction of migraine symptoms from a classification of severe or moderate to mild or none within two hours after taking the medication. As indicated in the prior table, *sumatriptan* injection has the earliest Tmax, reaching maximum blood concentration in

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## **Table of Contents**

12 minutes, as compared with one or more hours for the other marketed triptan products, and exhibits the highest percentage of patients reporting pain relief at two hours (81%-82%) as compared to all other marketed oral and nasal triptan products (37-77%). *Sumatriptan* injection is the only migraine product that explicitly reports pain relief at one hour in its Prescribing Information. The efficacy profile of *sumatriptan* injection has been suggested to be related to its faster rate (not extent) of drug absorption compared to oral and nasal forms of triptans. Nasal forms, while claimed by some to be fast-acting, have drug absorption profiles similar to oral forms because a large portion of the administered dose is usually swallowed prior to absorption.

### ***Unmet Needs in Acute Migraine Therapy***

Triptans have been widely used in clinical practice for more than 15 years and are generally considered to be safe and effective for many patients during their migraine episodes. However, more than half of all patients are unsatisfied with their current migraine therapy, as reported from a national survey of 500 migraine sufferers published by the NHF in June 2010 and supported by a grant from us and Astellas. Specifically, the NHF survey results indicate that three in four migraine sufferers said that their current medication did not work fast enough to get them back to their life when a migraine strikes suddenly or upon waking, and a majority of migraine sufferers said their prescription oral migraine medication was not useful for every migraine attack. Limitations of oral and nasal triptan formulations include:

*Slower onset of pain relief.* As shown in the prior table, compared to Sumavel DosePro, each oral and nasal triptan has a longer Tmax, which is correlated with a slower onset of pain relief.

*Lower degree of pain relief.* As shown in the prior table, oral and nasal triptans may have a lower percentage of patients reporting pain relief at one and two hours following treatment as compared to Sumavel DosePro.

*Significant numbers of non-responders.* According to our market research with physicians and patients, approximately 30% of migraine patients fail to respond to an oral or nasal triptan.

*Nasal route unpleasant.* The nasal route is an alternative to oral delivery; however, nasal spray can be unpleasant in taste. Some of these limitations are more pronounced depending on the type of migraine episode the patient is suffering. For example, when waking with a migraine already in progress, speed to onset of pain relief is important. In migraines with nausea and/or vomiting, a patient may not be able to ingest an oral treatment.

Despite its speed of onset and completeness of pain relief advantages over oral and nasal triptans, needle-based *sumatriptan* injection has been limited to less than 10% of the U.S. triptan market on a dollar basis and less than 3% on a total dose basis (Source<sup>®</sup> PHAST Institution/Retail January 2010 – December 2010). We believe this is largely due to limitations related to its delivery system which include:

*Needle-based.* Approximately 50% of patients refuse to use a needle-based injectable product for migraine because of needle anxiety or fear, or a lack of confidence in their ability to administer an injection correctly, according to physician market research conducted in 2006 by Palace Healthcare Group, Inc. on our behalf.

*Cumbersome to use.* The Imitrex STATdose System, or Imitrex STATdose, GSK's autoinjector for delivering *sumatriptan* with a needle, and its generic equivalents require more than 15 steps per their published instructions to prepare, administer and reload for its next use. This multi-step process, which patients have to complete during a migraine episode, is prone to error. Further, market research conducted by Palace Healthcare Group on our behalf finds that physicians report that the training required for Imitrex STATdose is a barrier to prescribing.

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*Needlestick risk.* Needle-based systems may require special handling and needle disposal, or sharps, containers to avoid needlestick injuries.

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## **Table of Contents**

Due to these limitations, there has historically been a limited prescriber base for injectable delivery forms of *sumatriptan*. Of an aggregate of over 350,000 prescribers of triptans in the United States, only an approximate 67,000 had written a prescription for *sumatriptan* injection (including Sumavel DosePro) in the 12 months ended December 2010 (Source<sup>®</sup> Prescriber January 2010 – December 2010). As a result, a limited number of patients are offered injectable delivery forms. Only 54% of migraine patients had ever been offered *sumatriptan* injection according to patient market research conducted by Boston Healthcare Associates, Inc. on our behalf.

### ***Our Solution: Sumavel DosePro***

Sumavel DosePro is a pre-filled, single-use disposable, needle-free drug delivery system that subcutaneously delivers 6 mg of *sumatriptan* in 0.5 mL of sterile liquid. Sumavel DosePro was designed to be portable, intuitive and easy-to-use. To use, the patient simply snaps off a plastic tip, flips back a lever and presses the end of the delivery system to the skin of the abdomen or thigh. Under the force of a small amount of compressed nitrogen gas, the liquid form of *sumatriptan* is expelled out of the device as a thin jet of medication, which pierces the skin and selectively deposits into the subcutaneous tissue. This process occurs in less than 1/10th of a second.

Due to its unique attributes, Sumavel DosePro has the potential to expand the dosage share for injectable *sumatriptan* beyond the traditional needle-based forms because it reduces the barriers inherent in needle-based delivery systems to being prescribed by physicians and accepted by patients. Sumavel DosePro may provide patients with the following benefits when compared to alternative triptan formulations:

*Rapid, more complete, migraine pain relief.* Sumavel DosePro can provide onset of migraine pain relief in as little as ten minutes for some patients, according to its Prescribing Information. The Prescribing Information for the product indicates that an average of 81% (vs. an average of 34% for placebo) of patients show pain relief at two hours following administration of Sumavel DosePro and that 49% of patients were pain free within 1 hour (vs. 9% for placebo) and 64% were pain free within two hours (vs. 15% for placebo) following administration.

*Help for sufferers of morning migraines, fast onset migraine and migraines with vomiting.* According to two studies published in the October 2006 issue of Clinical Therapeutics, 48% and 57% of patients with waking migraines were pain free at two hours (vs. 18% and 19% for placebo) following administration of *sumatriptan* injection. Subcutaneous *sumatriptan* is also as efficacious when administered early during a migraine attack as when the attack is full-blown. In addition, the pharmacokinetics of subcutaneously delivered *sumatriptan* is not affected by gastric stasis, nausea and/or vomiting.

*Help for triptan tablet non-responders.* Clinical research published in the January 2007 issue of Journal of Headache and Pain suggests injectable *sumatriptan* provides relief in up to 90% of migraine patients who have not responded to oral tablet triptans in at least two of their last three migraines. In this study, 43 patients who had failed to respond to oral triptans in at least two of their last three migraines were given *sumatriptan* injection for their next migraine. Of these patients, 91% reported pain relief at two hours, 56% reported being pain free at two hours and 32% reported sustained pain freedom through 24 hours following treatment of their first headache.

*Simplicity, through a new, convenient and easy-to-use option.* Sumavel DosePro is based on our unique delivery system which was designed to be portable, intuitive and easy-to-use, and can be disposed following use without the need of a sharps container. We believe healthcare providers appreciate the simplicity of DosePro because it is easy to train patients to use properly. Our usability study of Sumavel DosePro showed 98% of patients were able to self-administer Sumavel DosePro in the home during an acute migraine attack, without clinical supervision and with minimal prior training.

*Needle-free, eliminating needle-based issues.* Because it is needle-free, we believe Sumavel DosePro may eliminate the basis for patient needle phobia and fear. Additionally, it removes the risks of needlestick injury, the cost and inconvenience of needle disposal, issues resulting from poor injection

**Table of Contents**

technique and costs associated with professionally administered needle-based injections. Studies show when a choice between needle-based and needle-free injection is available, the majority of patients prefer needle-free injection. More specifically, in a head-to-head study conducted by GSK of Sumavel DosePro versus the European branded version of Imitrex STATdose, a needle-based delivery system, 61% of migraine patients preferred using Sumavel DosePro while only 18% preferred using the European branded version of Imitrex STATdose, with the remaining patients expressing no preference.

In addition, we believe that the unique attributes of Sumavel DosePro have the potential to reduce productivity loss in the workplace for patients suffering from migraine. According to a study published in the May 1998 issue of Archives of Internal Medicine, results from a placebo-controlled clinical study of 135 patients having migraine indicated that use of *sumatriptan* injection may reduce migraine-associated productivity loss. This decrease is a function of both a reduction in time lost due to reduced effectiveness while working and a reduction in time lost due to missing work altogether. Moreover, 52% of patients using *sumatriptan* injection (vs. 9% for placebo) returned to normal work performance within two hours after dosing.

***Sumavel DosePro Commercialization Strategy***

Working in collaboration with our co-promotion partner, Astellas, as well as third-party advertising and market research organizations, we developed and are executing a sophisticated and comprehensive commercialization strategy for Sumavel DosePro supported by a range of marketing programs. This strategy and tactical plan was built taking into consideration the unmet needs in the migraine market in conjunction with the unique product attributes of Sumavel DosePro. Key objectives of our commercialization strategy are to:

validate the unmet needs of patients during challenging migraine episodes and position Sumavel DosePro as an effective treatment solution with prescribers;

build awareness of Sumavel DosePro with migraine sufferers in order to drive patient requests;

enhance speed of physician adoption by focusing promotional efforts on prescribers of migraine medications across specialties;

ensure a positive first-dose experience for patients; and

achieve broad patient access to Sumavel DosePro by ensuring nationwide retail distribution and adequate third-party payor reimbursement status.

In support of these strategic objectives, we and Astellas are executing a variety of marketing programs to educate customers, which include direct-to-physician promotional materials, speaker programs, direct-to-patient programs, digital media, participation in selected medical conventions and reimbursement support programs. In addition, we and Astellas provide product samples to physicians so that their patients may try Sumavel DosePro during an acute migraine attack before filling their first prescription.

***Sumavel DosePro Regulatory Approval***

We sought and received FDA marketing approval of Sumavel DosePro under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or the FDCA, utilizing Imitrex *sumatriptan* injection as the reference listed product. Section 505(b)(2) of the FDCA 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. This expedited the development program for Sumavel DosePro by decreasing the overall scope of clinical and pre-clinical work required to be completed by us.

The clinical efficacy of subcutaneous injectable *sumatriptan* for migraine and cluster headache has been established by the reference listed product, Imitrex *sumatriptan* injection, which was approved in 1992. Based on our clinical bioequivalence studies, the FDA concluded that Sumavel DosePro is bioequivalent to injectable





**Table of Contents**

*sumatriptan* administered to the thigh or abdomen using Imitrex STATdose and is well tolerated when compared to this reference listed product. Our Sumavel DosePro NDA was approved by the FDA on July 15, 2009, and the Sumavel DosePro Prescribing Information includes the historical efficacy data of *sumatriptan* injection.

***Sumavel DosePro Pivotal Clinical Program***

Based on discussions with the FDA, and due to the existing body of data on injectable *sumatriptan*, our pivotal clinical program evaluated Sumavel DosePro in studies for pharmacokinetics, bioequivalence, safety, local injection site signs and reactions, and usability by patients with migraine. We conducted a single pivotal pharmacokinetics and bioequivalence clinical trial for the purpose of providing evidence of bioequivalence and safety of Sumavel DosePro as compared to Imitrex STATdose. This study, completed in April 2007, was a randomized, open-label, cross-over trial comparing safety, tolerability and pharmacokinetics in 54 subjects. The primary endpoint of bioequivalence was demonstrated in the commonly used abdomen and thigh injection sites. A separate 52-patient usability study was conducted in the second half of 2007 to evaluate the usability of Sumavel DosePro in patients during acute migraine attacks in an outpatient setting. In this study, 98% were able to use Sumavel DosePro correctly during a migraine attack on their first attempt, thus confirming the product candidate's ease of use. Further use of Sumavel DosePro by the same patients in their treatment of subsequent migraine attacks provided consistent evidence of usability in the outpatient setting. In addition, we concluded a successful safety trial with Sumavel DosePro in December 2007 to study the effect of repeat dosing and multiple injections. Adverse events seen in our clinical studies were consistent with previously reported adverse events for *sumatriptan* injection. The most common treatment-emergent adverse reactions (reported by at least 5% of patients) for *sumatriptan* injection as described in the Sumavel DosePro Prescribing Information summarizing two large placebo-controlled clinical trials were injection site reaction (59%), atypical sensations (42%), dizziness (12%), flushing (7%), chest discomfort (5%), weakness (5%), and neck pain/stiffness (5%).

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.

***Sumavel DosePro Post-Approval Clinical Program***

In addition to the clinical program completed in support of product approval, we have completed a Phase 4 open-label, multicenter study in the United States to evaluate treatment satisfaction, treatment confidence and subject preference for Sumavel DosePro in adult subjects diagnosed with migraine and currently treated with triptans. More than 200 subjects, who were predominantly taking oral triptan therapy, tried Sumavel DosePro to treat up to four migraines over a 60-day period. The study utilized the Patient Perception of Migraine Questionnaire-Revised, or PPMQ-R, to evaluate patient satisfaction with migraine treatment through analysis of efficacy, functionality, ease of use and tolerability/side effects. The primary endpoint PPMQ-R Overall Satisfaction score increased significantly from baseline to end of treatment ( $p=0.0007$ ), an improvement that met the criterion for clinical significance. From baseline to the end of treatment, PPMQ-R scores also improved significantly for efficacy ( $p<0.0001$ ), functionality ( $p<0.0001$ ) and tolerability ( $p=0.02$ ), but declined for ease of use ( $p<0.0001$ ). In addition, the percentage of patients confident or very confident in treating repeated migraine attacks increased from 41.0% at baseline to 64.6% at the end of treatment with Sumavel DosePro. The magnitude of improvement in treatment satisfaction from baseline to the end of the treatment period was even greater in a prospectively defined subset of 90 patients who were identified as requiring a change in therapy through use of the Migraine-ACT (Migraine Assessment of Current Therapy) questionnaire. The four-item questionnaire is an assessment tool for use by primary care physicians to identify patients who require a change in their current acute migraine treatment. Using Sumavel DosePro, 33% of the 669 treated migraine episodes in the study had pain relieved in 15 minutes, with 70% achieving pain relief within 30 minutes. Pain freedom was achieved in 61% of the treated attacks within two hours. These incidences of pain relief and pain-free response

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## **Table of Contents**

for needle-free Sumavel DosePro are consistent with those demonstrated by previous double-blind, placebo-controlled clinical studies of injectable *sumatriptan*. Given that rapid pain reduction is the primary determinant of patient satisfaction with migraine, these results may explain the high rate of satisfaction with Sumavel DosePro reported by patients in the current study.

### ***Sumavel DosePro 4mg Line Extension***

Based upon physician feedback, we have initiated development of a 4mg dosage strength of Sumavel DosePro. We believe this will require us to submit a supplemental NDA with the FDA to demonstrate the manufacturability and stability of the new dosage strength. We anticipate submitting the necessary information for regulatory approval of this line extension with the FDA by the end of 2012 and commercializing thereafter, if approved.

### ***DosePro and Sumavel DosePro Clinical Experience***

The DosePro drug delivery system has been in development for more than ten years. During this time, more than 9,000 injections have been administered in multiple clinical studies to assure the proper functioning of the system and to establish the safety and tolerability of needle-free administration by DosePro. While our experience indicates that some patients will experience pain upon injection with the DosePro technology, this pain sensation is consistent with the pain sensation associated with injection with a fine gauge needle and can be generally characterized as transient mild discomfort.

### ***Zohydro for the Treatment of Moderate to Severe Chronic Pain***

Our lead product candidate, Zohydro, is a novel, oral, single-entity extended-release formulation of *hydrocodone* currently in Phase 3 development for the treatment of moderate to severe chronic pain in patients requiring around-the-clock opioid therapy. We believe Zohydro has the potential to be an important therapeutic alternative to existing *hydrocodone* products, including the branded products Vicodin, Lortab and their generic equivalents, which contain the analgesic combination ingredient *acetaminophen* and, if taken in high quantities over time, can lead to serious side effects such as liver toxicity. Zohydro utilizes the SODAS Technology, Elan's proprietary multiparticulate drug delivery system that allows the development of customized extended-release profiles and serves to enhance the release profile of *hydrocodone* in Zohydro to provide consistent 12-hour pain relief. We believe these release properties have the potential to provide longer lasting and more consistent pain relief with fewer daily doses than the commercially available formulations of *hydrocodone*. As a result of its unique single-entity extended-release profile, we believe Zohydro will generate sales from both patients who use immediate-release products on a chronic basis and patients already using extended-release products in the prescription opioid market.

### ***The Chronic Pain Market***

Pain is a worldwide problem with serious health and economic consequences. The American Pain Society estimated in 1999 that 9% of the U.S. adult population suffers from moderate to severe non-cancer related chronic pain. Chronic pain may be defined as pain that lasts beyond the healing of an injury or that persists beyond three months. Common types of chronic pain include lower back pain, arthritis, headache and face and jaw pain. While mild pain does not typically stop an individual from participating in his or her daily activities, moderate pain may prevent an individual from participating in his or her daily activities and severe pain typically stops an individual from participating in his or her daily activities and induces a patient to exhibit pain avoidance behaviors.

Chronic pain treatment depends on the individual patients, their diagnosis and their pain severity. Chronic pain patients typically first attempt to self-medicate with over-the-counter drugs such as *acetaminophen*, aspirin or another non-steroidal anti-inflammatory drug, or NSAID. Patients with more constant and/or moderate to severe pain typically seek medical attention and prescription pain medication from a primary care physician and,

**Table of Contents**

if necessary, are referred to a neurologist or a physical medicine or pain specialist. Physicians generally assess the patient and, if appropriate, start treatment with a trial of opioid therapy to determine the optimal opioid regimen. At this point, physicians commonly prescribe opioids, including products from the *codeine* and *morphine* classes. The general objective of the physician is to safely achieve adequate control of pain.

Physicians generally prefer to start patients on less potent opioids where possible. A trial of opioid therapy usually begins with short-acting doses taken on an as-needed basis. This allows the clinician and patient to assess the total opioid requirement. Patients taking substantial doses of short-acting opioids multiple times per day may find substitution of an extended-release agent, taken one to two times per day, extremely helpful to provide more constant pain relief. In theory, the more constant opioid blood levels of extended-release products may provide better pain relief and better sleep quality. Dosing intervals less frequent than every four to six hours may also provide improved patient adherence to the prescribed regimen and improved patient convenience. Finally, individual patients may do poorly on one opioid, but better after switching to another. This practice is called opioid rotation and is regularly employed in chronic pain management. Opioids, while generally effective for pain treatment, are associated with numerous potential adverse effects, including opioid induced bowel dysfunction, sedation, nausea, vomiting, decreased respiratory function, addiction and, in some instances, death.

*Hydrocodone* is often used as a starter opioid to initiate opioid therapy because it is viewed by many physicians as a less potent opioid. Historically, *hydrocodone* preparations in the United States have been utilized primarily for treatment of acute pain following surgery or injury. For this purpose, they were combined with analgesics, including *acetaminophen* or an NSAID, which treat the acute inflammatory component of the pain. These analgesics are generally safe when used at lower doses or for short periods of time. However, at higher doses or over extended periods of time, they may significantly increase patient risk for gastrointestinal, liver and kidney damage.

As the practice of pain management has broadened to include chronic therapy for moderate to severe pain, physicians continue to broadly use *hydrocodone* combinations. In the United States, market research conducted by bioStrategies Group in 2011 on our behalf indicates that nearly 30% of the prescriptions of immediate-release combination products that include *hydrocodone* are for the treatment of chronic pain and that approximately half of those prescriptions, or 14%, would be replaced with an extended-release *hydrocodone* product if it were available. However, the non-opioid analgesic component in combination *hydrocodone* products can create a ceiling effect when physicians wish to escalate doses. For example, the most commonly prescribed dose of Vicodin (5mg *hydrocodone*/500 mg *acetaminophen*) given at a maximum dose of eight tablets per day delivers 4 g of *acetaminophen*, which approaches or exceeds recommended *acetaminophen* dosing, while only delivering 40 mg of *hydrocodone*, based on the Vicodin Prescribing Information. If a further increase in opioid dose is warranted, a physician is compelled to transition to an opioid not in combination, such as *oxycodone*, or more potent opioids such as *fentanyl* or *oxymorphone*.

In the 12 months ended December 2010, our target market, which we define as prescription non-injectable *codeine*-based and extended-release *morphine*-based pain products, generated sales of approximately \$13.5 billion in the United States on approximately 206 million prescriptions. Of the \$13.5 billion, *hydrocodone* products, the most commonly prescribed opioid and the most commonly prescribed pharmaceutical products in the United States, generated \$3.2 billion in sales on approximately 128 million prescriptions. (Source<sup>®</sup> PHAST Retail).

In June 2009, the FDA organized a joint meeting of the Drug Safety and Risk Management Advisory Committee, Nonprescription Drugs Advisory Committee, and the Anesthetic and Life Support Advisory Committee to discuss how to address the public health problem of liver injury related to the use of *acetaminophen* in both over-the-counter and prescription products. The expert panel specifically considered the elimination of combination prescription products containing *acetaminophen* (including Vicodin and its generics) from the U.S. market. Twenty of the 37 working group members (10 saying this was a high priority) voted in favor of removing such products from the market. The working group ultimately did not recommend withdrawal of these products stating that the benefits of access to Schedule III *acetaminophen*/*hydrocodone* combination

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## **Table of Contents**

products over Schedule II opioids outweighed the risk of removing the combinations from the market. The working group also noted that the logical choice to substitute for the combination products would be a single-entity formulation of *hydrocodone*. Subsequently, in January 2011, the FDA asked manufacturers of prescription combination products that contain *acetaminophen* to limit the amount of *acetaminophen* to no more than 325 mg in each tablet or capsule and will require manufacturers to update labels of all prescription combination *acetaminophen* products to warn of the potential risk for severe liver injury. There are currently no approved products formulated with *hydrocodone* alone, and we believe Zohydro has the potential to fill this treatment gap.

### ***Limitations of Current Opioid Pain Therapies***

While *hydrocodone* in combination products remains the most commonly prescribed opioid, currently available *hydrocodone* formulations have several major limitations, including:

*Hydrocodone only available in short-acting/immediate-release form.* There are currently no extended-release *hydrocodone* formulations on the market.

*Adherence dependent.* Because *hydrocodone* is available only in immediate-release formulations that are dosed every four to six hours, its around-the-clock efficacy is dependent on diligent adherence by the patient. Published studies across therapeutic categories, including the treatment of diabetes, hypertension and infectious disease, demonstrate that patient adherence to drug regimens declines as the number of daily drug doses increases.

*Inconsistent pain relief.* Because of the dosing issues noted above, many patients experience suboptimal pain relief due to variable opioid blood levels, particularly towards the end of dosing intervals.

*Opioid dose is limited by combination analgesics.* The overwhelming majority of currently approved *hydrocodone* products include *acetaminophen* in their formulation. Because of the potential side effects of chronic increasing *acetaminophen* doses, the *acetaminophen* component of these combination products can become a dose limiting factor. When this occurs, patients must limit their total *hydrocodone* dose to avoid potential liver and other side effects of *acetaminophen* and thus may receive a sub-optimal daily dose of *hydrocodone*, or they must switch to other single-entity opioids, such as *oxycodone*. *Hydrocodone* combinations with NSAIDs have similar dose limitations due to the gastrointestinal side effects associated with NSAIDs.

While extended-release, single-entity opioids exist, published study reports indicate that patients are regularly taking more daily doses of extended-release opioids than the recommended labeled dose, suggesting that not all of them provide true 12- or 24-hour dosing. For example, results from a study of 437 patients published in the May/June 2003 issue of the Journal of Managed Care Pharmacy indicated that despite the every 12-hours dosing regimen recommended in its Prescribing Information, patients taking extended-release *oxycodone* on average took 4.6 tablets per day, at an average dosing interval of only 7.8 hours. In the same study, among extended-release *oxycodone* patients, only 1.9% reported the duration of pain relief as 12 or more hours. A separate study published in the September/October 2004 issue of The Clinical Journal of Pain indicated that the prescribed frequency of dosing extended-release *oxycodone* determined through clinical practice was twice daily for 33% of patients, with 67% of patients requiring greater than twice daily dosing.

### ***Our Solution: Zohydro***

We believe that Zohydro, if approved, may provide patients and physicians with the following benefits when compared to existing opioid pain medications:

*Single-entity hydrocodone.* Zohydro, if successfully developed and approved by the FDA, is expected to be the first non-combination, extended-release *hydrocodone* product to be commercialized in the United States, giving physicians and patients a *hydrocodone* option unencumbered with *acetaminophen* or NSAIDs and their potential adverse effects.

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*Twice daily dosing provides true around-the-clock relief.* Zohydro, via its unique extended-release profile, is designed to provide consistent relief of moderate to severe chronic pain over a 12-hour period per dose. Clinical studies have shown a pharmacokinetic profile that supports the expected extended relief profile of Zohydro.

*Easier adherence/greater patient convenience.* Because of its twice daily dosing regimen, Zohydro requires fewer daily doses than currently available *hydrocodone* formulations, thereby increasing the likelihood of patient adherence and convenience.

**Table of Contents**

*Another opioid option for chronic medication rotation.* The unique profile of Zohydro provides another option for physicians investigating new alternatives to offer patients who require medication rotation due to tolerance, side effects or poor pain control.

***Zohydro Phase 3 Clinical Development Program***

We initiated a single pivotal Phase 3 efficacy trial (Study 801) in March 2010 and completed patient enrollment in February 2011. This trial is a randomized, 12-week, double-blind, placebo-controlled trial to evaluate the safety and efficacy of Zohydro for the treatment of moderate to severe chronic lower back pain in opioid-experienced adult subjects. Our trial utilizes a protocol design that has been used successfully to demonstrate the efficacy of other extended-release opioid therapies for chronic pain. Patients in this study were converted from their existing opioid treatment regimen to Zohydro and titrated to an effective dose of Zohydro during an initial up to 6-week open-label conversion and titration phase, and were then randomized to receive either placebo or active drug for a 12-week placebo-controlled treatment phase. During the entire study period, patients in both arms of the clinical trial had access to rescue medication. The primary efficacy endpoint in this trial is the mean change in average daily pain intensity scores between Zohydro and placebo. We confirmed the FDA's agreement on the trial design for Study 801 and the overall safety database requirements for an NDA submission at our End of Phase 2 meeting with the FDA conducted in June 2008. We did not seek a Special Protocol Assessment, or SPA, from the FDA for Study 801.

We reported positive top-line results for our pivotal Phase 3 efficacy trial in August 2011. The trial successfully met the primary efficacy endpoint in demonstrating a significant difference ( $p=0.008$ ) between the mean changes from Baseline to Week 12 or Final Visit in average daily pain intensity Numeric Rating Scale (NRS) scores obtained from patient diaries between Zohydro and placebo groups. The two key secondary endpoints were also met. With respect to the responder analysis secondary endpoint, the proportion of patients with at least 30% improvement in pain intensity from screening to end of study was significantly higher for Zohydro compared to placebo (67.5% versus 31.1%;  $p<0.001$ ). The proportion of patients with at least 50% improvement in pain intensity from screening to end of study was also significantly higher for Zohydro versus placebo (47.7% versus 23.3%;  $p<0.001$ ). The other key secondary endpoint, using the Subject Global Assessment of Medication questionnaire, showed that patients on Zohydro were significantly more satisfied ( $p<0.001$ ) with their pain treatment at the end of the study compared to their pre-study medication. The study further demonstrated that Zohydro was safe and generally well tolerated. The incidence of adverse events was 33.7% and 28.8% in the open label titration and double blind treatment periods, respectively. Overall, the most commonly reported adverse events (32%) were constipation, nausea, somnolence, vomiting, diarrhea, insomnia, fatigue, headache, dizziness and dry mouth. These are typical adverse events associated with chronic opioid therapy.

To further assess the safety and tolerability of Zohydro as a chronic pain therapy, we are also conducting an open-label Phase 3 trial in opioid-experienced adult subjects with any indication appropriate for continuous, around-the-clock opioid therapy for an extended period of time (Study 802). We completed patient enrollment for this trial in November 2010. The goal of this trial is to evaluate the safety and tolerability of Zohydro for up to 12 months of treatment. We expect to submit data from this trial as part of our NDA.

Based upon feedback from the FDA at our End of Phase 2 meeting, the positive results of our pivotal Phase 3 efficacy trial and assuming a positive outcome from the ongoing Phase 3 safety trial, we do not believe that additional Phase 3 safety and efficacy trials will be required to support our proposed label. Concurrent with our Phase 3 program, we are also conducting a small number of additional single-dose pharmacokinetic and clinical pharmacology trials and pre-clinical studies required for submission of the NDA and approval of this product candidate. Based upon the status and results of our ongoing Phase 3 clinical development program, we expect to submit an NDA with the FDA by early 2012.

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**Table of Contents*****Prior Clinical Development of Zohydro***

Our licensor for Zohydro, Elan, conducted pre-clinical and clinical studies of Zohydro under an IND initiated in 2002.

***Phase 1 and Phase 2 Clinical Development.*** In single and multiple dose pharmacokinetic evaluations, Zohydro demonstrated detectable plasma concentrations of *hydrocodone* within 15 minutes of administration. Zohydro also demonstrated a sustained release effect significantly longer than currently available *hydrocodone* combination products such as Vicodin, as well as dose proportional pharmacokinetics. Consistent, steady-state plasma levels, which are believed to be desirable for chronic pain patients who require around-the-clock opioid therapy, were achieved within one week of the initiation of dosing. In addition, Zohydro has been tested under both fed and fasted conditions and the amount of drug exposure was not affected by food, which we believe provides the basis for a flexible administration regimen for chronic pain. We believe that these prior pharmacokinetic studies demonstrate that Zohydro displays a consistent, extended-release profile, dose-proportional pharmacokinetics and an acceptable safety profile.

Zohydro has also been evaluated in two separate Phase 2 pain studies. The first study was a randomized, single-dose, parallel group, placebo-controlled, active-comparator study to evaluate the safety, efficacy and pharmacokinetics of increasing doses of Zohydro in opioid-naïve adults immediately following bunion removal surgery. This study was designed to evaluate pain prevention rather than pain treatment. In this 241-patient study, patients were treated with either one of four doses of Zohydro (10, 20, 30 or 40 mg extended-release *hydrocodone bitartrate*), an active immediate-release comparator consisting of 10 mg *hydrocodone bitartrate* plus 325 mg *acetaminophen*, or placebo. The primary efficacy measurement was the visual analog scale of pain intensity from 0 to 12 hours after dosing. The 40 mg dose of Zohydro was significantly more effective ( $p < 0.05$ ) versus placebo in controlling postoperative pain. In addition, efficacy of the 40 mg dose did not significantly differ from the *hydrocodone bitartrate/acetaminophen* active comparator in any of the efficacy outcome measures. None of the three lower doses of Zohydro were superior to placebo in the primary efficacy measurements. All four doses were found to be safe and well-tolerated. We believe this efficacy and safety information is useful in establishing proof-of-concept for Zohydro.

The second Phase 2 study was a four week, multiple-dose, safety, tolerability and pharmacokinetic dose-escalation study of Zohydro in opioid-experienced adults with chronic, moderate to severe osteoarthritis pain. The primary objective was to assess the safety, tolerability and pharmacokinetics of Zohydro at steady state over a range of escalating daily doses. Thirty-seven patients in two dosing cohorts received escalating doses of Zohydro over three weeks. This study demonstrated a clinically acceptable safety profile and a reduction in pain intensity for chronic moderate to severe osteoarthritis pain patients across multiple dosage strengths. We believe that the study also demonstrated a steady-state pharmacokinetic profile that is appropriate for the management of chronic pain. In both Phase 2 studies, patients experienced mild to moderate adverse events, such as nausea, vomiting, headache, dizziness, sweating, constipation and drowsiness, which are similar to the reported effects of opioids currently prescribed for chronic pain.

The data from these Phase 1 and Phase 2 studies were submitted to the FDA under our IND and were summarized in our End of Phase 2 meeting briefing package in support of progressing Zohydro into pivotal Phase 3 clinical studies.

***Relday for the Treatment of Schizophrenia***

Relday is a proprietary, long-acting injectable formulation of *risperidone* using Durect's SABER controlled-release formulation technology in combination with our DosePro needle-free, subcutaneous drug delivery system. If successfully developed and approved, we believe Relday may be the first once-monthly, subcutaneous antipsychotic product available in a needle-free delivery system to enter the long-acting injectable antipsychotic market. We believe the combination of our DosePro technology with Durect's SABER controlled-release technology will allow Relday to be delivered subcutaneously without a needle on a once-monthly basis with a simplified dosing regimen, improved pharmacokinetic profile and significant reduction in injection volume versus

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**Table of Contents**

currently marketed long-acting injectable antipsychotics. Based upon these characteristics, Relday may provide an important alternative to currently marketed long-acting injectable antipsychotics as well as a new long-acting treatment option for patients that currently use daily oral antipsychotic products. We intend to initiate clinical studies for Relday in patients with schizophrenia in early 2012 following the filing of an IND with the FDA. We completed a pre-IND meeting with the FDA in December 2009.

***The Antipsychotic Market***

Schizophrenia is a complex, chronic, severe and debilitating mental disorder that often develops between the ages of 16 and 30 years, and the NIMH estimates that the 12-month prevalence of schizophrenia is 1.1% of the U.S. adult population. The symptoms of schizophrenia are often categorized as positive, negative or cognitive in nature. Positive symptoms include hallucinations, delusions, disorganized thinking and movement disorders. Negative symptoms of schizophrenia can include flat affect, inability to feel pleasure and speaking little, and the cognitive symptoms of schizophrenia can include poor executive function, problems with working memory and attention deficits. This combination of symptoms often makes it challenging for many schizophrenic patients to care for themselves or hold jobs, resulting in significant societal costs. The direct and indirect costs of schizophrenia in the United States in 2002 were estimated at \$62.7 billion, including \$22.7 billion in direct medical costs for outpatient care, medications, inpatient care, and long-term care, according to an article published in 2005 in *The Journal of Clinical Psychiatry*.

Bipolar disorder, or manic depressive illness, is another chronic, recurring psychiatric illness that is characterized by extreme or unusual shifts in mood, energy and activity levels. In general, patients with bipolar disorder suffer over time from episodes of both mania and depression. The NIMH estimates that the average age of onset for bipolar disorder is 25 years, and the 12-month prevalence of bipolar disorder is 2.6% of the U.S. adult population. In many cases, the recurring episodes of mania and depression are so severe that the patient cannot maintain normal relationships or function normally at home, work or school, and suicide attempts occur in 25-50% of bipolar disorder patients.

First line therapy for most schizophrenia patients today are drugs generally known as atypical or second generation antipsychotics. These antipsychotics have been named atypical for their ability to treat a broader range of negative symptoms with improved side effect profiles versus the first-generation or typical antipsychotics, which were mostly introduced in the 1950s with drugs such as chlorpromazine and haloperidol. The first atypical antipsychotics to be approved by FDA in the United States were Clozaril (*clozapine*) in 1989, followed by Risperdal (*risperidone*) in 1993 and Zyprexa (*olanzapine*) in 1996. Similarly, over the last decade, atypical antipsychotics have become increasingly utilized in the treatment of bipolar disorder, either as monotherapy or as part of a polytherapy regimen, most often being prescribed in conjunction with a mood stabilizer such as lithium or valproic acid, and sometimes in conjunction with both a mood stabilizer and additional medications.

Patient compliance with medication has been a long-standing problem in the treatment of both schizophrenia and bipolar disorder. Results from the Clinical Antipsychotic Trials in Intervention Effectiveness conducted between 2001 and 2004, and published in *The New England Journal of Medicine* in 2005, indicated that over 70% of schizophrenia patients became non-compliant with their medication within 18 months of commencing therapy. Similarly a 2004 study of the VA National Psychosis Registry published in the journal *Bipolar Disorder* in October 2006 found that, of the 45% of bipolar patients who were being prescribed an antipsychotic, just over half of individuals appeared to be fully adherent with their antipsychotic medications, while the remaining individuals were either partially adherent or non-adherent with their antipsychotic medications.

In an attempt to improve patient compliance, physicians increasingly administer antipsychotic drugs through long-acting depot injections. Long-acting depot injections release medication slowly over weeks rather than over hours or days for conventional injections or oral medications, thereby dramatically reducing the number of times a patient needs to take their medication. Currently available long-acting injectable products include Risperdal Consta and Invega Sustenna, both marketed by Johnson & Johnson, and Zyprexa Relprevv, marketed by Eli Lilly & Co. These drugs provide two to four weeks of therapy per dose.



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## **Table of Contents**

Overall, the global atypical antipsychotic market is estimated to be in excess of \$16.3 billion in 2010, based upon published sales reports of certain pharmaceutical companies. In 2010, atypical antipsychotics comprised approximately 90% of all antipsychotic prescriptions in the United States, according to data from Wolters Kluwer (Source<sup>®</sup> PHAST Retail, January 2010 – December 2010). The existing long-acting injectable *risperidone* product, Risperdal Consta, achieved global net sales of \$1.5 billion in 2010, according to industry reports, and has a wholesale acquisition cost of approximately \$260 per bi-weekly dose, or more than \$500 per month, for the 25mg dosage strength (Source: Goldline). Finally, in the United States, prescribers of long-acting antipsychotics are highly concentrated with approximately 13,400 total prescribers of long-acting injectable products, including approximately 8,100 psychiatrists in 2010 (Source<sup>®</sup> PHAST Retail, January 2010 – December 2010).

### ***The Relday Opportunity***

Market research conducted on our behalf by bioStrategies Group in 2007 indicates that psychiatrists see significant potential advantages for Relday over the currently marketed long-acting *risperidone* injectable, specifically identifying the subcutaneous, needle-free, and once-monthly features of Relday as important differentiators versus the currently marketed long-acting antipsychotics. We believe on the basis of our preclinical development work and market research that, if successfully developed and approved, Relday could potentially provide a significant improvements over existing treatment options for patients suffering from schizophrenia as a result of:

*Subcutaneous delivery:* All the currently available long-acting atypical antipsychotics are administered intramuscularly and, other than the lowest dosage strength of Invega Sustenna, have injection volumes greater than Relday. Intramuscular injections have been associated with inadvertent vascular injection, leading to rapid release of the drug and related adverse events, and in addition can also result in slow, painful and or difficult injections. Utilizing the unique attributes of the Durect's SABER technology and the DosePro needle-free delivery system, Relday has been designed to be administered subcutaneously with an injection volume of 0.5mL or less.

*Needle-free delivery:* Relday is formulated to be administered using our proprietary DosePro needle-free delivery system. The currently available long-acting atypical antipsychotic products are delivered using a 23 gauge or larger needle, with Risperdal Consta requiring use of a 21 gauge or larger needle.

*No reconstitution:* Relday is formulated as a prefilled, single-dose product that does not require reconstitution, or the addition of a liquid diluent, prior to administration. Risperdal Consta and Zyprexa Relprevv both require reconstitution prior to injection, which is generally considered an inconvenience for busy healthcare practitioners.

*Once a month dosing with no oral supplementation:* Relday is formulated with a goal of providing a pharmacokinetic profile that will allow for once-monthly dosing without the need for supplementation with oral *risperidone*. Risperdal Consta provides therapy for only two weeks, resulting in more frequent physician visits and requires supplementation with oral *risperidone* for the first three weeks following initiation of therapy or following a missed dose of the injectable due to its pharmacokinetic profile.

*Preferred active ingredient:* Our market research indicated that in nearly all cases, long-acting injectable antipsychotics are prescribed to patients who have experience taking the same molecule orally and have demonstrated some level of acceptable efficacy and tolerability. Oral *risperidone* is now the second most commonly prescribed atypical antipsychotic compound in the United States, accounting for nearly 23% of total prescriptions in the twelve months ended December 2010 (Source<sup>®</sup> PHAST Retail, January 2010 – December 2010).

We intend to initiate clinical studies for Relday in patients with schizophrenia in early 2012 following filing of an IND application. We completed a pre-IND meeting with the FDA in December 2009. Following initiation of clinical trials in the United States, we plan to seek a development and commercialization partner or partners for Relday in territories outside of the United States such as Europe and Japan. While our current development

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## Table of Contents

plans are focused on schizophrenia, in the future we may consider expanding the program to address additional indications, such as bi-polar disorder. If successfully developed and approved by the FDA, we plan to commercialize Relday in the United States further leveraging our commercial infrastructure and sales force.

### **Our DosePro Technology and Pre-clinical Pipeline**

Our proprietary DosePro technology is a first-in-class, easy-to-use drug delivery system designed for self-administration of a pre-filled, single dose of liquid drug, subcutaneously, without a needle. The DosePro technology (formerly known as Intraject) has undergone more than ten years of design, process engineering, clinical evaluation and development work, including significant capital investment by the predecessor owners of the technology, Weston Medical Group, plc and Aradigm Corporation, or Aradigm. We believe the approval and launch of Sumavel DosePro in the United States validates the technology's commercial viability and readiness for other potential drug applications.

We believe that DosePro offers several benefits to patients compared to other subcutaneous delivery methods, and that it has the potential to become a preferred delivery option for patients and physicians for many injected medicines beyond *sumatriptan*, particularly those that are self-administered. These benefits include less anxiety or fear due to the lack of a needle, easier disposal without the need for a sharps container, no risk of needlestick injury or contamination, an easy-to-use three step process, no need to fill or manipulate the device, reliable performance, discreet use and portability. In several clinical trials and market research studies, DosePro has been shown to be preferred by patients over conventional needle-based systems. For example, in a head-to-head study conducted by GSK of Sumavel DosePro versus the European branded version of Imitrex STATdose, a needle-based delivery system, 61% of migraine patients preferred using Sumavel DosePro while only 18% preferred using the European branded version of Imitrex STATdose, with the remaining patients expressing no preference. In addition, in a market study conducted on our behalf by Boston Healthcare Associates, Inc., 76% of patients preferred Sumavel DosePro as a delivery method over Imitrex STATdose. In addition, DosePro requires less time from physicians and other caregivers to train patients to use the device.

Physician preference for DosePro as a needle-free alternative to conventional needle-based injections has also been demonstrated in market research studies. For example, in a study conducted by Palace Healthcare Group, Inc. on our behalf, 94% of primary care physicians and 98% of neurologists indicated they would be more willing to prescribe an injectable migraine product if it were needle-free.

In order to further enhance the DosePro technology and Sumavel DosePro, we have completed additional engineering and design work aimed at significantly reducing the sound emitted by the DosePro device upon drug delivery. Rather than the current loud burst of air, best described as a "whoosh," heard upon delivery with the current DosePro device, this enhanced version will sound more like the click of a pen upon drug delivery. We expect to submit this minor manufacturing change to the FDA in 2012, and expect to introduce this change to the commercial product shortly thereafter, depending on the FDA's agreement.

Clinical studies suggest that DosePro will have significant versatility in its ability to deliver various types of therapeutic compounds, including both small molecules and biologic products where the dose volume is 0.5 mL or less. In addition to positive results using DosePro in clinical studies performed with saline and *sumatriptan*, there have been three positive single-dose human pilot studies conducted with a combination of a protein pharmaceutical and DosePro. These studies include pharmacokinetic bioequivalence studies comparing DosePro to a conventional needle injection for human growth hormone and erythropoietin, or EPO, and pharmacodynamic equivalence study using granulocyte colony-stimulating factor, or GCSF. Pre-clinical work with monoclonal antibodies evaluating bioavailability, pharmacokinetics and a lack of immunogenicity has also been conducted. *In vitro* studies with DosePro technology have demonstrated the potential to allow the subcutaneous delivery of highly viscous formulations, which can be a limiting factor for use of traditional needle-based delivery systems. As a result of the versatility of DosePro to deliver various types of drug products, this technology may have significant market potential across a broad range of therapeutic areas, including those typically treated with small volume injectable products, such as hepatitis, infertility, multiple sclerosis and rheumatoid arthritis.

## **Table of Contents**

Since some drug formulations cannot be accommodated in a 0.5 mL dose volume, we have initiated early stage design and development of a larger volume, second generation version of our DosePro technology, which if successfully developed, would allow for a broader range of potential applications for our technology. However, the full development of such technology will require substantial investment and we may consider entering into a third-party collaboration in order to fully-develop such technology. There is no guarantee that we or any potential future third-party collaborator will be able to successfully develop such a device technology, whether for financial or technical reasons or otherwise.

Given its multiple benefits and therapeutic versatility, we believe the DosePro technology provides us with an opportunity to develop our own product candidates by pairing DosePro with proven drugs to enhance their commercial attractiveness such as with Relday. We are also evaluating the market potential, formulation requirements and clinical development pathway of an additional CNS compound that could be paired with DosePro to enhance its commercial attractiveness. We also believe DosePro provides an attractive licensing option for other pharmaceutical and biotech companies seeking to enhance, differentiate or extend the life-cycle of their own injectable products, and we are continuing to explore such arrangements with several established pharmaceutical companies. These opportunities include both currently marketed products as well as development stage product candidates.

### **Sales and Marketing**

We have built a highly experienced sales and marketing organization in the United States focused on marketing and selling Sumavel DosePro to physicians, nurses and other healthcare professionals. Our sales and marketing organization is comprised of approximately 100 professionals. Our field sales force of approximately 80 representatives is promoting Sumavel DosePro primarily to neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. We believe the key factors in the continued successful adoption of Sumavel DosePro will include expanding its use as an alternative to oral and nasal triptan therapy, converting current *sumatriptan* injectable users to Sumavel DosePro and building patient awareness and trial. We are specifically positioning Sumavel DosePro as a therapeutic alternative for oral triptan non-responders and dissatisfied patients, including those with morning migraines, fast progressing migraines and migraines accompanied by nausea and/or vomiting.

We believe our sales force is differentiated by its level of experience and background in the industry and accountability for sales results. Our field sales representatives have an average of 12 years of prior experience promoting pharmaceutical products and most have prior experience in the neurology and/or migraine space. In addition, our sales management team has on average 19 years of pharmaceutical industry experience, including an average of eight years of sales management experience. Each of our sales representatives and regional business directors undergoes a formal training program focused on disease background, our product, competitive products and territory management, as well as compliance with applicable laws. Our training program also includes significant ongoing and field-based learning to provide a comprehensive understanding and perspective as to our markets and disease states and the needs of both physicians and patients.

In addition to our field sales team, we also have an experienced team of field-based managed markets and trade directors. This team works closely with our regional business directors to engage with third-party payors to ensure and expand reimbursement coverage and patient access for our product and implement pharmacy based educational programs. To date, we have entered into a limited number of contracts with private health insurers, managed care organizations, government entities and other third-party payors that provide coverage for our products.

We are supporting this field based organization with an internal team which includes product management, communications, commercial analytics and sales operations staff. This team is focused on the implementation of a variety of marketing programs to educate customers, which include direct-to-physician promotional materials, speaker programs, direct-to-patient programs, digital media, participation in selected medical conventions and reimbursement support programs.

## **Table of Contents**

In addition, in July 2009, we entered into an exclusive agreement with Astellas under which Sumavel DosePro is currently being marketed by Astellas in the United States and promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists by approximately 400 Astellas sales representatives. This allows us to effectively market and sell to a broader physician audience than could be reached by our sales force alone.

In March 2008, we entered into a licensing and distribution agreement with Desitin, a private German pharmaceutical company focused on the development, manufacturing and distribution of products for the treatment of CNS disorders. Under the terms of the agreement, we licensed to Desitin the exclusive development and commercialization rights to Sumavel DosePro for the European Union, Norway, Switzerland and Turkey. Desitin will oversee, and be responsible for the expenses related to, all clinical development, regulatory approval and commercialization efforts required to market Sumavel DosePro in the territories in which Desitin elects to develop and market Sumavel DosePro. Desitin received approval to market Sumavel DosePro in Denmark in November 2010 followed by approval in the United Kingdom and Germany in January 2011 and Norway in February 2011. We have agreed to manufacture and supply the product to Desitin for commercial sale. Desitin has agreed to pay us a specified transfer price for commercial product and a low single-digit percentage royalty on net sales of the product. We retain full commercial rights to Sumavel DosePro in all other countries not licensed under the Desitin agreement, including the United States, Canada and the countries in Asia. We continue to evaluate potential partnerships to expand the future sale of Sumavel DosePro to additional markets outside of Europe and the United States.

To build upon our continued success in growing Sumavel DosePro prescriptions, we have initiated activities to expand our sales force in the United States to approximately 95 sales representatives by the end of the third quarter of 2011. For the launch of Zohydro, if approved, we intend to further expand our sales and marketing infrastructure, including expanding our field sales force to 250 or more representatives to allow us to reach a broad range of opioid prescribers in our target market and continue to support Sumavel DosePro. We expect our primary target audiences may expand to include anesthesiologists, pain specialists, physical medicine specialists and additional primary care physicians. In addition, we expect that we will also consider opportunities to partner Zohydro to reach a broader physician audience. We will also evaluate third-party co-promotion opportunities that would allow us to strategically leverage our commercial resources and generate additional revenue in the United States.

## **Competition**

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary therapeutics. We face competition from a number of sources, some of which may target the same indications as our product or product candidates, including large pharmaceutical companies, smaller pharmaceutical companies, biotechnology companies, academic institutions, government agencies and private and public research institutions, many of which have greater financial resources, sales and marketing capabilities, including larger, well established sales forces, manufacturing capabilities, experience in obtaining regulatory approvals for product candidates and other resources than us. We face competition not only in the commercialization of Sumavel DosePro or any product candidates for which we obtain marketing approval from the FDA or other regulatory authorities, but also for the in-licensing or acquisition of additional product candidates, and the out-licensing of our DosePro drug delivery technology.

### ***Sumavel DosePro***

Sumavel DosePro competes against other marketed migraine therapeutics. The largest class of marketed prescription products for treatment of migraine is the triptan class. The largest selling triptan is *sumatriptan*, with the branded products Imitrex and Treximet marketed by GSK and Sumavel DosePro marketed by us. There are six other branded triptan therapies being sold by pharmaceutical companies including AstraZeneca PLC, Endo Pharmaceuticals Holdings Inc., Johnson & Johnson, Merck, and Pfizer, Inc. in the United States.

**Table of Contents**

We also face competition from generic *sumatriptan* injectable, now marketed in the United States as an authorized generic of Imitrex STATdose by Par Pharmaceutical Companies 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 and alternative autoinjector forms of *sumatriptan* injection may not be directly substituted for Sumavel DosePro, generic versions of injectable *sumatriptan* 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. In addition to these migraine therapeutics, there are other marketed non-triptan migraine therapeutics, such as Cambia sold by Nautilus Neurosciences, Inc. and Migranal sold by Valeant Pharmaceuticals International. Moreover, there are several product candidates under development that could potentially be used to treat migraines and compete with Sumavel DosePro, including products under development by large pharmaceutical companies such as GSK and Merck and smaller companies such as NuPathe, Inc. and MAP Pharmaceuticals, Inc. In addition, Allergan, Inc. is now marketing BOTOX botulinum toxin for the treatment of chronic migraine.

**Zohydro**

If approved for the treatment of moderate to severe chronic pain, Zohydro will compete against other marketed branded and generic pain therapeutics and may compete with additional product candidates currently under development or developed in the future. Current competitors in the opioid pain therapeutics space include, but are not limited to, Abbott Laboratories, Cephalon, Inc., Endo Pharmaceuticals Holdings Inc., Johnson & Johnson, Mallinckrodt Inc., Pfizer, Purdue Pharma L.P., Teva Pharmaceutical Industries Limited and Watson Pharmaceuticals, Inc. There are at least 15 opioid product candidates under development, including abuse and diversion resistant formulations of currently available opioids, novel opioids and alternative delivery forms of various opioids under development at other pharmaceutical companies, including single-entity extended-release *hydrocodone* product candidates being developed by Cephalon, Inc., Egalet A/S, Pfizer and Purdue Pharma L.P. Zohydro may also face competition from non-opioid products, including new chemical entities, as well as alternative delivery forms of NSAIDs. In addition to the previously named companies, a number of pharmaceutical companies are developing new product candidates for pain including, but not limited to, Acura Pharmaceuticals, Inc., Altea Therapeutics Corporation, Collegium Pharmaceutical, Inc., Eli Lilly and Company, Elite Pharmaceuticals, Inc., Hospira, Inc., Inspirion Delivery Technologies, LLC, Intellipharmaceutics International Inc. and QRxPharma Ltd.

**Relday**

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

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**Table of Contents**

companies listed above, as well as by other pharmaceutical companies such as Alkermes, Inc., NuPathe, Inc. and Novartis AG, each of which has announced they are developing long-acting antipsychotic product candidates.

***DosePro Technology***

Traditional needle and syringe remain the primary method for administering intramuscular and subcutaneous injections. The injectable drug market is increasingly adopting new injection systems including pre-filled syringes, pen injectors and autoinjector devices. The majority of these devices, however, still employ a needle. We will compete with companies operating in the needle-based drug delivery market. These companies include, but are not limited to, Becton, Dickinson and Company, Owen Mumford Ltd. and Ypsomed. Additional competition may come from companies focused on out-licensing needle-free technology including Antares Pharma Inc. and Bioject Inc., which have both commercialized spring-driven, multiple-use, patient-filled, needle-free injectors, primarily for injecting human growth hormone or insulin for diabetes. We believe that market acceptance of these devices has been limited due to a combination of the cost of the devices, their large size and their complexity of use. Other companies may also be developing single-use, pre-filled, needle-free delivery systems. We also may experience future competition from alternative delivery systems which bypass the need for an injection, including inhaled, nasal, sublingual or transdermal technologies.

**Distribution**

We primarily sell Sumavel DosePro to wholesale pharmaceutical distributors, who, in turn, sell the products to pharmacies, hospitals and other customers. Three wholesale pharmaceutical distributors, Cardinal Health, Inc., McKesson Corporation and AmerisourceBergen Corporation, individually comprised 46.2% , 34.8% and 11.1%, respectively, of our total gross sales of Sumavel DosePro for the six months ended June 30, 2011.

We use a third-party logistics provider, Cardinal Health 105, Inc. (a/k/a Specialty Pharmaceutical Services), for key services related to logistics, warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management and call center management. In addition, we utilize third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services.

The following are distribution agreements that we believe are material to the ongoing operation of our business.

***Cardinal Health Inc.***

In December 2009 and January 2010, we entered into a wholesale purchase agreement and distribution services agreement, respectively, with Cardinal Health, Inc. and its affiliates, or collectively Cardinal Health, pursuant to which it provides us with distribution and inventory management services for Sumavel DosePro. The wholesale purchase agreement covers general terms related to the distribution and inventory management services provided by Cardinal Health, including with respect to the purchase of Sumavel DosePro from us and chargebacks and returns related to such purchases. The distribution services agreement covers the fees payable by us to Cardinal Health for the performance of such services. Under the distribution services agreement, we pay Cardinal Health a quarterly fee based on the volume of Sumavel DosePro purchased by Cardinal Health from us during that quarter.

The distribution services agreement has an initial three-year term, which expires in January 2013, and the wholesale purchase agreement has a one-year term, which expires in December 2011. Each agreement automatically renews for successive one-year periods unless either party provides the other party with written notice of non-renewal within a specified period prior to the expiration of the then-current term. Either party may

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**Table of Contents**

terminate either agreement (1) upon mutual written agreement of the parties, (2) upon written notice if the other party has failed to cure a breach of any of the terms of the agreement within a specified period following receipt of written notice of such breach, or (3) upon institution (whether voluntary or involuntary) of bankruptcy, insolvency, liquidation or similar proceedings by or against the other party or the assignment of the other party's assets for the benefit of creditors. In addition, either party may terminate the distribution services agreement 60 days following termination of the agreement pursuant to which an affiliate of Cardinal Health, Cardinal Health 105, Inc. (a/k/a Specialty Pharmaceutical Services) provides third-party logistics services for us. Cardinal Health may also terminate the distribution services agreement following a change of control of our company if Cardinal Health determines that the transaction gives rise to credit or financial risks. Either party may also terminate the wholesale purchase agreement for any reason by giving the other party specified written notice.

***McKesson Corporation***

In December 2009, we entered into a strategic redistribution center and core distribution agreement with McKesson Corporation, or McKesson, pursuant to which McKesson provides us with distribution and inventory management services for Sumavel DosePro. We pay McKesson a quarterly fee based on the volume of Sumavel DosePro purchased by McKesson from us during that quarter. The agreement remains in effect unless terminated by either party upon specified written notice to the other party.

**Manufacturing**

Sumavel DosePro and our DosePro technology are manufactured by contract manufacturers, component fabricators and secondary service providers. Suppliers of components, subassemblies and other materials are located in the United Kingdom, Germany, Ireland and the United States. All contract manufacturers and component suppliers have been selected for their specific competencies in the manufacturing processes and materials that make up the DosePro system. FDA regulations require that materials be produced under current Good Manufacturing Practices, or cGMPs, or Quality System Regulations, or QSR, as required for the respective unit operation within the manufacturing process. Manufacturing equipment specific to the production of critical DosePro components and assemblies was developed and purchased by us and the prior owners of the DosePro technology and is currently owned by us.

We manage the supply chain for Sumavel DosePro, consisting of the DosePro system and the active pharmaceutical ingredient, or API, internally with experienced operations professionals, including employees residing in the United Kingdom who oversee European contract manufacturing operations. We have entered into supply agreements relating to Sumavel DosePro with our critical contract manufacturers, most component fabricators and secondary service providers to secure commercial supply for Sumavel DosePro and expect manufacturing capacity to adequately support our projected Sumavel DosePro demand through 2012. Each of these manufacturers and each other company that supplies, fabricates or manufactures any component used in our DosePro device is currently the sole qualified source of their respective components. In order to support projected demand after 2012, or if demand exceeds our expectation before then, we will be required to expand the capacity of some of our existing contract manufacturers and suppliers or qualify new manufacturers or suppliers.

DosePro systems intended for clinical trials of DosePro-based products other than Sumavel DosePro are provided by using the existing manufacturing infrastructure, supplemented with clinical scale aseptic fill/finish as appropriate for the stage and scale of the product under clinical development.

Clinical materials for our Zohydro clinical program are manufactured by Elan Drug Delivery, Inc. under the terms of our license agreement with Elan described under "Collaborations, Commercial and License Agreements" below.

The following are manufacturing and supply arrangements and agreements that we believe are material to the ongoing operation of our business.

**Table of Contents*****Patheon UK Limited***

In November 2008, we entered into a manufacturing services agreement with Patheon UK Limited, or Patheon, located in Swindon, United Kingdom, a specialist in the aseptic fill/finish of injectables and other sterile pharmaceutical products. Under the terms of the agreement, Patheon serves as our exclusive manufacturer for the aseptic capsule assembly, filling and inspection, final device assembly and packaging of Sumavel DosePro, as well as other manufacturing and support services. Although we are not required to have any minimum quantity of Sumavel DosePro manufactured under the agreement, we have agreed to provide Patheon with forecasts of the required volumes of Sumavel DosePro we need, and we are required to pay Patheon a monthly manufacturing fee of £283,000, or approximately \$453,298 (based on the exchange rate as of June 30, 2011), over the remaining term of the agreement, aggregating to £9,633,000, or approximately \$15,429,800. Under the agreement, we are also required to pay support and service fees, with the level of service fees increasing if annual production exceeds a specified volume. The agreement has an initial five-year term, which expires October 31, 2013. The parties may mutually agree in writing to renew the term for additional terms prior to the expiration of the then-current term. Either party may terminate the agreement (1) upon specified written notice to the other party, (2) upon written notice if the other party has failed to remedy a material breach of any of its representations, warranties or other obligations under the agreement within a specified period following receipt of written notice of such breach, and (3) immediately upon written notice to the other party in the event that the other party is declared insolvent or bankrupt by a court of competent jurisdiction, a voluntary petition of bankruptcy is filed in any court of competent jurisdiction by such other party or the agreement is assigned by such other party for the benefit of creditors. Patheon may also terminate the agreement upon specified written notice if we assign the agreement to certain specified parties.

***Nypro Limited***

Nypro Limited, located in Bray, Ireland, manufactures the actuator assemblies and injection molded components for our DosePro device pursuant to purchase orders. We do not currently have a long-term commercial supply agreement with Nypro.

***MGlas AG***

In May 2009, we entered into a commercial manufacturing and supply agreement with MGlas AG, located in Schweinfurt, Germany. Under the terms of the agreement, MGlas is our exclusive supplier of the glass capsule that houses the *sumatriptan* API in Sumavel DosePro (and will be the exclusive supplier of glass capsules for any future 0.5 mL DosePro product candidates or products). The agreement has an initial three-year term, which expires in May 2012. Either party may terminate the agreement by providing the other party with specified written notice. In addition, either party may terminate the agreement immediately by written notice if the other party commits a material breach of its obligations which is either incapable of remedy or is not remedied within a specified period following receipt of written notice of such breach, or in the event the other party becomes insolvent or is subject to insolvency-related proceedings.

***Dr. Reddy s Laboratories, Inc.***

We are party to a supply agreement with Dr. Reddy s Laboratories, Inc., or Dr. Reddy s, which was originally entered into between Aradigm and Dr. Reddy s in September 2004. Under the terms of the agreement, Dr. Reddy s, a global pharmaceutical company and supplier of bulk API located in India, agreed to supply us with the *sumatriptan* API for Sumavel DosePro at a specified price. Dr. Reddy s has agreed to sell to us, and we agreed to purchase on a non-exclusive basis from Dr. Reddy s, not less than 50% of our quarterly requirements for *sumatriptan* in the United States, Canada and the European Union. The initial term of the agreement expires in 2020. The term of the agreement may be extended by us for successive one-year periods by written notice to Dr. Reddy s, unless Dr. Reddy s gives written notice to us that it does not wish to extend the term. We may terminate the agreement upon written notice if Dr. Reddy s is unable to deliver sufficient amounts of *sumatriptan* over a specified period of time. We may also terminate the agreement if we are negotiating an agreement with a third party to commercialize such third party s formulation of *sumatriptan* and such agreement would preclude



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**Table of Contents**

us from sourcing *sumatriptan* from any party other than such third party. Either party may terminate the agreement upon written notice if the other party commits a material breach of its obligations and fails to remedy the breach within a specified time period, if the other party becomes insolvent or subject to bankruptcy proceedings, or where a force majeure event continues for a specified period of time.

**Collaborations, Commercial and License Agreements**

***Durect Corporation Development and License Agreement***

In July 2011, we entered into a development and license agreement with Durect. Under the terms of the agreement, we will be responsible for the clinical development and commercialization of Relday. Durect will be responsible for non-clinical, formulation and CMC development responsibilities. Durect will be reimbursed by us for its research and development efforts on the product.

We paid a non-refundable upfront fee to Durect of \$2.25 million. We are obligated to pay Durect up to \$103 million in total future milestone payments with respect to the product subject to and upon the achievement of various development, regulatory and sales milestones. We are also required to pay a mid single-digit to low double-digit percentage patent royalty on annual net sales of the product determined on a jurisdiction-by-jurisdiction basis. The patent royalty term is equal to the later of the expiration of all Durect technology patents or joint patent rights in a particular jurisdiction, the expiration of marketing exclusivity rights in such jurisdiction, or 15 years from first commercial sale in such jurisdiction. After the patent royalty term, we will continue to pay royalties on annual net sales of the product at a reduced rate for so long as we continue to sell the product in the jurisdiction. We are also required to pay to Durect a tiered percentage of fees received in connection with any sublicense of the licensed rights.

Durect granted to us an exclusive worldwide license, with sub-license rights, to Durect intellectual property rights related to Durect's proprietary polymeric and non-polymeric controlled-release formulation technology to make and have made, use, offer for sale, sell and import *risperidone* products, where *risperidone* is the sole active agent, for administration by injection in the treatment of schizophrenia, bipolar disorder or other psychiatric related disorders in humans. Durect retains the right to supply our Phase 3 clinical trial and commercial product requirements on the terms set forth in the agreement.

Durect may terminate the agreement with respect to specific countries if we fail to advance the development of the product in such country within a specified time period, either directly or through a sublicensee. In addition, either party may terminate the agreement upon insolvency or bankruptcy of the other party, upon written notice of a material uncured breach or if the other party takes any act that attempts to impair such other party's relevant intellectual property rights. We may terminate the agreement upon written notice if during the development or commercialization of the product, the product becomes subject to one or more serious adverse drug experiences or if either party receives notice from a regulatory authority, independent review committee, data safety monitoring board or other similar body alleging significant concern regarding a patient safety issue and, as a result, we believe the long-term viability of the product would be seriously impacted. We may also terminate the agreement with or without cause, at any time upon prior written notice.

***Astellas Co-Promotion Agreement***

In July 2009, we entered into a co-promotion agreement with Astellas. Under the terms of the agreement, we granted Astellas the co-exclusive right (with us) to market and sell Sumavel DosePro in the United States (excluding Puerto Rico and the other territories and possessions of the United States) until June 30, 2013. Astellas has the option to extend the term of the agreement by an additional year in its sole discretion (and contingent upon Astellas' payment to us of a predetermined option fee). In addition, Astellas has a right to opt-in to the commercialization of potential line extensions of Sumavel DosePro. Under the agreement, both Astellas and we are 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 2011 and throughout the remainder of the

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**Table of Contents**

term, these minimum sales efforts are set forth as a minimum number of annual primary detail equivalents. We are responsible for the manufacture, supply, and distribution of commercial product for sale in the United States. In addition, we will supply product samples to Astellas, and Astellas will pay us for such samples, at an agreed upon transfer price.

The target audience for Astellas sales efforts is primarily comprised of prescribers classified as primary care physicians (including internal medicine, family practice and general practice), OB/GYNs, emergency medicine physicians and urologists, or collectively the Astellas Segment. The target audience for our sales effort is primarily comprised of neurologists and other prescribers of migraine medicines who fall outside the Astellas Segment. In addition, our representatives have the right to call upon a specified number of prescribers within the Astellas Segment; conversely Astellas representatives have the right to call upon a specified number of neurologists.

Under the agreement, Astellas has paid us upfront and milestone payments in an aggregate amount of \$20.0 million through June 30, 2011. Astellas is not obligated to pay us any additional milestone payments. In consideration for Astellas performance of its commercial efforts, we are 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. Astellas is not compensated for Sumavel DosePro sales to neurologists, any other prescribers not included in the Astellas Segment or for non-retail sales. In addition, upon completion of the co-promotion term, Astellas will be eligible to receive two additional annual tail payments calculated as decreasing fixed percentages (ranging from a mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion.

Astellas may terminate the agreement for any reason or no reason upon 180-days written notice to us or at any time in the event we undergo a change of control (as defined in the agreement). In addition, Astellas may terminate the agreement if a governmental authority takes action that prevents or makes it unlawful for Astellas to perform its obligations under the agreement, in the event of our inability to supply commercial product, under certain circumstances where a third party asserts that the making or selling of Sumavel DosePro infringes the intellectual property rights of a third party, or if we materially breach our minimum sales effort obligations and do not cure such breach within a specified period. We may terminate the agreement in the event that Astellas materially breaches its minimum sales effort obligations and does not cure such breach within a specified period; however, we would be required to pay Astellas the first of the two annual tail payments described above in connection with such termination. Either party may terminate the agreement upon the occurrence of a large scale recall or market withdrawal of Sumavel DosePro, a failure of the Sumavel DosePro brand to achieve certain minimum sales levels in 2011, a material uncured breach by the other party, insolvency or bankruptcy of the other party, or other event which affects the other party's ability to perform its obligations under the agreement. Based on our net product revenue through June 30, 2011, we do not expect to meet the specified 2011 minimum sales levels for Sumavel DosePro, and therefore expect that both we and Astellas will have the right to terminate the agreement on this basis. If either party were to exercise this termination right, it must provide 90 days written notice to the other party, such notice to be provided within 30 days after the actual net sales of Sumavel DosePro through December 31, 2011 have been provided to Astellas pursuant to the terms of the co-promotion agreement. In the event of such a termination relating to sales levels of Sumavel DosePro, we would be required to make the two annual tail payments described above. In the event of a termination by us or Astellas, we would expect to either expand our sales force to promote Sumavel DosePro to certain physicians within the Astellas Segment, and/or seek another co-promotion partner, if available, in order to support the future sales and marketing of Sumavel DosePro.

***Desitin License and Distribution Agreement***

In March 2008, we entered into a licensing and distribution agreement with Desitin. Under the terms of the agreement, we granted Desitin the exclusive right under our intellectual property rights related to Sumavel DosePro to develop, use, distribute, sell, offer for sale, and import Sumavel DosePro and any potential modified versions of Sumavel DosePro in the European Union, Norway, Switzerland and Turkey. Under the agreement, Desitin has the right, but with the exception of Germany not the obligation, at its own expense, to develop, obtain

**Table of Contents**

marketing approval and commercialize Sumavel DosePro in these territories. In addition, Desitin has a right of first refusal on the commercialization of any potential line extensions of Sumavel DosePro. We will manufacture and supply the product to Desitin for commercial sale in the licensed territories. Desitin will pay us a specified transfer price for commercial product and a low single-digit percentage royalty on net sales of the product for an initial term, on a country to country basis until the greater of ten years after the first commercial sale in that country or the expiration, in such country, of the last patent right to expire under the licensed technology. After the initial term, in countries where the product has had commercial sales, the agreement will be automatically renewed on a country-by-country basis by additional successive specified periods unless it is terminated by either party giving a specified prior written notice.

Either party may terminate the agreement upon a material uncured breach, insolvency or bankruptcy, adverse event which affects the other party's ability to perform its obligations under the agreement or upon the enactment of any law, decree or regulation which would impair or restrict either our right, title or interest in the intellectual property, or Desitin's right to market or distribute the product in accordance with the agreement, either party's right to terminate or elect not to renew the agreement as provided therein, or our right to collect the purchase price or royalties under the agreement. Either party may also terminate the agreement by giving 90 days prior written notice if continued marketing in the relevant territories is no longer possible due to advice from a relevant regulatory authority or clinical review board in such countries or due to serious adverse events caused by Sumavel DosePro anywhere in the world. Desitin may terminate the agreement upon a competent regulatory authority in the territories either imposing therapeutic indications not acceptable to Desitin or requiring the product to be marketed as a generic drug. Desitin also may terminate the agreement if more than one study regarding bioequivalence is required to obtain marketing authorization. We may terminate the agreement upon a specified prior written notice if in each of a specified number of consecutive calendar years Desitin fails to meet a specified percentage of sales forecasts to be mutually agreed upon under the agreement, if Desitin takes any act impairing our intellectual property rights or if Desitin ceases to carry on business in the marketing of pharmaceutical products in the territories. Desitin may also terminate the agreement, upon written notice, if the price at which we supply our product to Desitin exceeds a specified threshold.

***Elan Pharma International Limited License Agreement***

In November 2007, we entered into a license agreement with Elan, which was amended in September 2009. Under the terms of this license agreement, Elan granted to us an exclusive license in the United States and its possessions and territories, with defined sub-license rights to third parties other than certain technological competitors of Elan, to certain Elan intellectual property rights related to our Zohydro product candidate. The agreement grants us the exclusive right under certain Elan patents and patent applications to import, use, offer for sale and sell oral controlled-release capsule or tablet formulations of *hydrocodone*, where *hydrocodone* is the sole active ingredient, for oral prescriptions in the treatment or relief of pain, pain syndromes or pain associated with medical conditions or procedures in the United States. This right enables us to exclusively develop and sell Zohydro in the United States. Elan has retained the exclusive right to take action in the event of infringement or threatened infringement by a third party of Elan's intellectual property rights under the agreement. We have the right to pursue an infringement claim against the alleged infringer should Elan decline to take or continue an action.

Under the terms of the agreement, the parties agreed that, subject to the future negotiation of a commercial manufacture and supply agreement, Elan, or an affiliate of Elan, will have the sole and exclusive right to manufacture and supply finished commercial product of Zohydro to us under agreed upon financial terms.

Elan also granted to us, in the event that Elan is unwilling or unable to manufacture or supply commercial product to us, a non-exclusive license to make product under Elan's intellectual property rights. This non-exclusive license also includes the right to sublicense product manufacturing to a third party, other than certain technological competitors of Elan.

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**Table of Contents**

Under the license agreement, we paid an upfront fee to Elan of \$500,000. We paid an additional milestone payment in the amount of \$750,000 to Elan in August 2011 in connection with the completion of the treatment phase of our pivotal efficacy Phase 3 clinical trial, Study 801. We may be obligated to pay Elan up to \$3.75 million in total future milestone payments with respect to Zohydro depending upon the achievement of various development and regulatory events. We are also required to pay a mid single-digit percentage royalty on net sales of the product for an initial royalty term equal to the longer of the expiration of Elan's patents covering the product in the United States, or 15 years after commercial launch, if Elan does not have patents covering the product in the United States. After the initial royalty term, the license agreement will continue automatically for three-year rolling periods during which we will continue to pay royalties on net sales of the product at a reduced low single-digit percentage rate in accordance with the terms of the license agreement.

Either party may terminate the agreement upon a material, uncured default or certain insolvency events of the other party or upon 12 months written notice prior to the end of the initial royalty term or any additional three-year rolling period. Elan may terminate the agreement in the event that we fail to meet specified development and commercialization milestones within specified time periods. We may terminate this agreement if the sale of Zohydro is prohibited by regulatory authorities, or if, despite commercially reasonable efforts, we are unable to obtain regulatory approval for Zohydro. We may also terminate the agreement, with or without cause, at any time upon six months' written notice prior to NDA approval for Zohydro and at any time upon 12 months' prior written notice after NDA approval for Zohydro.

In May 2011, Elan announced the execution of a definitive agreement under which Alkermes, Inc. will acquire and merge with an Elan entity which will include rights as licensor under our license agreement. According to Elan, the transaction is expected to close during the third quarter of 2011. Although Alkermes will succeed Elan as the party in interest to our license agreement, we do not anticipate any other changes in the rights under our license agreement in connection with the proposed transaction.

***Aradigm Corporation Asset Purchase Agreement***

In August 2006, we entered into an asset purchase agreement with Aradigm. Under the terms of the agreement, Aradigm assigned and transferred to us all of its right, title and interest to tangible assets and intellectual property related to the DosePro (formerly known as Intraject) needle-free drug delivery system. Aradigm also granted to us a non-exclusive, fully paid, worldwide, perpetual, irrevocable, transferable, sublicensable license under all other intellectual property of Aradigm that was owned, controlled or employed by Aradigm prior to the closing of the asset purchase and that is necessary or useful to the development, manufacture or commercialization of the DosePro delivery system. Aradigm also retained a worldwide, royalty-free, non-exclusive license, with a right to sublicense, under all transferred intellectual property rights solely for purposes of the pulmonary field, and we granted Aradigm a license under other intellectual property rights solely for use in the pulmonary field.

At the time of the closing of the asset purchase, we paid to Aradigm a sum of \$4.0 million as consideration. Under the agreement, we also paid a subsequent milestone payment to Aradigm of \$4.0 million upon the U.S. commercialization of Sumavel DosePro in February 2010. We are also required to pay a 3% royalty on global net sales of Sumavel DosePro, by us or one of our licensees, if any, until the later of January 2020 or the expiration of the last valid claim of the transferred patents covering the manufacture, use, or sale of the product.

In addition, in the event we or one of our future licensees, if any, commercializes a non-*sumatriptan* product in the DosePro delivery system, we will be required to pay Aradigm, at our election, either a 3% royalty on net sales of each non-*sumatriptan* product commercialized, or a fixed low-twenties percentage of the royalty revenues received by us from the licensee, if any, until the later of the ten year anniversary of the first commercial sale of the product in the United States or the expiration of the last valid claim of the transferred patents covering the manufacture, use or sale of the product. Royalty revenues under this agreement include, if

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## **Table of Contents**

applicable, running royalties on the net sales of non-*sumatriptan* products, license or milestone fees not allocable to development or other related costs incurred by us, payments in consideration of goods or products in excess of their cost, or payments in consideration for equity in excess of the then fair market value of the equity.

### **Intellectual Property**

Our success will depend to a significant extent on our ability to obtain, expand and protect our intellectual property estate, enforce patents, maintain trade secret and trademark protection and operate without infringing the proprietary rights of other parties.

#### ***Needle-free Drug Delivery Technologies***

Sumavel DosePro is a new drug-device combination that subcutaneously delivers *sumatriptan* utilizing our proprietary needle-free drug delivery system to treat migraine and cluster headache. Our patent portfolio is directed to various types and components of needle-free and other drug delivery systems. As of August 16, 2011, we have 16 issued U.S. patents, 13 pending U.S. patent applications, 47 issued foreign patents and 23 pending foreign patent applications. Of the above, we have eight issued U.S. patents, three pending U.S. patent applications, 38 issued foreign patents and three pending foreign patent applications relating to various aspects of Sumavel DosePro and our DosePro technology.

Our issued U.S. Patent No. 5,891,086 covers a particular actuator mechanism forming a part of the needleless injector device, and is expected to expire in 2014. We have a corresponding patent in Canada, and two each in Germany, Spain, France, United Kingdom, Italy and Japan, which are all expected to expire in 2013. Our issued U.S. Patent No. 6,135,979 covers a needleless injector with particular safety mechanisms, and is expected to expire in 2017. We have corresponding patents in Germany, France, United Kingdom and Japan, which are all expected to expire in 2016. Our issued U.S. Patent No. 5,957,886 claims a needleless injector system using a viscous damping medium, and is expected to expire in 2016. We have corresponding foreign patents (one each in Canada, Germany, France, United Kingdom and Japan), which are all expected to expire in 2015. Our issued U.S. Patent No. 7,776,007 covers the cap and latch mechanism, and is expected to expire in 2026. We have a corresponding patent in Japan. Our issued U.S. Patent No. 7,901,385 covers a casing for enclosing the injection device, and is expected to expire in 2026. We have corresponding patents in Australia, Germany, Spain, France, Great Britain, Italy, and Japan. U.S. Patents 5,891,086; 6,135,979; 5,957,886; 7,776,007; and 7,901,385 are listed in the FDA Orange Book for Sumavel DosePro.

In addition, we have two U.S. patents (U.S. Patent Nos. 7,231,945 and 7,320,346) and two pending foreign patent applications in Canada and Europe corresponding to methods of proof testing glass drug containers, such as those used in the manufacture of Sumavel DosePro. These patents, and applications if they issue, are expected to expire in 2023. We also have one U.S. patent (U.S. Patent No. 7,150,297) and one each in Canada, Germany, France and the United Kingdom corresponding to methods of filling needle-free injector capsules, such as those used in the manufacture of Sumavel DosePro. These patents, and applications if they issue, are expected to expire in 2022.

We also have three pending U.S. patent applications, four foreign patents (one each in Germany, France, Japan and the United Kingdom), and one pending foreign patent application in Canada corresponding to needle-free injector drug capsules and methods for filling capsules with liquid drug, such as those used in the manufacture of Sumavel DosePro. These patents, and applications if they issue, are expected to expire in 2022.

Our remaining issued U.S. patents, pending U.S. patent applications, issued foreign patents, and pending foreign patent applications are not currently used in Sumavel DosePro, but may be used with alternate versions of, or future product candidates utilizing, our DosePro technology.

We do not have patent protection for Sumavel DosePro in a significant number of countries, including large territories such as India, Russia and China, and we will be unable to prevent infringement in those countries.

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## **Table of Contents**

Additionally, the five U.S. patents listed in the FDA Orange Book for Sumavel DosePro expire in 2014, 2016, 2017 and 2026. Upon expiration, we will lose certain advantages that come with Orange Book listing of patents and will no longer be able to prevent others in the U.S. from practicing the inventions claimed by the five patents.

### ***Zohydro***

Zohydro is an oral version of an opioid pain reliever, which is designed to offer an extended-release profile that utilizes Elan's proprietary SODAS delivery system. Our in-licensed patents from Elan relating to Zohydro include one issued U.S. Patent No. 6,902,742 and a pending U.S. Patent Application No. 11/372,857. The license agreement is described above in further detail. The issued patent is expected to expire in November 2019. Absent any award of patent term adjustments or extensions, the patent application, if it issues, is not expected to expire later than this date.

### ***Relday***

Because Relday utilizes the DosePro technology, the patents and intellectual property that protect the DosePro device will also provide protection for Relday. Zogenix has licensed a number of United States and foreign patent applications from Durect that are intended to cover the formulation of Relday and its delivery. However, as the formulation and delivery of Relday are the subject of on-going research it remains uncertain if the Durect patents or applications, should they issue as patents, will cover the final formulation or delivery of Relday.

## **Government Regulation**

### ***FDA Approval Process***

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The FFDCAs and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable FDA or other requirements may subject a company to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, a clinical hold, warning letters, recall or seizure of products, partial or total suspension of production, withdrawal of the product from the market, injunctions, fines, civil penalties or criminal prosecution.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves:

completion of pre-clinical laboratory and animal testing and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;

submission to the FDA of an IND for human clinical testing which must become effective before human clinical trials may begin in the United States;

approval by an independent institutional review board, or IRB, at each clinical trial site before each trial may be initiated;

performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each intended use;

satisfactory completion of an FDA pre-approval inspection of the facility or facilities at which the product is manufactured to assess compliance with the FDA's cGMP regulations, and for devices and device components, the QSR, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;



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**Table of Contents**

submission to the FDA of a new drug application, or NDA;

satisfactory completion of an FDA advisory committee review, if applicable; and

FDA review and approval of the NDA.

The pre-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Pre-clinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The results of pre-clinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to the FDA. Some pre-clinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions relating to one or more proposed clinical trials and places the clinical trial on a clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, our submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Further, an independent IRB, covering each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and informed consent information for subjects before the trial commences at that site and it must monitor the study until completed. The FDA, the IRB, or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk or for failure to comply with the IRB's requirements, or may impose other conditions.

As a separate amendment to an IND, a sponsor may submit a request for an SPA from the FDA. Under the SPA procedure, a sponsor may seek the FDA's agreement on the proposed design and size of a clinical trial intended to form the primary basis for determining a product's efficacy. Upon specific request by a sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis within 45 days of receipt of the request with the goal of reaching an agreement that the Phase III trial protocol design, clinical endpoints, and statistical analyses are acceptable to support regulatory approval of the drug product candidate with respect to effectiveness for the indication studied. Under an SPA, the FDA agrees to not later alter its position with respect to adequacy of the design, execution, or analyses of the clinical trial intended to form the primary basis of an effectiveness claim in an NDA, without the sponsor's agreement, unless the FDA identifies a substantial scientific issue essential to determining the safety or efficacy of the drug after testing begins. Moreover, any change to a study protocol after agreement with the FDA is reached can invalidate an SPA. Agreements and disagreements between the FDA and the sponsor regarding an SPA are documented by the FDA in an SPA letter to the sponsor or in the minutes of a meeting between the sponsor and the FDA.

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Sponsors of clinical trials generally must register and report, at the NIH-maintained website [ClinicalTrials.gov](http://ClinicalTrials.gov), key parameters of certain clinical trials. For purposes of an NDA submission and approval, human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

*Phase 1:* The drug is initially introduced into healthy human subjects or patients and tested for safety, dose tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness.



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**Table of Contents**

*Phase 2:* The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications and to determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more extensive Phase 3 clinical trials.

*Phase 3:* These are commonly referred to as pivotal studies. When Phase 2 evaluations demonstrate that a dose range of the product appears to be effective and has an acceptable safety profile, Phase 3 trials are undertaken in large patient populations to further evaluate dosage, to obtain additional evidence of clinical efficacy and safety in an expanded patient population at multiple, geographically-dispersed clinical trial sites, to establish the overall risk-benefit relationship of the drug and to provide adequate information for the labeling of the drug.

*Phase 4:* In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after NDA approval. Such post-approval trials are typically referred to as Phase 4 studies.

The results of product development, pre-clinical studies and clinical trials are submitted to the FDA as part of an NDA. NDAs must also contain extensive information relating to the product's pharmacology, CMC and proposed labeling, among other things.

For some drugs, especially controlled substances, the FDA may require a risk evaluation and mitigation strategy, or REMS, which could include measures imposed by the FDA such as prescribing restrictions, requirements for post-marketing studies or certain restrictions on distribution and use. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information and is subject to payment of additional user fees. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once the submission has been accepted for filing, the FDA begins an in-depth substantive review. Under the Prescription Drug User Fee Act, or PDUFA, the FDA agrees to specific performance goals for NDA review time through a two-tiered classification system, Standard Review and Priority Review. Standard Review NDAs have a goal of being completed within a ten-month timeframe. A Priority Review designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. The goal for completing a Priority Review is six months. It is likely that our product candidates will be granted a Standard Review. The review process may be extended by the FDA for three additional months to consider certain information or obtain clarification regarding information already provided in the submission. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully when making decisions. In addition, for combination products like Sumavel DosePro or future product candidates utilizing the DosePro technology, the FDA's review may include the participation of both the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health, which may complicate or prolong the review.

Before approving an NDA, the FDA may inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP, and if applicable, QSR, requirements and are adequate to assure consistent production of the product within required specifications. Additionally, the FDA will typically inspect one or more clinical sites to assure compliance with GCP before approving an NDA.

## **Table of Contents**

After the FDA evaluates the NDA and, in some cases, the related manufacturing facilities, it may issue an approval letter or a Complete Response Letter, or CRL, to indicate that the review cycle for an application is complete and that the application is not ready for approval. CRLs generally outline the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when the deficiencies have been addressed to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Once issued, the FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems are identified after the product reaches the market. In addition, the FDA may require post-approval testing, including Phase 4 studies, and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label, and, even if the FDA approves a product, it may limit the approved indications for use for the product or impose other conditions, including labeling or distribution restrictions or other risk-management mechanisms. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require us to develop additional data or conduct additional pre-clinical studies and clinical trials.

### ***Post-Approval Requirements***

Once an NDA is approved, a product will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug/device listing, recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. There also are extensive U.S. Drug Enforcement Agency, or DEA, regulations applicable to marketed controlled substances.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and generally require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;

fines, warning letters or holds on post-approval clinical trials;

refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;

product seizure or detention, or refusal to permit the import or export of products; or

injunctions or the imposition of civil or criminal penalties.



## **Table of Contents**

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. While physicians may prescribe for off label uses, manufacturers may only promote for the approved indications and in accordance with the provisions of the approved label. 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.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution, including a drug pedigree which tracks the distribution of prescription drugs.

The FDA may require post-approval studies and clinical trials if the FDA finds that scientific data, including information regarding related drugs, deem it appropriate. The purpose of such studies would be to assess a known serious risk or signals of serious risk related to the drug or to identify an unexpected serious risk when available data indicate the potential for a serious risk. The FDA may also require a labeling change if it becomes aware of new safety information that it believes should be included in the labeling of a drug.

The FDA also has the authority to require a drug-specific risk evaluation and mitigation strategy, or REMS, to ensure the safe use of the drug. In determining whether a REMS is necessary, FDA must 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, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. 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, 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 at 18 months, three years, and seven years after the strategy's approval. The FDA may also impose a REMS requirement on a drug already on the market if the FDA determines, based on new safety information, that a REMS is necessary to ensure that the drug's benefits outweigh its risks.

In February 2009, the FDA informed drug manufacturers that it will require a REMS for sustained release opioid drug products. Subsequently, the FDA initiated efforts to develop a new standardized REMS for these opioid medications to ensure their safe use. An extended-release formulation of *hydrocodone* would also be required to have a REMS. The FDA's authority to take this action is based on risk management and post market safety provisions within the FDAAA. In April 2011, after several public meetings, the FDA released the final REMS for extended-release opioids. The REMS consists of a Medication Guide, elements to assure safe use (including an education program for prescribers and materials for prescribers to educate patients), and a timetable for submission of assessments of at least six months, 12 months, and annually after the REMS is approved. The FDA recommends that sponsors of extended-release opioids cooperate to establish a single monitoring system for these assessments. We intend to submit a REMS at the time of the NDA submission for Zohydro.

With respect to post-market product advertising and promotion, the FDA imposes a number of complex regulations on entities that advertise and promote pharmaceuticals, which include, among others, standards for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the internet. The FDA has very broad enforcement authority under the FDCA, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing entities to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA, and state and federal civil and criminal investigations and prosecutions.

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**Table of Contents*****Section 505(b)(2) New Drug Applications***

As an alternate path to FDA approval for modifications to formulations or uses of products previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, and 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. The applicant may rely upon published literature and the FDA's findings of safety and effectiveness based on certain pre-clinical or clinical studies conducted for an approved product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that a Section 505(b)(2) NDA relies on studies conducted for a previously approved drug product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book. Specifically, the applicant must certify for each listed patent that (1) the required patent information has not been filed; (2) the listed patent has expired; (3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patent is invalid, unenforceable or will not be infringed by the new product. A certification that the new product will not infringe the already approved product's listed patent or that such patent is invalid is known as a Paragraph IV certification. If the applicant does not challenge the listed patents through a Paragraph IV certification, the Section 505(b)(2) NDA application will not be approved until all the listed patents claiming the referenced product have expired. The Section 505(b)(2) NDA application also will not be accepted or approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a New Chemical Entity, listed in the Orange Book for the referenced product, has expired.

If the 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the referenced NDA and patent holders once the 505(b)(2) NDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a legal challenge to the Paragraph IV certification. Under the FDCA, the filing of a patent infringement lawsuit within 45 days of their receipt of a Paragraph IV certification in most cases automatically prevents the FDA from approving the Section 505(b)(2) NDA for 30 months, or until a court decision or settlement finding that the patent is invalid, unenforceable or not infringed, whichever is earlier. The court also has the ability to shorten or lengthen the 30 month stay if either party is found not to be reasonably cooperating in expediting the litigation. Thus, the Section 505(b)(2) applicant may invest a significant amount of time and expense in the development of its product only to be subject to significant delay and patent litigation before its product may be commercialized.

The 505(b)(2) NDA applicant also may be eligible for its own regulatory exclusivity period, such as three-year exclusivity. The first approved 505(b)(2) applicant for a particular condition of approval, or change to a marketed product, such as a new extended release formulation for a previously approved product, may be granted three-year Hatch-Waxman exclusivity if one or more clinical studies, other than bioavailability or bioequivalence studies, was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, the FDA would be precluded from making effective any other application for the same condition of use or for a change to the drug product that was granted exclusivity until after that three-year exclusivity period has run. Additional exclusivities may also apply.

Additionally, the 505(b)(2) NDA applicant may have relevant patents in the Orange Book, and if it does can initiate patent infringement litigation against those applicants that challenge such patents, which could result in a thirty-month stay delaying those applicants.

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## **Table of Contents**

### ***DEA Regulation***

One of our product candidates, Zohydro, will be regulated as a controlled substance as defined in the Controlled Substances Act of 1970, or CSA, which establishes registration, security, recordkeeping, reporting, storage, distribution and other requirements administered by the DEA. The DEA is concerned with the control of handlers of controlled substances, and with the equipment and raw materials used in their manufacture and packaging, in order to prevent loss and diversion into illicit channels of commerce.

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, our proprietary oral, extended-release version of *hydrocodone*, is expected to be listed by the DEA as a Schedule II controlled substance under the CSA. Consequently, its manufacture, shipment, storage, sale and use will be subject to a high degree of regulation. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized.

The DEA typically inspects a facility to review its security measures prior to issuing a registration. Security requirements vary by controlled substance schedule, with the most stringent requirements applying to Schedule I and Schedule II substances. Required security measures include background checks on employees and physical control of inventory through measures such as cages, surveillance cameras and inventory reconciliations. Records must be maintained for the handling of all controlled substances, and periodic reports made to the DEA, for example distribution reports for Schedule I and II controlled substances, Schedule III substances that are narcotics, and other designated substances. Reports must also be made for thefts or losses of any controlled substance, and to obtain authorization to destroy any controlled substance. In addition, special authorization and notification requirements apply to imports and exports.

In addition, a DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. Distributions of any Schedule I or II controlled substance must also be accompanied by special order forms, with copies provided to the DEA. Because Zohydro, an oral, extended-release version of *hydrocodone*, is expected to be regulated as a Schedule II controlled substance, it will be 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. We and our contract manufacturers must receive an annual quota from the DEA in order to produce or procure any Schedule I or Schedule II substance, including *hydrocodone* for use in manufacturing Zohydro. 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. Our, or our contract manufacturers', quota of an active ingredient may not be sufficient to meet commercial demand or complete clinical trials. Any delay or refusal by the DEA in establishing our, or our contract manufacturers', quota for controlled substances could delay or stop our clinical trials or product launches, which could have a material adverse effect on our business, financial position and results of operations.

To meet its responsibilities, the DEA conducts periodic inspections of registered establishments that handle controlled substances. Failure to maintain compliance with applicable requirements, particularly as manifested in loss or diversion, can result in enforcement action that could have a material adverse effect on our business,

## **Table of Contents**

results of operations and financial condition. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to revoke those registrations. In certain circumstances, violations could eventuate in criminal proceedings.

Individual states also regulate controlled substances, and we and our contract manufacturers will be subject to state regulation on distribution of these products.

### ***International Regulation***

In addition to regulations in the United States, we are subject to a variety of foreign regulations regarding safety and efficacy and governing, among other things, clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional review periods, and the time may be longer or shorter than that required to obtain FDA approval and, if applicable, DEA classification. The requirements governing, among other things, the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. 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 negatively impact the regulatory process in others.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

In addition to regulations in Europe and the United States, we are subject to a variety of other foreign regulations governing, among other things, the conduct of clinical trials, pricing and reimbursement and commercial distribution of our products. If we fail to comply with applicable foreign regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

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. In November 2010, Desitin received marketing approval in Denmark and has received subsequent approvals in Germany, Sweden and United Kingdom.

### ***Healthcare Fraud and Abuse Laws***

We are subject to various federal, state and local laws targeting fraud and abuse in the healthcare industry. For example, in the United States, there are federal and state anti-kickback laws that prohibit the payment or receipt of kickbacks, bribes or other remuneration intended to induce the purchase or recommendation of healthcare products and services or reward past purchases or recommendations. Violations of these laws can lead to civil and criminal penalties, including fines, imprisonment and exclusion from participation in federal healthcare programs. These laws are potentially applicable to manufacturers of products regulated by the FDA, such as us, and hospitals, physicians and other potential purchasers of such products.

In particular, the federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program such as the TRICARE, Medicare and Medicaid programs. The term remuneration is not defined in the federal Anti-Kickback Statute and has been broadly interpreted to include anything of value,

**Table of Contents**

including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests and providing anything at less than its fair market value. In addition, the recently enacted Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the PPACA, among other things, amends the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b effective March 23, 2010. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of 42 U.S.C. § 1320a-7b constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes fines against any person who is determined to have presented or caused to be presented claims to a federal health care program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Moreover, the lack of uniform court interpretation of the Anti-Kickback Statute makes compliance with the law difficult.

Recognizing that the Anti-Kickback Statute is broad and may technically prohibit many innocuous or beneficial arrangements within the healthcare industry, the U.S. Department of Health and Human Services' Office of Inspector General, or OIG, issued regulations in July of 1991, and periodically since that time, which the OIG refers to as safe harbors. These safe harbor regulations set forth certain provisions which, if met in form and substance, will assure pharmaceutical companies, healthcare providers and other parties that they will not be prosecuted under the federal Anti-Kickback Statute. Additional safe harbor provisions providing similar protections have been published intermittently since 1991. Although full compliance with these provisions ensures against prosecution under the federal Anti-Kickback Statute, the failure of a transaction or arrangement to fit within a specific safe harbor does not necessarily mean that the transaction or arrangement is illegal or that prosecution under the federal Anti-Kickback Statute will be pursued. However, conduct and business arrangements that do not fully satisfy each applicable safe harbor may result in increased scrutiny by government enforcement authorities, such as the OIG or federal prosecutors. Additionally, there are certain statutory exceptions to the federal Anti-Kickback Statute, one or more of which could be used to protect a business arrangement, although we understand that OIG is of the view that an arrangement that does not meet the requirements of a safe harbor cannot satisfy the corresponding statutory exception, if any, under the federal Anti-Kickback Statute.

Additionally, many states have adopted laws similar to the federal Anti-Kickback Statute. Some of these state prohibitions apply to referral of patients for healthcare items or services reimbursed by any third-party payor, not only the Medicare and Medicaid programs in at least some cases, and do not contain safe harbors or statutory exceptions. Government officials have focused their enforcement efforts on marketing of healthcare services and products, among other activities, and have brought cases against numerous pharmaceutical and medical device companies, and certain sales and marketing personnel for allegedly offering unlawful inducements to potential or existing customers in an attempt to procure their business or reward past purchases or recommendations.

Another development affecting the healthcare industry is the increased use of the federal civil False Claims Act and, in particular, actions brought pursuant to the False Claims Act's whistleblower or qui tam provisions. The civil False Claims Act imposes liability on any person or entity who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The qui tam provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically. In addition, various states have enacted false claim laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third-party payor and not merely a federal healthcare program. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties of



**Table of Contents**

\$5,500 to \$11,000 for each separate false claim. There are many potential bases for liability under the False Claims Act. Liability arises, primarily, when an entity knowingly submits, or causes another to submit, a false claim for reimbursement to the federal government. The False Claims Act has been used to assert liability on the basis of inadequate care, kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price or Average Manufacturer Price, improper use of Medicare numbers when detailing the provider of services, improper promotion of off-label uses (i.e., uses not expressly approved by FDA in a drug's label), and allegations as to misrepresentations with respect to the services rendered. Our activities relating to the reporting of discount and rebate information and other information affecting federal, state and third party reimbursement of our products, and the sale and marketing of our products and our service arrangements or data purchases, among other activities, may be subject to scrutiny under these laws. We are unable to predict whether we would be subject to actions under the False Claims Act or a similar state law, or the impact of such actions. However, the cost of defending such claims, as well as any sanctions imposed, could adversely affect our financial performance.

Also, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, created several new federal crimes, including health care fraud, and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private third-party payors. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services.

The PPACA also imposes new reporting and disclosure requirements on drug manufacturers for any transfer of value made or distributed to prescribers and other healthcare providers, effective March 30, 2013. Such information will be made publicly available in a searchable format beginning September 30, 2013. In addition, drug manufacturers will also be required to report and disclose any investment interests held by physicians and their immediate family members during the preceding calendar year. Failure to submit required information may result in civil monetary penalties of up to an aggregate of \$150,000 per year (and up to an aggregate of \$1 million per year for knowing failures), for all payments, transfers of value or ownership or investment interests not reported in an annual submission.

In addition, under California law, pharmaceutical companies must adopt a comprehensive compliance program that is in accordance with both the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers, or OIG Guidance, and the Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals, or the PhRMA Code. The PhRMA Code seeks to promote transparency in relationships between health care professionals and the pharmaceutical industry and to ensure that pharmaceutical marketing activities comport with the highest ethical standards. The PhRMA Code contains strict limitations on certain interactions between health care professionals and the pharmaceutical industry relating to gifts, meals, entertainment and speaker programs, among others. Also, certain states, such as Massachusetts, Vermont and Minnesota, have imposed restrictions on the types of interactions that pharmaceutical and medical device companies or their agents (e.g., sales representatives) may have with health care professionals, including bans or strict limitations on the provision of meals, entertainment, hospitality, travel and lodging expenses, and other financial support, including funding for continuing medical education activities.

***Healthcare Privacy and Security Laws***

We may be subject to, or our marketing activities may be limited by, HIPAA, and its implementing regulations, which established uniform standards for certain covered entities (healthcare providers, health plans and healthcare clearinghouses) governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of protected health information. The American Recovery and Reinvestment Act of 2009, commonly referred to as the economic stimulus package, included sweeping expansion of HIPAA's privacy and security standards called the Health Information Technology for Economic and Clinical Health Act, or HITECH, which became effective on February 17, 2010. Among other things, the new law makes HIPAA's privacy and

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## **Table of Contents**

security standards directly applicable to business associates independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions.

### ***Third-Party Payor Coverage and Reimbursement***

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

Changes in third-party payor coverage and reimbursement rules can impact our business. For example, the PPACA changes include increased rebates a manufacturer must pay to the Medicaid program and established a new Medicare Part D coverage gap discount program, in which manufacturers must provide 50% point-of-sale discounts on products covered under Part D beginning in 2011. Further, also beginning in 2011, the new law imposes a significant annual, nondeductible fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with health care practitioners. A number of states have challenged the constitutionality of certain provisions of the PPACA, and many of these challenges are still pending final adjudication in several jurisdictions. Congress has also proposed a number of legislative initiatives, including possible repeal of the PPACA. At this time, it remains unclear whether there will be any changes made to the PPACA, whether to certain provisions or its entirety. We will not know the full effects of PPACA until applicable federal and state agencies issue regulations or guidance under the new law and these provisions are implemented. Although it is too early to determine the full effect of PPACA, the new law appears likely to continue the pressure on pharmaceutical pricing, and may also increase our regulatory burdens and operating costs.

Moreover, other legislative changes have been proposed and adopted since the PPACA was enacted. Most recently, on August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, creates the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. In the event that the Joint Select Committee is unable to achieve a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, or Congress does not act on the committee's recommendation, without amendment, by December 23, 2011, an automatic reduction is triggered. These automatic cuts would be made to several government programs and, with respect to Medicare, would include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. In the coming years, additional changes could be made to governmental healthcare programs that could significantly impact the success of our products.

In addition, the cost of pharmaceuticals and devices continues to generate substantial governmental and third party payor interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed health care, the increasing influence of managed care organizations and additional legislative proposals. Our results of operations and business could be adversely affected by current and future third-party payor policies as well as health care legislative reforms.

Some third-party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse health care providers who use such therapies. While we cannot predict

## **Table of Contents**

whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, these requirements or any announcement or adoption of such proposals could have a material adverse effect on our ability to obtain adequate prices for Sumavel DosePro and our product candidates and to operate profitably.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. There can be no assurance that our products will be considered medically reasonable and necessary for a specific indication, that our products will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be available or that the third-party payors' reimbursement policies will not adversely affect our ability to sell our products profitably.

### ***Manufacturing Requirements***

We and our third-party manufacturers must comply with applicable FDA regulations relating to FDA's cGMP regulations and, if applicable, QSR requirements. The cGMP regulations include requirements relating to, among other things, organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet cGMP requirements to the satisfaction of the FDA pursuant to a pre-approval inspection before we can use them to manufacture our products. We and our third-party manufacturers are also subject to periodic unannounced inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations. Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including, among other things, warning letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and criminal penalties.

### ***Other Regulatory Requirements***

We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, the FDA has broad regulatory and enforcement powers, including, among other things, the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals, any one or more of which could have a material adverse effect on us.

## **Legal Proceedings**

We are not currently a party to any legal proceeding.

## **Employees**

As of July 31, 2011, we employed 150 full-time employees. Of the full-time employees, 107 were engaged in sales and marketing, 8 were engaged in manufacturing operations, 18 were engaged in product development, quality assurance and clinical and regulatory activities and 17 were engaged in general and administrative activities (including business and corporate development). To build upon our success in growing Sumavel DosePro prescriptions, we have initiated activities to expand our sales force by approximately 15 sales representatives by the end of the third quarter of 2011. In addition, if our co-promotion agreement with Astellas is amended, terminated or otherwise restructured, we may expand our sales force to support the future sales and marketing of Sumavel DosePro. Otherwise, we do not anticipate significant growth in the number of our full-time employees unless and until we need to prepare for the launch of Zohydro. None of our employees are represented by a labor union, and we consider our employee relations to be good. We currently utilize TriNet Employer Group, Inc., an employer services company, to provide human resource services. TriNet Employer Group is the employer of record for payroll, benefits, employee relations and other employment-related administration.

## **Table of Contents**

### **Company Information**

We were formed as a Delaware corporation on May 11, 2006 as SJ2 Therapeutics, Inc. We commenced our operations on August 25, 2006 and changed our name to Zogenix, Inc. on August 28, 2006. Our principal executive offices are located at 12671 High Bluff Drive, Suite 200, San Diego, CA 92130, and our telephone number is 1-866-ZOGENIX (1-866-964-3649). We formed a wholly-owned subsidiary, Zogenix Europe Limited, in June 2010, a company organized under the laws of England and Wales and which is located in the United Kingdom, and whose principal operations are to support the manufacture of the DosePro technology. Our website address is www.zogenix.com. The information on, or accessible through, our website is not part of this prospectus.

### **Facilities**

Our facilities are located in San Diego and Emeryville, California. Our general and administrative and sales and marketing personnel are located at our San Diego facility. Our manufacturing operations, product development, quality assurance and clinical and regulatory personnel are located in our Emeryville facility.

We occupy 12,128 square feet of office and laboratory space in Emeryville under a lease which expires in 2015. We believe that the space in Emeryville is adequate to meet our needs there, and that, if necessary, additional space can be leased to accommodate any future growth.

We occupy 12,929 square feet of office space in San Diego under a lease which expires in 2012. We believe additional space can be leased to accommodate our potential growth.

The manufacturing equipment used to produce our DosePro technology is currently located at our contract manufacturers and component suppliers facilities in Europe where we occupy an aggregate of more than 20,000 square feet of space that is used to manufacture Sumavel DosePro.

### **Research and Development**

We invested \$17.4 million, \$11.4 million, \$28.6 million, \$21.4 million and \$33.9 million in research and development in the six months ended June 30, 2011 and 2010 and in the years ended December 31, 2010, 2009 and 2008, respectively.

### **Financial Information about Segments**

We operate only in one business segment, which is the commercialization and development of pharmaceutical products. See note 2 to our consolidated financial statements included in this prospectus. For financial information regarding our business, see Management's Discussion and Analysis of Financial Condition and Results of Operations and those financial statements and related notes.

**Table of Contents****MANAGEMENT****Executive Officers, Key Employees and Directors**

The following table sets forth certain information about our executive officers, key employees and directors as of July 31, 2011:

<b>Name</b>	<b>Age</b>	<b>Position</b>
<i>Executive Officers</i>		
Roger L. Hawley	58	Chief Executive Officer and Director
Stephen J. Farr, Ph.D.	52	President, Chief Operating Officer and Director
Ann D. Rhoads	46	Executive Vice President, Chief Financial Officer, Treasurer and Secretary
Cynthia Y. Robinson, Ph.D.	52	Chief Development Officer
<i>Key Employees</i>		
Jeff Durlinger	50	Vice President of Technical Operations and Product Supply
Stephen H. Jenner	43	Vice President, Marketing
Bret E. Megargel	42	Vice President, Corporate Development
Edward F. Smith III, Ph.D., RAC	58	Vice President, Regulatory Affairs and Safety
Mark R. Thompson	59	Vice President, Sales & Managed Markets
John J. Turanin	53	Vice President & General Manager, Zogenix Technologies
<i>Directors</i>		
Cam L. Garner <sup>(1)(2)</sup>	63	Chairman of the Board of Directors
James C. Blair, Ph.D. <sup>(1)</sup>	72	Director
Louis C. Bock <sup>(3)</sup>	46	Director
Erle T. Mast <sup>(2)(3)</sup>	49	Director
Arda M. Minocherhomjee, Ph.D. <sup>(1)(3)</sup>	57	Director
Kurt C. Wheeler <sup>(1)</sup>	58	Director
Mark Wiggins <sup>(2)</sup>	55	Director

(1) Member of the Compensation Committee.

(2) Member of the Nominating/Corporate Governance Committee.

(3) Member of the Audit Committee.

**Executive Officers**

*Roger L. Hawley* is one of our co-founders and has served as our Chief Executive Officer and as a member of our board of directors since August 2006. From January 2006 to August 2006, Mr. Hawley served as a consultant to CG Pharma, Inc. From August 2003 to January 2006 he served as Executive Vice President, Commercial and Technical Operations for InterMune, Inc., a biopharmaceutical company focused on therapies in hepatology and pulmonology. From October 2002 to July 2003, Mr. Hawley was the Chief Commercial Officer at Prometheus Laboratories Inc., a specialty pharmaceutical and diagnostics company. From 2001 to 2002, Mr. Hawley served as General Manager & Vice President of Sales and Marketing at Elan Pharmaceuticals, Inc. From 1987 to 2001, Mr. Hawley held a broad range of management positions in commercial operations, alliance/partnership management, and regional sales and corporate finance at GlaxoSmithKline, or GSK. His last position at GSK was Vice President of Sales-CNS/GI Division. From 1976 to 1987, he held various financial management positions with Marathon Oil Company, including serving four years in London, England. While at Marathon, he was a certified treasury manager and a certified public accountant. Mr. Hawley served as a member of the board of directors of Cypress Bioscience, Inc., a publicly traded pharmaceutical company, until December 2010. Mr. Hawley holds a B.Sc. in Accounting from Eastern Illinois University. As one of our co-founders and having served as our Chief Executive Officer since August 2006, Mr. Hawley's extensive knowledge of our

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**Table of Contents**

business, history and culture, as well as over 20 years of experience in the pharmaceutical industry, including providing strong executive leadership to numerous biopharmaceutical companies, contributed to our board of directors' conclusion that he should serve as a director of our company.

*Stephen J. Farr, Ph.D.* is one of our co-founders and has served as our President and as a member of our board of directors since our inception in May 2006. From May 2006 to August 2006, Dr. Farr also served as our Chief Executive Officer and since August 2006, Dr. Farr has served as our Chief Operating Officer. From 1995 to August 2006, Dr. Farr held positions of increasing responsibility within pharmaceutical sciences and research and development at Aradigm Corporation, and he served most recently as Senior Vice President and Chief Scientific Officer. In 2003, he played a key role in identifying and acquiring the DosePro technology and became technical director and executive sponsor for the development of *sumatriptan* DosePro at Aradigm Corporation. From 1986 to 1994, Dr. Farr was a tenured professor at the Welsh School of Pharmacy, Cardiff University, United Kingdom, concentrating in the areas of physical pharmacy and biopharmaceutics. He is a fellow of the American Association of Pharmaceutical Scientists and visiting Associate Professor in the Department of Pharmaceutics, School of Pharmacy, Virginia Commonwealth University. Dr. Farr is a registered pharmacist in the United Kingdom and obtained his Ph.D. degree in Pharmaceutics from the University of Wales. As one of our co-founders and having served as our President since May 2006, Dr. Farr's extensive knowledge of our business, history and culture, including his in-depth involvement with the DosePro technology and the development of Sumavel DosePro, as well as his significant experience in research and development and thorough knowledge of the pharmaceutical product development process, contributed to our board of directors' conclusion that he should serve as a director of our company.

*Ann D. Rhoads* has served as our Executive Vice President, Chief Financial Officer, Treasurer and Secretary since March 2010. From 2000 to December 2009, Ms. Rhoads was the Chief Financial Officer and Senior Vice President for Premier, Inc., a healthcare service company, where she had responsibility for all areas of financial management, strategic planning, business development, information technology, and ethics and compliance. From August 1998 to 2000, Ms. Rhoads served as Vice President for strategic initiatives at Premier, where she was responsible for overseeing strategic investments, including a venture capital fund, as well as assisting Premier operating divisions with long range strategic planning. Prior to joining Premier, Ms. Rhoads held various positions at Sprout Group, a venture capital affiliate of Donaldson, Lufkin & Jenrette (now part of Credit Suisse First Boston), Bain & Company and Merrill Lynch Capital Partners (now known as Stonington Partners). Ms. Rhoads is a member of the boards of directors of Novellus Systems, Inc. and Globus Medical, Inc. Ms. Rhoads received a B.S. from the University of Arkansas and an M.B.A. from the Harvard Business School.

*Cynthia Y. Robinson, Ph.D.* has served as our Chief Development Officer since April 2008, after consulting for us from April 2007 to April 2008. From November 2004 to July 2007, Dr. Robinson served as Senior Vice President, Development Operations at InterMune, Inc. From April 1989 to August 2004, Dr. Robinson held positions of increasing responsibility at Elan Pharmaceuticals, Inc., serving most recently as Vice President, Project Management, where she oversaw a portfolio of 14 global development programs from pre-clinical through commercialization, including multiple products in the therapeutic areas of CNS and pain. These efforts resulted in nine U.S. New Drug Applications, four European Marketing Authorization Applications and four U.S. product launches. Dr. Robinson holds a B.S. in Chemistry and a Ph.D. in Organic Chemistry from the University of Alabama.

***Key Employees***

*Jeff Durflinger* has served as our Vice President of Technical Operations and Product Supply since March 2011. Mr. Durflinger previously served as our Senior Director of Manufacturing from October 2008 and prior to that as our Director of Supply Chain Operations, beginning in January 2007. From 2004 to January 2007, Mr. Durflinger served as Director of Supply Chain Operations at Chiron Corporation (acquired by Novartis Pharmaceuticals), a publicly-held multinational biopharmaceutical company, where he led supply chain activities for Betaseron®, Proleukin® and vaccine operations. Prior to joining Chiron, Mr. Durflinger held various

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**Table of Contents**

operating and technical positions with Optime Therapeutics, a private pharmaceutical company, where he led technical and business development of the company's proprietary manufacturing and drug delivery technologies; Dow Pharmaceutical Sciences, a manufacturing services provider; Stedim, a designer and manufacturer of custom single-use, sterile bio-processing supplies; Elan Pharmaceuticals, a biopharmaceutical company; and ALZA Corporation (acquired by Johnson and Johnson), a publicly-held drug delivery company. Mr. Durlinger holds a B.S. in Industrial Technology from California State University, Chico and an M.S. in Business from Golden Gate University.

*Stephen H. Jenner* has served as our Vice President of Marketing since January 2011. From July 2008 to January 2011, Mr. Jenner served as our Senior Director of Marketing. From November 2007 to July 2008, Mr. Jenner served as the Senior Vice President of Client Services at MedAccess Communications, an advertising agency specializing in the pharmaceutical industry. From June 2005 to November 2007, Mr. Jenner served as the Senior Director of Marketing for Valeant Pharmaceuticals International, a publicly-held pharmaceutical company, where he led the Neurology Marketing Department. From July 2003 to June 2005, Mr. Jenner was the Senior Product Manager for Allergan Pharmaceuticals, a publicly-held pharmaceutical company, where he was the lead marketer for all Direct to Consumer activities related to BOTOX Cosmetic. From October 1998 to July 2003, Mr. Jenner held positions of increasing responsibility at Elan Pharmaceuticals, a publicly-held pharmaceutical company, most recently as Product Manager for the CNS/Movement Disorder Franchise. Mr. Jenner holds a B.S. in Business Administration from California Lutheran University and an M.B.A. from the University of Florida.

*Bret E. Megargel* is one of our co-founders and has served as our Vice President of Corporate Development since August 2006. From December 2005 to August 2006, Mr. Megargel served as a consultant to CG Pharma, Inc. From January 2005 to August 2007, Mr. Megargel served as Vice President of Planet Technologies, Inc., an allergy products company, where he was responsible for the general management of the company's Allergy Free business. From 2002 to December 2004, Mr. Megargel served as Vice President of Business Development for Avera Pharmaceuticals, Inc., a private, central nervous system-focused development company. From 1999 to 2002, Mr. Megargel served as a Venture Partner for Windamere Venture Partners, LLC. During his tenure at Windamere, Mr. Megargel served as Vice President of Business Development for MD Edge, Inc., and Director of Business Development for Converge Medical, Inc. and was a member of the founding team of Dexcom, Inc. From 1991 to 1996, Mr. Megargel served as a consultant for The Healthcare Group of Marketing Corporation of America (now a Division of The InterPublic Group), where he was a case manager for projects that included major product development, licensing and acquisition, and marketing strategy assignments for pharmaceutical clients. Mr. Megargel received a B.A. in Economics from Dartmouth College and an M.B.A. at the Stanford University Graduate School of Business.

*Edward F. Smith III, Ph.D., RAC* has served as our Vice President, Regulatory Affairs and Drug Safety since October 2008. From April 2007 to October 2008, he was our Senior Director, Regulatory Affairs. From July 2006 to April 2007, he was the Senior Director, Regulatory Affairs at Connetics, a specialty pharmaceutical company focused on the development and commercialization of innovative therapeutics for the dermatology market. From October 2004 to July 2006, he was the Director, Regulatory Affairs at Nektar Therapeutics, a biopharmaceutical company. Dr. Smith has authored over 90 peer-reviewed scientific articles and has submitted numerous U.S. Food and Drug Administration and European Medicines Agency submissions. He was a Postdoctoral Fellow at the Medical University of South Carolina and the Institute of Pharmacology at the University of Koln in West Germany. Dr. Smith received a B.S. in Biology from Montana State University, an M.B.A. at Washington University and a Ph.D. in Physiology at Thomas Jefferson University.

*Mark R. Thompson* has served as our Vice President, Sales and Managed Markets since April 2008. From January 2006 to July 2007, Mr. Thompson served as Vice President, Sales of Valeant Pharmaceuticals International, a multinational specialty pharmaceutical company, where he led both the hepatology and neuroscience sales teams, as well as management of sales operations, analytics, and training. From March 2004 to December 2005, Mr. Thompson was the Vice President, Sales at InterMune, Inc., a biopharmaceutical

**Table of Contents**

company. From October 2002 to March 2004, Mr. Thompson was the Vice President, Sales at SkinMedica, Inc., a company focused on developing, acquiring and commercializing products that treat dermatologic conditions and improve the appearance of skin, and from August 2001 to October 2002 he served as Senior Director, National Sales for Elan Biopharmaceuticals, Inc., Primary Care Division leading a sales team of approximately 500 people. From July 1980 to August 2001, Mr. Thompson held positions of increasing responsibility at GSK serving most recently as Regional Vice President, where his responsibilities included sales of Imitrex® and other CNS products. Mr. Thompson holds a M.Ed. in Administration and Supervision from the University of North Carolina, Chapel Hill.

*John J. Turanin* is one of our co-founders and has served as our Vice President and General Manager, Zogenix Technologies since August 2010 and prior to that as our Vice President, Operations since our inception in May 2006. From 1997 to April 2006, Mr. Turanin served as Vice President, Corporate Planning and Program Management and held positions as Senior Director of Program Management, Director of New Product Planning, and Director of Respiratory Products Business Unit at Aradigm Corporation, a specialty pharmaceutical company, where he was responsible for leading numerous product development programs and strategic alliances. Mr. Turanin was also responsible for directing Aradigm's integration of the DosePro technology acquisition and serving as program director for the *sumatriptan* DosePro development program. From 1987 to 1996, Mr. Turanin was General Manager of operations, quality, product development, and marketing for the respiratory therapeutics division at Invacare Corporation, a global manufacturer of home medical products. Mr. Turanin holds a B.A. in Business from Indiana University of Pennsylvania and an M.B.A. from the University of Pittsburgh.

***Board of Directors***

*Cam L. Garner* is one of our co-founders and has served as chairman of our board of directors since August 2006. Mr. Garner co-founded specialty pharmaceutical companies Cadence Pharmaceuticals, Inc., Somaxon Pharmaceuticals, Inc., Evoke Pharma, Inc., Elevation Pharmaceuticals, Inc., DJ Pharma, Verus Pharmaceuticals, Inc., Xcel Pharmaceuticals, Inc. and Meritage Pharma, Inc. He has served as chairman of Cadence, Verus, Evoke, Elevation and Meritage since May 2004, November 2002, January 2007, December 2007 and February 2008, respectively. Xcel was acquired in March 2005 by Valeant Pharmaceuticals International and DJ Pharma was sold to Biovail in 2000. He was Chief Executive Officer of Dura Pharmaceuticals, Inc. from 1989 to 1995 and its Chairman and Chief Executive Officer from 1995 to 2000 until it was sold to Elan in November 2000. Mr. Garner also serves on the board of directors of Aegis Therapeutics, Inc. Mr. Garner earned his B.A. in Biology from Virginia Wesleyan College and an M.B.A. from Baldwin-Wallace College. As one of our co-founders and having served as our chairman since August 2006, Mr. Garner's extensive knowledge of our business, history and culture, his extensive experience as a board member of multiple publicly-traded and privately-held companies, and expertise in developing, financing and providing strong executive leadership to numerous biopharmaceutical companies, contributed to our board of directors' conclusion that he should serve as a director of our company.

*James C. Blair, Ph.D.* has served as a member of our board of directors since August 2006. Dr. Blair is a Managing Member of Domain Associates, LLC, and he has been a Partner of Domain since its founding in 1985. Dr. Blair's present board memberships include Astute Medical Inc., Cadence Pharmaceuticals, Cell Biosciences, Clovis Oncology, Inc., CoDa Therapeutics, Five Prime Therapeutics, GenVault, IntegenX, Inc., Meritage Pharma and NeuroPace. Dr. Blair has over 40 years experience with venture and emerging growth companies. In the course of this experience, he has been involved in the creation and successful development at the board level of over 40 life sciences ventures, including Amgen, Aurora Biosciences, Amylin Pharmaceuticals, Applied Biosystems, Dura Pharmaceuticals, GeneOhm Sciences, Molecular Dynamics, Nuvasive, Pharmion and Volcano. A former managing director of Rothschild Inc., Dr. Blair was directly involved at a senior level with Rothschild/New Court venture capital activities from 1978 to 1985. From 1969 to 1978, he was associated with F.S. Smithers and Co. and White, Weld and Co., two investment banking firms actively involved with new ventures and emerging growth companies. From 1961 to 1969, Dr. Blair was an engineering manager with RCA Corporation, during which time he received a David Sarnoff Fellowship. Dr. Blair currently serves on the board



**Table of Contents**

of directors of the Prostate Cancer Foundation, and he is on the Advisory Boards of the Department of Molecular Biology at Princeton University, the Department of Biomedical Engineering at the University of Pennsylvania, the USC Stevens Institute for Innovation and the Division of Chemistry and Chemical Engineering at the California Institute of Technology. Dr. Blair received a B.S.E. from Princeton University and an M.S.E and Ph.D. from the University of Pennsylvania. With more than forty years' experience at the board level with venture and emerging growth companies, Dr. Blair's extensive expertise in the evaluation of financing alternatives, strategic planning for life sciences companies, and substantial executive leadership skills, contributed to our board of directors' conclusion that he should serve as a director of our company.

*Louis C. Bock* has served as a member of our board of directors since August 2006. Mr. Bock is a Managing Director of Scale Venture Partners, a venture capital firm. Mr. Bock joined Scale Venture Partners in September 1997 from Gilead Sciences, Inc., a biopharmaceutical company, where he held positions in research, project management, business development and sales from September 1989 to September 1997. Prior to Gilead, he was a research associate at Genentech, Inc. from November 1987 to September 1989. He currently serves as a director of Ascenta Therapeutics, Inc., diaDexus, Inc., VaxGen, Inc., Horizon Pharma, Inc., Orexigen Therapeutics, Inc. and Sonexa Therapeutics, Inc. and is responsible for Scale Venture Partners' prior investments in Seattle Genetics, Prestwick Pharmaceuticals, Inc. and Somaxon Pharmaceuticals, Inc. Mr. Bock received his B.S. in Biology from California State University, Chico and an M.B.A. from California State University, San Francisco. Mr. Bock's extensive clinical and leadership experience in the biotechnology and biopharmaceutical industries, including experience in research, project management, business development and sales from his time at Gilead, and his membership on other companies' boards of directors, including positions on other audit and nominating/corporate governance committees, contributed to our board of directors' conclusion that he should serve as a director of our company.

*Erle T. Mast* has served as a member of our board of directors since May 2008. Mr. Mast is a co-founder of and has served as Executive Vice President, Chief Financial Officer with Clovis Oncology, Inc. since May 2009. From July 2002 to May 2008, Mr. Mast served as Executive Vice President and Chief Financial Officer of Pharmion Corporation, until its acquisition by Celgene Corporation. From 2000 to 2002, after Elan Pharma International Ltd. acquired Dura Pharmaceuticals, Inc., Mr. Mast served as Chief Financial Officer for the Global Biopharmaceuticals business unit of Elan. From 1997 to 2000, Mr. Mast served as Vice President of Finance for Dura Pharmaceuticals. From 1984 to 1997, Mr. Mast held positions of increasing responsibility at Deloitte & Touche, LLP, serving most recently as Partner, where he provided accounting, auditing and business consulting services to companies in various industries, including the healthcare, pharmaceutical, biotech and manufacturing industries. Mr. Mast also serves on the board of directors of Somaxon Pharmaceuticals, Inc. Mr. Mast received a degree in Business Administration from California State University, Bakersfield. Mr. Mast's experience as a chief financial officer of various companies in the healthcare industry and in providing accounting, auditing and consulting services while at Deloitte & Touche, LLP, as well as his expertise in management, accounting, treasury, and finance functions, contributed to our board of directors' conclusion that he should serve as a director of our company.

*Arda M. Minocherhomjee, Ph.D.* has served as a member of our board of directors since December 2009. Dr. Minocherhomjee has been a Partner of Chicago Growth Partners since he co-founded the firm in 2004. Prior to founding Chicago Growth Partners, Dr. Minocherhomjee was a Managing Director at William Blair Capital Partners and currently is a Managing Director and member of the Board of Managers of WBCP VI and VII. Prior to that, Dr. Minocherhomjee was a Senior Healthcare Analyst at William Blair & Company. As head of the firm's Healthcare Research Group, Dr. Minocherhomjee covered several sectors, including drugs/drug delivery, medical devices and selected healthcare services. He was a Wall Street Journal All-Star Analyst in both medical device and pharmaceutical sectors. Dr. Minocherhomjee's current and past directorships include: DJ Pharma, EndoGastric Solutions, Genoptix, Lanx, Morton Grove Pharmaceuticals, NovaVision, NuVasive, PharmaResearch Corporation, Proteome, TargeGen, and Xoft. Dr. Minocherhomjee received a MS (Pharmacology) from the University of Toronto, a Ph.D. and a M.B.A. from the University of British Columbia, and was a post-doctoral fellow in Pharmacology at the University of Washington Medical School.

**Table of Contents**

Dr. Minocherhomjee's experience as a founder of a private equity firm, significant participation on the boards of directors of various pharmaceutical companies and substantial knowledge of the pharmaceutical industry, contributed to our board of directors' conclusion that he should serve as a director of our company.

*Kurt C. Wheeler* has served as a member of our board of directors since August 2006. Mr. Wheeler is a Managing Director of Clarus Ventures, a venture capital firm, a position he has held since February 2005, and is a General Partner of MPM Capital BioVentures II and III funds, a position he has held since March 2000. From March 1992 to September 1998, Mr. Wheeler was Chairman and Chief Executive Officer of InControl, Inc., a publicly traded medical device company that designed, developed, and marketed implantable medical devices to treat irregular heart rhythms, which was sold to Guidant Corporation. Mr. Wheeler serves on the board of directors of several private medical device and biopharmaceutical companies. Mr. Wheeler holds a B.A. degree from Brigham Young University and a M.B.A. degree from Northwestern University, where he serves on the Kellogg Alumni Advisory Board. Mr. Wheeler's background as a chief executive officer of a large, publicly-traded company, his extensive experience at the board level in various biopharmaceutical companies and his experience as a venture capitalist focused in the biopharmaceutical industry, bring to our board critical skills related to financial oversight of complex organizations, financing and strategic planning, and contributed to our board of directors' conclusion that he should serve as a director of our company.

*Mark Wiggins* has served as a member of our board of directors since May 2011. Mr. Wiggins joined Mpex Pharmaceuticals, a biopharmaceutical company, in April 2009 as Chief Business Officer. From May 1998 to February 2009, Mr. Wiggins was employed at Biogen Idec, Inc., and its predecessor Idec Pharmaceuticals, Corp., biotechnology companies, where he served as head of Business Development, later as Vice President of Marketing and Business Development and most recently as Executive Vice President of Corporate and Business Development. At Idec Pharmaceuticals, Mr. Wiggins was a member of the management committee for the collaboration with Genentech on Rituxan®. Mr. Wiggins has substantial experience in pharmaceutical marketing and business development activities. Prior to Biogen Idec, Mr. Wiggins spent fifteen years in a number of positions of increasing responsibility in marketing, marketing research and business development at Hybridon, Inc., Schering-Plough Corporation (now Merck), Johnson & Johnson and Pfizer, Inc. Mr. Wiggins' business development transaction experience includes closing over twenty licensing deals and several global corporate partnerships and company acquisitions. Mr. Wiggins earned his B.S. degree in Finance from Syracuse University and an M.B.A. from the University of Arizona. Mr. Wiggins' expertise in business development activities and the marketing of pharmaceutical products, as well as his extensive management experience within the biopharmaceutical industry, contributed to our board of directors' conclusion that he should serve as a director of our company.

**Board Composition and Election of Directors**

Our board of directors is currently authorized to have nine members and is currently composed of seven non-employee members, our current Chief Executive Officer, Roger L. Hawley, and our current President and Chief Operating Officer, Stephen J. Farr, Ph.D. Each of our non-employee directors, Cam L. Garner, James C. Blair, Ph.D., Louis C. Bock, Erle T. Mast, Arda M. Minocherhomjee, Ph.D., Kurt C. Wheeler and Mark Wiggins, is independent within the meaning of the independent director standards of the Securities and Exchange Commission, or SEC, and the Nasdaq Stock Market, or Nasdaq. Our amended and restated certificate of incorporation provides for a classified board of directors consisting of three classes of directors, each serving staggered three-year terms. As a result, a portion of our board of directors will be elected each year. Our Class I directors, whose terms will expire at the 2014 annual meeting of stockholders, are Messrs. Bock, Garner and Wiggins. Our Class II directors, whose terms will expire at the 2012 annual meeting of stockholders, are Drs. Blair, Farr and Minocherhomjee. Our Class III directors, whose terms will expire at the 2013 annual meeting of stockholders, are Messrs. Hawley, Mast and Wheeler. This classification of our board of directors may have the effect of delaying or preventing changes in our control or management. Our directors may be removed only for cause by the affirmative vote of the holders of at least 66 2/3% of our outstanding voting stock then entitled to vote in the election of directors.

## **Table of Contents**

### **Risk Oversight**

Our board of directors has responsibility for the oversight of the company's risk management processes and, either as a whole or through its committees, regularly discusses with management our major risk exposures, their potential impact on our business and the steps we take to manage them. The risk oversight process includes receiving regular reports from board committees and members of senior management to enable our board to understand the company's risk identification, risk management and risk mitigation strategies with respect to areas of potential material risk, including operations, finance, legal, regulatory, strategic and reputational risk.

The audit committee reviews information regarding liquidity and operations, and oversees our management of financial risks. Periodically, the audit committee reviews our policies with respect to risk assessment, risk management, loss prevention and regulatory compliance. Oversight by the audit committee includes direct communication with our external auditors, and discussions with management regarding significant risk exposures and the actions management has taken to limit, monitor or control such exposures. The compensation committee is responsible for assessing whether any of our compensation policies or programs has the potential to encourage excessive risk-taking. The nominating/corporate governance committee manages risks associated with the independence of the board, corporate disclosure practices, and potential conflicts of interest. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, the entire board is regularly informed through committee reports about such risks. Matters of significant strategic risk are considered by our board as a whole.

### **Board Diversity**

Our nominating/corporate governance committee is responsible for reviewing with the board of directors the appropriate characteristics, skills and experience required for the board of directors as a whole and its individual members. In evaluating the suitability of individual candidates (both new candidates and current members), the nominating/corporate governance committee, in recommending candidates for election, and the board of directors, in approving (and, in the case of vacancies, appointing) such candidates, takes into account many factors, including: personal and professional integrity, ethics and values; experience in corporate management, such as serving as an officer or former officer of a publicly held company; commercialization experience in large pharmaceutical companies; strong finance experience; experience relevant to our industry; experience as a board member of another publicly held company; diversity of expertise and experience in substantive matters pertaining to our business relative to other board members; diversity of background and perspective; and practical and mature business judgment. The board of directors evaluates each individual in the context of the board of directors as a whole, with the objective of assembling a group that can best maximize the success of our business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

### **Board Committees**

Our board of directors has established three standing committees: the audit committee, the compensation committee and the nominating/corporate governance committee. Our board of directors may establish other committees to facilitate the management of our business. Each of these committees has a written charter approved by our board of directors. A copy of each charter can be found under the Investor Relations Corporate Governance section of our website at [www.zogenix.com](http://www.zogenix.com).

#### ***Audit Committee***

The audit committee of our board of directors currently consists of Messrs. Mast (chairman and audit committee financial expert) and Bock and Dr. Minocherhomjee. The audit committee met four times during fiscal year 2010, including telephonic meetings. Our board of directors has determined that all members of the

**Table of Contents**

audit committee are independent directors, as defined in the Nasdaq qualification standards and by Section 10A of the Securities Exchange Act of 1934, as amended. In addition, our board of directors has determined that Mr. Mast qualifies as an audit committee financial expert as that phrase is defined under the regulations promulgated by the SEC. The audit committee is governed by a written charter adopted by our board of directors. The audit committee's main function is to oversee our accounting and financial reporting processes, internal systems of control, independent registered public accounting firm relationships and the audits of our financial statements. The audit committee's responsibilities include, among other things:

selecting and engaging our independent registered public accounting firm;

evaluating the qualifications, independence and performance of our independent registered public accounting firm;

approving the audit and non-audit services to be performed by our independent registered public accounting firm;

reviewing the design, implementation, adequacy and effectiveness of our internal controls and our critical accounting policies;

discussing with management and the independent registered public accounting firm the results of our annual audit and the review of our quarterly unaudited financial statements;

reviewing, overseeing and monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to financial statements or accounting matters;

reviewing with management and our auditors any earnings announcements and other public announcements regarding our results of operations;

preparing the report that the SEC requires in our annual proxy statement;

reviewing and approving any related party transactions and reviewing and monitoring compliance with our code of conduct and ethics; and

reviewing and evaluating, at least annually, the performance of the audit committee and its members including compliance of the audit committee with its charter.

***Compensation Committee***

The compensation committee of our board of directors currently consists of Drs. Blair and Minocherhomjee and Messrs. Garner (chairman) and Wheeler. The compensation committee met six times during fiscal year 2010, including telephonic meetings. Our board of directors has determined that all members of the compensation committee are independent directors, as defined in the Nasdaq qualification standards. The compensation committee is governed by a written charter approved by our board of directors. The compensation committee's purpose is to assist our board of directors in determining the development plans and compensation for our senior management and directors and recommend these plans to our board of directors. The compensation committee's responsibilities include, among other things:

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reviewing our compensation philosophy, including our policies and strategy relative to executive compensation;

reviewing and recommending to the full board for approval the compensation of our Chief Executive Officer;

reviewing and approving the compensation of our other executive officers, including executive employment and severance agreements;

reviewing and recommending to the full board for approval the compensation policies for members of our board of directors and board committees;

## **Table of Contents**

reviewing, approving and administering our benefit plans and the issuance of stock options and other awards under our equity incentive plans (other than any such awards that must be approved by the full board);

reviewing and discussing with management our compensation discussion and analysis to be included in our annual proxy report or annual report on Form 10-K and producing the report that the SEC requires in our annual proxy statement; and

reviewing and evaluating, at least annually, the performance of the compensation committee and its members including compliance of the compensation committee with its charter.

### ***Nominating/Corporate Governance Committee***

The nominating/corporate governance committee of our board of directors currently consists of Messrs. Garner (chairman), Mast and Wiggins. The nominating/corporate governance committee met two times during fiscal year 2010, including telephonic meetings. Our board of directors has determined that all members of the nominating/corporate governance committee are independent directors, as defined in the Nasdaq qualification standards. The nominating/corporate governance committee is governed by a written charter approved by our board of directors. The nominating/corporate governance committee's purpose is to assist our board of directors by identifying individuals qualified to become members of our board of directors, consistent with criteria set by our board, and to develop our corporate governance principles. The nominating/corporate governance committee's responsibilities include, among other things:

evaluating the composition, size and governance of our board of directors and its committees and making recommendations regarding future planning and the appointment of directors to our committees;

administering a policy for considering stockholder nominees for election to our board of directors;

evaluating and recommending candidates for election to our board of directors;

developing guidelines for board compensation;

overseeing our board of directors' performance and self-evaluation process;

reviewing our corporate governance principles and providing recommendations to the board regarding possible changes; and

reviewing and evaluating, at least annually, the performance of the nominating/corporate governance committee and its members including compliance of the nominating/corporate governance committee with its charter.

### **Compensation Committee Interlocks and Insider Participation**

None of the members of our compensation committee has ever been one of our officers or employees. None of our executive officers currently serves, or has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or compensation committee. See "Certain Relationships and Related Party Transactions" below.

### **Code of Business Conduct and Ethics**

We have adopted a code of business conduct and ethics that applies to our officers, directors and employees. Our code of business conduct and ethics is available under the Investor Relations - Corporate Governance section of our website at [www.zogenix.com](http://www.zogenix.com). Any amendments to the

code, or waivers to its requirements, will be disclosed on our website.

**Table of Contents**

**COMPENSATION DISCUSSION AND ANALYSIS**

**Overview**

This compensation discussion and analysis provides information about the material components of our executive compensation program for our named executive officers, consisting of the following persons:

Roger L. Hawley, our Chief Executive Officer;

Stephen J. Farr, Ph.D., our President and Chief Operating Officer;

Ann D. Rhoads, our Executive Vice President, Chief Financial Officer, Treasurer and Secretary;

Cynthia Y. Robinson, Ph.D., our Chief Development Officer;

David W. Nassif, J.D., our former Executive Vice President, Chief Financial Officer, Treasurer and Secretary; and

J.D. Haldeman, our former Chief Commercial Officer.

Mr. Nassif resigned from his position as Executive Vice President, Chief Financial Officer, Treasurer and Secretary in February 2010. In March 2010, we appointed Ann Rhoads as our new Executive Vice President, Chief Financial Officer, Treasurer and Secretary.

Ms. Haldeman resigned from her position as Chief Commercial Officer in July 2010.

Specifically, this compensation discussion and analysis provides an overview of our executive compensation philosophy, the overall objectives of our executive compensation program, and each compensation component that we provide. In addition, we explain how and why the compensation committee and our board of directors arrived at specific compensation policies and decisions involving our executive officers during the year ended December 31, 2010.

**Executive Summary**

We recognize that the ability to excel depends on the integrity, knowledge, imagination, skill, diversity and teamwork of our employees. To this end, the key objectives of our executive compensation program are to:

attract, engage and retain an executive team who will provide leadership for our future success by providing competitive total pay opportunities;

establish a direct link between our business results, individual executive performance and total executive compensation; and

align the interests of our executive officers with those of our stockholders.

The primary elements of our executive compensation program are (1) base salary, (2) annual short-term cash incentives, (3) long-term equity incentives, (4) post-termination benefits, and (5) other benefits, such as health insurance and retirement benefits. We believe that each component aligns the interests of our named executive officers with the interests of our stockholders in different ways, whether through focusing



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on short-term and long-term performance goals, promoting an ownership mentality toward one's job or linking individual performance to our performance.

In general, the majority of our named executive officers' total compensation is tied directly to corporate and individual performance, increases in our stock price, or both. Specific elements of our executive compensation program that demonstrate our pay-for-performance philosophy include:

the performance measures in our short-term cash incentive program are linked to key corporate objectives;

## **Table of Contents**

corporate achievement represents the majority of each executive's annual bonus opportunity and achievement relative to corporate objectives is used to determine the overall funding level of executive bonuses; and

our long-term equity incentives are granted in the form of stock options, which provide value to our executives only if our stock price increases.

This mix of compensation is intended to ensure that total compensation reflects our overall success or failure and to motivate executive officers to meet appropriate performance measures. In determining each element of compensation for any given year, our board of directors and our compensation committee consider and determine each element individually and then review the resulting total compensation and determine whether it is reasonable and competitive. We do not have a pre-established policy or target for the allocation between either cash and non-cash or short-term and long-term incentive compensation.

We believe that the total compensation received by our named executive officers relating to 2010 was appropriate when viewed in light of our key corporate achievements during 2010, guided by our named executive officers, including the successful completion of our initial public offering, the launch of our first product, Sumavel DosePro, ongoing clinical advancement and initiation of Phase 3 clinical development of our next product candidate, Zohydro, and the validation of our commercial manufacturing capabilities. Specifically, while our compensation committee acknowledged our corporate achievements and the high level of individual performance of our named executive officers during 2010, we did not meet all of our stated corporate objectives and annual bonus payments were reduced accordingly.

### **Compensation Determination Process**

The compensation committee of our board of directors develops, reviews and approves each of the elements of our executive compensation program. The compensation committee also regularly assesses the effectiveness and competitiveness of our compensation programs.

In the first quarter of each year, the compensation committee reviews the performance of each of our named executive officers during the previous year. At this time the compensation committee also reviews our performance relative to the corporate performance objectives set by the board of directors for the year under review and makes the final bonus payment determinations based on our performance and the compensation committee's evaluation of each named executive officer's performance for the year under review. In connection with this review, the compensation committee also reviews and adjusts, as appropriate, annual base salaries for our named executive officers and grants, as appropriate, additional stock option awards to our named executive officers and certain other eligible employees for the then current fiscal year.

During the fourth quarter of each year our compensation committee also reviews the corporate performance objectives for purposes of our performance bonus programs for the following year, but such objectives historically have been recommended to the full board of directors for approval. Our Chief Executive Officer, with the assistance and support of our Chief Financial Officer and our human resources department, aids the compensation committee by providing annual recommendations regarding the compensation of all of our named executive officers, other than himself. The compensation committee also, on occasion, meets with our Chief Executive Officer to obtain recommendations with respect to our compensation programs and practices generally. The compensation committee considers, but is not bound to accept, the Chief Executive Officer's recommendations with respect to named executive officer compensation. In the beginning of each year, our named executive officers work with our Chief Executive Officer to establish their individual performance goals for the year, based on their respective roles within the company.

Our Chief Executive Officer generally attends all of the compensation committee meetings, but the compensation committee also holds executive sessions that are not attended by any members of management or non-independent directors, as needed from time to time. Any decisions regarding our Chief Executive Officer's compensation are made without him present.

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**Table of Contents**

In May 2011, our stockholders voted to approve, on an advisory basis, the compensation of our named executive officers. Our stockholders also voted to approve the board's recommendation that an advisory stockholder vote on executive compensation be held on a triennial basis. Although both stockholder votes were non-binding, our compensation committee and board of directors value the opinions of our stockholders and consider these votes to indicate the stockholders' support for our current pay practices. Although we have made no new compensation decisions and have implemented no new compensation policies since the annual stockholder meeting in May, we anticipate that the compensation committee and board of directors will consider such stockholder sentiment in their future review of compensation practices.

***Role of Compensation Consultant and Comparable Company Information***

Our compensation committee has not historically established compensation levels based on benchmarking. Our compensation committee has instead relied upon the judgment of its members in making compensation decisions, after reviewing our performance and carefully evaluating a named executive officer's performance during the year against established goals, leadership qualities, operational performance, business responsibilities, career with our company, current compensation arrangements and long-term potential to enhance stockholder value.

The compensation committee is authorized to retain the services of third-party compensation consultants and other outside advisors from time to time, as the committee sees fit, in connection with compensation matters. Compensation consultants and other advisors retained by the compensation committee will report directly to the compensation committee which has the authority to select, retain and terminate any such consultants or advisors.

In May 2010, upon the recommendation of management, our compensation committee engaged Compensia, Inc., or Compensia, to provide compensation consulting services and to assist the compensation committee in the determination of the key elements of our executive compensation programs. Specifically, for 2010, the compensation committee requested Compensia to advise it on a variety of compensation-related issues, including:

compiling, analyzing and presenting third-party survey data regarding the compensation of executives at comparable companies;

evaluating our current executive compensation program relative to this survey data, including base salary, bonus and equity ownership levels; and

providing general information concerning executive compensation trends and developments.

Compensia did not provide any other services to us in 2010 beyond its engagement as an advisor to the compensation committee on executive compensation matters.

The comparable company information presented to the compensation committee by Compensia in May 2010 consisted of industry survey data for two groups of companies: private companies and public companies. The compensation committee reviewed data from The Radford Global Life Sciences Compensation Survey, which consists of public companies throughout the United States primarily from the life sciences industry with between 50 and 150 employees. The compensation committee also reviewed data from the Advanced HR Option Impact Pre-IPO Compensation Database, which consists of private companies throughout the United States. The data from this survey reviewed by our compensation committee was for companies from the life sciences industry, with between 50 and 150 employees and that had raised more than \$100 million in capital. This survey data was presented separately to the compensation committee, so that it could see the relative compensation levels for both private and public companies. With respect to the survey data presented to the compensation committee, the identities of the individual companies included in the survey were not provided to the compensation committee, and the compensation committee did not refer to individual compensation information for such companies. We believe that by utilizing both sets of survey data, our compensation committee is able to review an appropriate set of competitive data for use in making compensation decisions.

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**Table of Contents**

While our compensation committee reviewed the foregoing third party survey data in connection with its determinations of the 2010 base salaries, target bonuses and equity awards for our named executive officers, our committee did not attempt to set those compensation levels or awards at a certain target percentile with respect to the third party survey data or otherwise rely entirely on that data to determine named executive officer compensation. Instead, as described above and consistent with past practice, the compensation committee members relied on their judgment and experience in setting those compensation levels and making those awards.

We expect that the compensation committee will continue to review comparable company survey data in connection with setting the compensation we offer our named executive officers to help ensure that our compensation programs are competitive and fair.

We strive to achieve an appropriate mix between equity incentive awards and cash payments in order to meet our objectives. Any apportionment goal is not applied rigidly and does not control our compensation decisions, and our compensation committee does not have any formal policies for allocating compensation between long-term and short-term compensation or cash and non-cash compensation.

The compensation levels of the named executive officers reflect to a significant degree the varying roles and responsibilities of such executives. As a result of the compensation committee's and the board of director's assessment of our Chief Executive Officer's and President and Chief Operating Officer's roles and responsibilities within our company, there are significant compensation differentials between these named executive officers and our other named executive officers.

We do not yet have a formal policy to adjust or recover awards or payments if the relevant performance measures upon which they are based are restated or are otherwise adjusted in a manner that would otherwise reduce the size of the initial payment or award.

**Executive Compensation Components**

The following describes each component of our executive compensation program, the rationale for each, and how compensation amounts are determined.

***Base Salaries***

In general, base salaries for our named executive officers are initially established through arm's length negotiation at the time the executive is hired, taking into account such executive's qualifications, experience and prior salary. Base salaries of our named executive officers are approved and reviewed annually by our compensation committee and adjustments to base salaries are based on the scope of an executive's responsibilities, individual contribution, prior experience and sustained performance. Decisions regarding salary increases may take into account an executive officer's current salary, equity ownership, and the amounts paid to an executive officer's peers inside our company by conducting an internal analysis, which compares the pay of an executive officer to other members of the management team. Base salaries are also reviewed in the case of promotions or other significant changes in responsibility. Base salaries are not automatically increased if the compensation committee believes that other elements of the named executive officer's compensation are more appropriate in light of our stated objectives. This strategy is consistent with our intent of offering compensation that is both cost-effective, competitive and contingent on the achievement of performance objectives.

Our Chief Executive Officer's base salary is based upon the same policies and criteria used for other named executive officers as described above. Each year the compensation committee reviews the Chief Executive Officer's compensation arrangements and his individual performance for the previous fiscal year, as well as our performance as a whole, and makes recommendations to the full board of directors of adjustments to such compensation, if appropriate.

**Table of Contents**

In March 2010, Ann Rhoads commenced employment as our Executive Vice President, Chief Financial Officer, Treasurer and Secretary, and the compensation committee set her initial base salary at \$325,000 per year based on its review and consideration of the factors described in the first paragraph above.

In May 2010, the compensation committee reviewed the base salaries of our named executive officers. The compensation committee, in consultation with our Chief Executive Officer (with respect to the salaries of our other named executive officers) and Compensia, determined to increase base salaries of our named executive officers for 2010, effective April 1, 2010, subject to improvement of our financial condition. In August 2010, in light of our improved financial condition based on our debt restructuring, our compensation committee approved the implementation of the base salary increases of our named executive officers (and the full board of directors approved the increase for Mr. Hawley). As Ms. Haldeman resigned her position in July 2010, she did not receive this adjustment. The base salaries for our named executive officers as of April 1, 2010 were as shown in the following table.

In March 2011, the compensation committee reviewed the base salaries of our named executive officers. The compensation committee, in consultation with our Chief Executive Officer (with respect to the salaries of our other named executive officers) and Compensia, determined to increase base salaries of our named executive officers for 2011, effective April 1, 2011. The base salaries for our named executive officers as of April 1, 2011 are as shown in the following table.

Named Executive Officer	2009 Base Salary	Base Salary as of April 1, 2010	Base Salary as of April 1, 2011
Roger L. Hawley	\$ 400,000	\$ 420,000	\$ 435,000
Stephen J. Farr, Ph.D.	\$ 325,000	\$ 341,250	\$ 350,000
Ann D. Rhoads	N/A	\$ 325,000	\$ 335,000
Cynthia Robinson, Ph.D.	\$ 260,000	\$ 272,000	\$ 280,000

The actual base salaries paid to all of our named executive officers for 2010 are set forth in the Summary Compensation Table below.

**Annual Incentive Plan**

In May 2011, our board of directors adopted the Zogenix, Inc. Annual Incentive Plan, which provides for discretionary annual bonus payments to our named executive officers based on achievement of individual performance and corporate performance goals and other factors determined by the compensation committee. This bonus program is consistent with the terms of our 2010 bonus program and our general bonus practices, as described above.

**Performance Bonuses**

Each named executive officer is also eligible for a performance bonus based upon the achievement of certain corporate performance goals and objectives approved by our board of directors and, with respect to our named executive officers other than Mr. Hawley, individual performance.

Bonuses are set based on the executive's base salary as of the end of the bonus year, and are expected to be paid out in the first quarter of the following year. The target levels for executive bonuses are currently as follows: 50% of base salary for the Chief Executive Officer (100% of which is based on corporate objectives), 45% of base salary for our President and Chief Operating Officer and Executive Vice President and Chief Financial Officer (80% of which is based on corporate objectives and 20% of which is based on individual performance), and 35% of base salary for all other named executive officers (60% of which is based on corporate objectives and 40% of which is based on individual performance).

At the beginning of each year, the board of directors (considering the recommendations of the compensation committee and management) sets corporate goals and milestones for the year. These goals and milestones and the proportional emphasis placed on each are set by the board of directors after considering management input and

**Table of Contents**

our overall strategic objectives. These goals generally relate to factors such as financial targets, achievement of product development objectives and establishment of new collaborative arrangements. The board of directors, upon recommendation of the compensation committee, determines the level of achievement of the corporate goals for each year. This achievement level is then applied to each named executive officer's target bonus to determine that year's total bonus opportunity, before any determination of the individual component of the award. The individual component of each named executive's bonus award is not necessarily based on the achievement of any predetermined criteria or guidelines but rather on the compensation committee's subjective assessment of the officer's overall performance of his or her duties. In coming to this determination, our compensation committee does not follow any guidelines, nor are there such standing guidelines regarding the exercise of such discretion.

All final bonus payments to our named executive officers are determined by our compensation committee, other than the bonus payments to our Chief Executive Officer, whose compensation is approved by the full board of directors. The actual bonuses awarded in any year, if any, may be more or less than the target, depending on individual performance and the achievement of corporate objectives and may also vary based on other factors at the discretion of the compensation committee (or the full board of directors, with respect to our Chief Executive Officer).

*2010 Performance Bonuses.* For 2010, corporate objectives generally fell into the following categories: the successful commercialization of Sumavel DosePro (65%); ensuring product availability of Sumavel DosePro and cost effectiveness during 2010 (10%); realizing value from our core assets, including Sumavel DosePro (15%); and progressing the Hydrocodone CR program through key development milestones to ensure the submission of an NDA to the FDA (10%). Objectives were weighted based on their level of importance to the business plan.

In evaluating management's performance against our 2010 corporate goals, our board of directors determined to award a corporate achievement level of 57.5% relative to those goals. As stated above, quantitative measures were not established for the corporate objectives during 2010. Instead these performance objectives were used as a guide by the board of directors in subjectively determining overall corporate performance as they represented those areas in which the named executive officers and our employees generally were expected to focus their efforts. The board of directors believed that it was better to evaluate our overall performance in these areas throughout the year and without regard to pre-determined targets or goals in light of the general economic and industry conditions in which we operate and the limited proceeds generated in connection with our initial public offering in November 2010. In coming to its final determination regarding the overall corporate achievement percentage, and the resulting funding of our annual bonus program, our board of directors awarded half credit for corporate performance relative to the first objective, noting that, together with our co-promotion partner, we successfully launched Sumavel DosePro during 2010. The board of directors, however, did not award full credit for this objective in its discretion as it determined that full credit would have resulted in a funding level for the executive and employee bonus pool that was too high based on our overall performance, together with our co-promotion partner, in this area during 2010. With respect to the second objective, our board of directors awarded substantially full credit in recognition of the satisfactory validation of our commercial manufacturing capabilities. With respect to the third objective, our board of directors awarded one-third credit for this objective. The board noted that while no new strategic business arrangements were secured in 2010, we did successfully progress Sumavel DosePro into new territories through our partnership with Desitin Pharma and progressed the product profile of an early stage product candidate to the satisfaction of the board of directors. With respect to the final objective, our board of directors awarded us an achievement level in excess of the expected level based on our initiation of Phase 3 clinical development of our next product candidate, Zohydro, in an efficient manner.

This achievement level was then used to determine each named executive officer's bonus. For Mr. Hawley, as his entire bonus is based on corporate achievement, his 2010 annual bonus represents the 57.5% of his target bonus. For the other named executive officers, each of his or her target bonus was first multiplied by 57.5%. The resulting amount was then split into its corporate and individual components, based on the weighting applicable to such named executive officer as described above.

**Table of Contents**

The compensation committee's determination of the individual components of the 2010 bonus awards for our named executive officers was not based on the achievement of any predetermined individual performance objectives, criteria or guidelines, but rather on the compensation committee's subjective assessment of each officer's overall performance of their duties during 2010.

The bonuses paid to our named executive officers for 2010 are set forth in the following table:

<b>Named Executive Officer</b>	<b>2010 Bonus (\$)</b>
Roger L. Hawley	120,750
Stephen J. Farr, Ph.D.	88,311
Ann D. Rhoads	84,094
Cynthia Robinson, Ph.D.	54,740

***Long-Term Equity Incentives***

The goals of our long-term, equity-based incentive awards are to align the interests of our named executive officers and other employees, non-employee directors and consultants with the interests of our stockholders. Because vesting is based on continued employment, our equity-based incentives also encourage the retention of our named executive officers through the vesting period of the awards. In determining the size of the long-term equity incentives to be awarded to our named executive officers, we take into account a number of internal factors, such as the relative job scope, the value of existing long-term incentive awards, individual performance history, prior contributions to us and the size of prior grants. For 2010, while our compensation committee reviewed competitive market data prepared by Compensia in connection with its grant of long-term equity incentive awards to the named executive officers, such awards were not determined by reference to any specific target level of compensation or benchmarking. Based upon these factors, the compensation committee determines the size of the long-term equity incentives at levels it considers appropriate to create a meaningful opportunity for reward predicated on the creation of long-term stockholder value. We have not granted any equity awards other than stock options to date.

To reward and retain our named executive officers in a manner that best aligns employees' interests with stockholders' interests, we use stock options as the primary incentive vehicles for long-term compensation. We believe that stock options are an effective tool for meeting our compensation goal of increasing long-term stockholder value by tying the value of the stock options to our future performance. Because employees are able to profit from stock options only if our stock price increases relative to the stock option's exercise price, we believe stock options provide meaningful incentives to employees to achieve increases in the value of our stock over time.

We use stock options to compensate our named executive officers both in the form of initial grants in connection with the commencement of employment and annual refresher grants. Annual grants of options are typically approved by the compensation committee during the first quarter of each year. While we intend that the majority of stock option awards to our employees be made pursuant to initial grants or our annual grant program, the compensation committee retains discretion to make stock option awards to employees at other times, including in connection with the promotion of an employee, to reward an employee, for retention purposes or for other circumstances recommended by management or the compensation committee.

The exercise price of each stock option grant is the fair market value of our common stock on the grant date, as determined by our board of directors from time to time. Stock option awards to our named executive officers have generally vested over a four-year period as follows: 25% of the shares underlying the option vest on the first anniversary of the date of the vesting commencement date and the remainder of the shares underlying the option vest in equal monthly installments over the remaining 36 months thereafter. From time to time, our compensation committee may, however, determine that a different vesting schedule is appropriate. Also, commencing in 2011, annual stock option awards to our named executive officers will vest monthly over a four-year period. For a

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**Table of Contents**

description of certain accelerated vesting provisions applicable to such options, see Employee Equity Incentive Plans 2010 Equity Incentive Award Plan and Employee Equity Incentive Plans 2006 Equity Incentive Plan below. We do not have any stock ownership requirements for our named executive officers.

In May 2010, the compensation committee granted Ms. Rhoads stock options to purchase 150,000 shares of our common stock in consideration of her commencement of employment as our Executive Vice President, Chief Financial Officer, Treasurer and Secretary. The compensation committee established this award based on its review and consideration of the factors described in the first paragraph above. This option award vests monthly over the four-year period following Ms. Rhoads' date of hire, which was March 2010.

In May 2010, the compensation committee, and the board of directors with respect to our Chief Executive Officer, awarded the following options to our named executive officers: Mr. Hawley, options to purchase 150,000 shares; Dr. Farr, options to purchase 100,000 shares; Ms. Rhoads, options to purchase 20,000 shares; Dr. Robinson, options to purchase 32,000 shares; and Ms. Haldeman, options to purchase 10,000 shares. Each of these option awards vests over a four-year period as follows: 25% of the shares underlying the option vest on the first anniversary of the date of the vesting commencement date and the remainder of the shares underlying the option vest in equal monthly installments over the remaining 36 months thereafter. The compensation committee's recommendation regarding each named executive officer's award amount was not based on any quantifiable factors, but instead was based on the compensation committee's subjective analysis of the award levels the committee deemed appropriate for each executive in light of various factors, including: our clinical, commercial and operational successes during 2010 despite our limited cash resources; and the need to continue to incentivize our executives. Each of these factors was taken into consideration by the compensation committee for each executive, as was management's recommendations regarding the appropriate award levels. The final award levels, however, were entirely based on the compensation committee's subjective analysis of these general factors and internal pay equity considerations.

In March 2011, the compensation committee awarded the following options to our named executive officers: Mr. Hawley, options to purchase 300,000 shares; Dr. Farr, options to purchase 250,000 shares; Ms. Rhoads, options to purchase 180,000 shares; and Dr. Robinson, options to purchase 110,000 shares. Each of these option awards vests monthly over a four-year period. The compensation committee's recommendation regarding each named executive officer's award amount was not based on any quantifiable factors, but instead was based on the compensation committee's subjective analysis of the award levels the committee deemed appropriate for each executive in light of various factors, including the dilution created as a result of our initial public offering and the need to continue to incentivize our executives. Each of these factors was taken into consideration by the compensation committee for each executive, as was management's recommendations regarding the appropriate award levels. The final award levels, however, were entirely based on the compensation committee's subjective analysis of these general factors and internal pay equity considerations.

We have had no program, plan or practice pertaining to the timing of stock option grants to named executive officers coinciding with the release of material non-public information.

***Retirement Savings***

All of our full-time employees in the U.S., including our named executive officers, are eligible to participate in our 401(k) plan. Pursuant to our 401(k) plan, employees may elect to reduce their current compensation by up to the statutorily prescribed annual limit (\$16,500 in 2011) (additional salary deferrals not to exceed \$5,500 are available to those employees 50 years of age or older) and to have the amount of this reduction contributed to our 401(k) plan. While we may elect to make matching contributions, no such contributions have been made.

***Health and Welfare Benefits, Perquisites and Other Compensation***

The establishment of competitive benefit packages for our employees is an important factor in attracting and retaining highly qualified personnel.



## **Table of Contents**

*Health and Welfare Benefits.* Our named executive officers are eligible to participate in all of our employee benefit plans, including our medical, dental, vision, group life and disability insurance plans, in each case on the same basis as other employees. We believe that these health and welfare benefits help ensure that we have a productive and focused workforce through reliable and competitive health and other benefits.

*Perquisites.* We do not provide significant perquisites or personal benefits to our named executive officers. We do, however, pay the premiums for term life insurance for our named executive officers.

### ***Post Termination Benefits***

We have entered into employment agreements which provide for certain severance benefits in the event a named executive officer's employment is involuntarily or constructively terminated. Such severance benefits are intended and designed to alleviate the financial impact of an involuntary termination and maintain a stable work environment through salary continuation and equity award vesting acceleration. We provide severance benefits because they are essential to help us fulfill our objective of attracting and retaining key managerial talent. While these arrangements form an integral part of the total compensation provided to these individuals and are considered by the compensation committee when determining executive officer compensation, the decision to offer these benefits did not influence the compensation committee's determinations concerning other direct compensation or benefit levels. The compensation committee has determined that such arrangements offer protection that is competitive within our industry and for our company size and are designed to attract highly qualified individuals and maintain their employment with us. In determining the severance benefits payable pursuant to the executive employment agreements, the compensation committee considered what level of severance benefits would be sufficient to retain our current executive team and to recruit talented executives in the future, which determination was based in part on input from management and our board of directors. For a description of these employment agreements, see [Employment and Release Agreements](#) [Employment Agreements](#) below.

### **Tax Deductibility of Executive Compensation**

The compensation committee and our board of directors have considered the potential future effects of Section 162(m) of the Internal Revenue Code on the compensation paid to our executive officers. Section 162(m) disallows a tax deduction for any publicly held corporation for individual compensation exceeding \$1.0 million in any taxable year for our Chief Executive Officer and each of the other named executive officers (other than our Chief Financial Officer), unless compensation is performance based. As we are only recently a publicly-traded company, our board of directors has not previously taken the deductibility limit imposed by Section 162(m) into consideration in setting compensation. Our compensation committee, however, has adopted a policy that, where reasonably practicable, we will seek to qualify the variable compensation paid to our executive officers for an exemption from the deductibility limitations of Section 162(m).

In approving the amount and form of compensation for our executive officers, the compensation committee will continue to consider all elements of the cost to our company of providing such compensation, including the potential impact of Section 162(m).

### **Accounting for Stock-Based Compensation**

We follow Financial Accounting Standards Board Accounting Standards Codification Topic 718 (formerly known as SFAS No. 123(R)), or ASC Topic 718, for our stock-based compensation awards. ASC Topic 718 requires companies to calculate the grant date fair value of their stock-based awards using a variety of assumptions. This calculation is performed for accounting purposes and reported in the compensation tables below, even though recipients may never realize any value from their awards. ASC Topic 718 also requires companies to recognize the compensation cost of their stock-based awards in their income statements over the period that an employee is required to render service in exchange for the award.

**Table of Contents****Summary Compensation Table**

The following table shows information regarding the compensation earned by our named executive officers during the fiscal years ended December 31, 2010, 2009, and 2008.

Name and Principal Position	Year	Annual Compensation		Long Term Compensation		Non-Equity Incentive Plan	All Other Compensation	Total (\$)
		Salary (\$) <sup>(1)</sup>	Bonus (\$) <sup>(2)</sup>	Stock Awards (\$)	Option Awards (\$) <sup>(3)</sup>	Compensation (\$) <sup>(4)</sup>	(\$) <sup>(5)</sup>	
Roger L. Hawley <i>Chief Executive Officer</i>	2010	415,000			1,795,707	120,750	79	2,331,536
	2009	381,667	100,000		156,223		79	637,969
	2008	400,000			880,290		93	1,280,383
Stephen J. Farr, Ph.D. <i>President and Chief Operating Officer</i>	2010	337,225			1,197,138	88,311	79	1,622,753
	2009	310,104	81,250		110,658		79	502,091
	2008	325,000			73,358		93	398,451
Ann D. Rhoads <sup>(6)</sup> <i>Executive Vice President and Chief Financial Officer</i>	2010	270,833			2,035,135	84,094	66	2,390,128
Cynthia Robinson, Ph.D. <sup>(7)</sup> <i>Chief Development Officer</i>	2010	269,000			383,084	54,740	79	706,903
	2009	248,083	65,000		26,037		79	339,199
	2008	208,333			471,552		89,035	768,920
David W. Nassif, J.D. <sup>(8)</sup> <i>Former Executive Vice President and Chief Financial Officer</i>	2010	73,333					334,080	407,413
	2009	248,083	65,000				79	313,162
	2008	260,000					93	260,093
J.D. Haldeman <sup>(9)</sup> <i>Former Chief Commercial Officer</i>	2010	173,411			119,714		260,050	553,175
	2009	243,313	63,750		52,074		79	359,216
	2008	251,073					93	251,166

- (1) The salaries paid for 2009 are lower than those for 2008, reflecting the 10% voluntary salary reduction taken by the named executive officers for a portion of 2009.
- (2) For 2009, represents amounts paid under a retention bonus program.
- (3) Represents the grant date fair value of the awards granted in the relevant fiscal year as computed in accordance with ASC Topic 718. For a discussion of the valuation assumptions, see Note 9 to our consolidated financial statements for the year ended December 31, 2010 included elsewhere in this prospectus.
- (4) These amounts represent 2010 performance bonuses under our executive bonus program, which is described above under Compensation Discussion and Analysis Performance Bonuses. No bonuses were earned for 2009 or 2008 performance under the executive bonus program due to the need to conserve cash.
- (5) Reflects premiums paid by us for term life insurance for our named executive officers. The amounts shown for Mr. Nassif for 2010 also include consulting fees of \$59,775 paid to him by us during the period February 2010 through December 2010, following his cessation of service as our Executive Vice President and Chief Financial Officer, and severance payments of \$274,292. The amounts shown for Ms. Robinson for 2008 also include consulting fees of \$88,975 paid to her by us during the period January 2008 through March 2008, when she commenced employment as our Chief Development Officer. The amounts shown for Ms. Haldeman for 2010 also include severance payments of \$260,004.
- (6) For 2010, reflects a pro-rated salary for Ms. Rhoads due to the fact the Ms. Rhoads was appointed Executive Vice President, Chief Financial Officer, Treasurer and Secretary in March 2010.
- (7) For 2008, reflects a pro-rated salary for Ms. Robinson due to the fact the Ms. Robinson was appointed Chief Development Officer in April 2008.
- (8) Effective February 26, 2010, Mr. Nassif resigned his positions with us. Beginning March 1, 2010, he began providing executive consulting services to us.
- (9) For 2010, reflects a pro-rated salary for Ms. Haldeman. Effective July 26, 2010, Ms. Haldeman resigned her position with us.



**Table of Contents****2010 Grants of Plan-Based Awards**

The following table sets forth summary information regarding grants of plan-based awards made to our named executive officers during the year ended December 31, 2010.

Name	Grant Date <sup>(1)</sup>	Estimated Possible Payouts Under Non-Equity Incentive Plan Awards Target (\$) <sup>(2)</sup>	All Other Stock Awards: Number of Shares of Stock or Units (#)	All Other Option Awards: Number of Securities Underlying Options (#)	Exercise or Base Price of Option Awards (\$/Sh) <sup>(3)</sup>	Grant Date Fair Value of Stock and Option Awards <sup>(4)</sup>
Roger L. Hawley	5/25/2010	210,000		150,000	4.00	1,795,707
Stephen J. Farr, Ph.D.	5/25/2010	153,563		100,000	4.00	1,197,138
Ann D. Rhoads	5/25/2010	146,250		150,000	4.00 <sup>(5)</sup>	1,795,707
	5/25/2010			20,000	4.00	239,428
Cynthia Robinson, Ph.D.	5/25/2010	95,200		32,000	4.00	383,084
J.D. Haldeman	5/25/2010	89,250		10,000	4.00	119,714

- (1) Unless otherwise indicated, 25% of the shares underlying options vest on the first anniversary of the vesting commencement date and the remaining options vest on a monthly basis over the subsequent three-year period of continuous service and all options have a 10-year term from the date of grant. All options are immediately exercisable. Unvested options are subject to a right of repurchase within 90 days of termination of employment.
- (2) These amounts represent the target 2010 performance bonuses under our executive bonus program, which is described above under Compensation Discussion and Analysis – Performance Bonuses.
- (3) Reflects the fair market value per share of our common stock on the grant date as determined by our board of directors.
- (4) Represents the grant date fair value of the awards as computed in accordance with ASC Topic 718. For a discussion of the valuation assumptions, see Note 9 to our consolidated financial statements for the year ended December 31, 2010 included elsewhere in this prospectus.
- (5) The options vest on a monthly basis over a four-year period of continuous service following Ms. Rhoads' date of hire in March 2010 and have a 10-term from the date of grant.

**Discussion of Summary Compensation and Grants of Plan-Based Awards Tables**

Our executive compensation policies and practices, pursuant to which the compensation set forth in the Summary Compensation Table and the 2010 Grants of Plan-Based Awards table was paid or awarded, are described above under Compensation Discussion and Analysis. A summary of certain material terms of our employment agreements and compensation plans and arrangements is set forth below.

**Employment and Release Agreements****Employment Agreements**

In May 2008, our board of directors approved our entering into employment agreements with each of our named executive officers. In March 2010, we entered into an employment agreement with Ms. Rhoads in connection with her commencement of employment as our Executive Vice President, Chief Financial Officer, Treasurer and Secretary.

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**Table of Contents**

Pursuant to each of the employment agreements, if we terminate such officer's employment without cause (as defined below) or such officer resigns for good reason (as defined below) or such officer's employment is terminated as a result of his or her death or following his or her permanent disability, the executive officer or his or her estate, as applicable, is entitled to the following payments and benefits: (1) his or her fully earned but unpaid base salary through the date of termination at the rate then in effect, plus all other benefits, if any, under any group retirement plan, nonqualified deferred compensation plan, equity award or agreement, health benefits plan or other group benefit plan to which he or she may be entitled to under the terms of such plans or agreements; (2) a lump sum cash payment in an amount equal to 12 months of his or her base salary as in effect immediately prior to the date of termination; (3) continuation of health benefits for a period of 12 months following the date of termination; and (4) the automatic acceleration of the vesting and exercisability of outstanding unvested stock awards as to the number of stock awards that would have vested over the 12-month period following termination had such officer remained continuously employed by us during such period.

If a named executive officer is terminated without cause or resigns for good reason during the period commencing 60 days prior to a change in control (as defined below) or 12 months following a change in control, such officer shall be entitled to receive, in addition to the severance benefits described above, the following payments and benefits: (1) a lump sum cash payment in an amount equal to his or her bonus (as defined below) for the year in which the termination of employment occurs; and (2) in the case of Mr. Hawley, an additional lump sum cash payment in an amount equal to six months of his base salary as in effect immediately prior to the date of termination. In addition, in the event of a change in control, the vesting and exercisability of 50% of the executive officer's outstanding unvested stock awards shall be automatically accelerated and, in the event an executive officer is terminated without cause or resigns for good reason within three months prior to or 12 months following a change in control, the vesting and exercisability of 100% of the executive officer's outstanding unvested stock awards shall be automatically accelerated. For a further description of the potential compensation payable to our named executive officers under their employment agreements, please see Potential Payments Upon Termination or Change in Control below.

For purposes of the employment agreements, cause generally means an executive officer's (1) commission of an act of fraud, embezzlement or dishonesty or some other illegal act that has a material adverse impact on us or any successor or affiliate of ours, (2) conviction of, or entry into a plea of guilty or no contest to, a felony, (3) unauthorized use or disclosure of our confidential information or trade secrets or any successor or affiliate of ours that has, or may reasonably be expected to have, a material adverse impact on any such entity, (4) gross negligence, insubordination or material violation of any duty of loyalty to us or any successor or affiliate of ours, or any other material misconduct on the part of the executive officer, (5) ongoing and repeated failure or refusal to perform or neglect of his or her duties as required by his or her employment agreement, which failure, refusal or neglect continues for 15 days following his or receipt of written notice from our board of directors, Chief Executive Officer or supervising officer, as applicable, stating with specificity the nature of such failure, refusal or neglect, or (6) breach of any policy of ours or any material provision of his or her employment agreement.

For purposes of the employment agreements, good reason generally means (1) a material diminution in the executive officer's authority, duties or responsibilities, (2) a material diminution in the executive officer's base compensation, unless such a reduction is imposed across-the-board to senior management of the company, (3) a material change in the geographic location at which the executive officer must perform his or her duties, or (4) any other action or inaction that constitutes a material breach by us or any successor or affiliate of ours of its obligations to the executive officer under his or her employment agreement.

For purposes of the employment agreements, bonus generally means an amount equal to the average of the bonuses awarded to the named executive officer for each of the three fiscal years prior to the date of his or her termination of employment, or such lesser number of years as may be applicable if the executive officer has not been employed for three full years on the date of termination of employment. However, to the extent the executive officer has not received any bonus prior to the date of his or her termination of employment due to the

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## **Table of Contents**

fact that his or her employment commenced during the fiscal year in which the termination occurs, **bonus** means an amount equal to his or her target bonus for the fiscal year in which such termination occurs (calculated by reference to the target bonus level in effect on the date of termination) multiplied by the corporate performance achievement percentage approved by the board of directors or its designee with respect to the payment of executive bonuses for the preceding fiscal year.

For purposes of the employment agreements, **change in control** has the same meaning as such term is given under the terms of our 2010 equity incentive award plan, as described below.

### ***Release Agreements***

In February 2010, we entered into a general release of claims with Mr. Nassif, which release superseded his employment agreement. Pursuant to the release, (1) we paid him a cash payment equal to \$260,000, representing his annual base salary as in effect immediately prior to his termination of employment, (2) we agreed to continue his health benefits for a period of 12 months following the date of his termination of employment, and (3) the vesting and exercisability of all of his outstanding unvested stock awards was accelerated. Following his termination of employment, Mr. Nassif commenced consulting for us in March 2010.

In August 2010, we entered into a general release of claims with Ms. Haldeman, which release superseded her employment agreement. Pursuant to the release (1) we paid her a cash payment equal to \$255,000, representing her annual base salary as in effect immediately prior to her resignation, (2) we agreed to continue her health benefits for a period of 12 months following the date of her resignation, (3) the vesting and exercisability of her outstanding unvested stock awards was accelerated as to the number of stock awards that would have vested over the 12-month period following her resignation, and (4) the expiration date of Ms. Haldeman's vested options was extended until July 26, 2011. In addition, in the event of a change in control on or before September 26, 2010, we agreed to pay Ms. Haldeman an additional cash amount of \$52,085, representing her bonus as of the date of her resignation. In the event of a change in control on or before October 26, 2010, the vesting and exercisability of 100% of Ms. Haldeman's outstanding unvested stock awards as of her date of resignation would have been automatically accelerated.

## **Employee Equity Incentive Plans**

### ***2010 Equity Incentive Award Plan***

We adopted our 2010 equity incentive award plan, or the 2010 Plan, in connection with our initial public offering. The 2010 Plan became effective in November 2010. A total of 2,000,000 shares of our common stock, plus 233,689 shares which were authorized for issuance but not issued under our 2006 equity incentive award plan, or the 2006 Plan, as of the effective date of the 2010 Plan, were initially reserved for issuance under the 2010 Plan. The number of shares reserved for issuance under the 2010 Plan may be increased from time to time by the number of shares of common stock related to awards granted under our 2006 Plan that are repurchased, forfeited, expired or are cancelled on or after the effective date of the 2010 Plan. As of July 31, 2011, awards to purchase 53,707 shares issued under the 2006 Plan had been repurchased, forfeited or cancelled, increasing the number of shares reserved under the 2010 Plan accordingly.

The 2010 Plan contains an **evergreen provision** that allows for an annual increase in the number of shares available for issuance under the 2010 Plan commencing on January 1, 2011, and on each January 1 thereafter during the ten-year term of the 2010 Plan. The annual increase in the number of shares shall be equal to the least of:

4% of our outstanding common stock on the applicable January 1;

1,000,000 shares; and

a lesser number of shares as determined by our board of directors.

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**Table of Contents**

Pursuant to the evergreen provision, the number of shares reserved for issuance under the 2010 Plan was automatically increased on January 1, 2011 by 1,000,000 shares. As of July 31, 2011, the aggregate number of shares authorized for issuance under the 2010 Plan was 3,287,396, the aggregate number of shares of common stock subject to outstanding awards under the 2010 Plan was 1,983,104, no shares of common stock have been issued pursuant to the exercise of stock options under the 2010 Plan, and a total of 1,304,292 shares of common stock remained available for future issuance under the 2010 Plan.

The 2010 Plan provides for an aggregate limit of 14,034,000 shares of common stock that may be issued under the 2010 Plan over the course of its ten-year term. The material terms of the 2010 Plan are summarized below. The 2010 Plan is incorporated by reference as an exhibit to the registration statement of which this prospectus is a part.

*Administration.* The compensation committee of our board of directors administers the 2010 Plan (except with respect to any award granted to independent directors (as defined in the 2010 Plan), which must be administered by our full board of directors). To administer the 2010 Plan, our compensation committee must consist solely of at least two members of our board of directors, each of whom is a non-employee director for purposes of Rule 16b-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and, with respect to awards that are intended to constitute performance-based compensation under Section 162(m) of the Internal Revenue Code of 1986, as amended, an outside director for purposes of Section 162(m). Subject to the terms and conditions of the 2010 Plan, our compensation committee has the authority to select the persons to whom awards are to be made, to determine the type or types of awards to be granted to each person, the number of awards to grant, the number of shares to be subject to such awards, and the terms and conditions of such awards, and to make all other determinations and decisions and to take all other actions necessary or advisable for the administration of the 2010 Plan. Our compensation committee is also authorized to establish, adopt, amend or revise rules relating to administration of the 2010 Plan. Our board of directors may at any time revert in itself the authority to administer the 2010 Plan.

*Eligibility.* Options, stock appreciation rights, or SARs, restricted stock and other awards under the 2010 Plan may be granted to individuals who are then our officers or employees or are the officers or employees of any of our subsidiaries. Such awards may also be granted to our non-employee directors and consultants but only employees may be granted incentive stock options, or ISOs. As of July 31, 2011, there were seven non-employee directors and 150 employees who would have been eligible for awards under the 2010 Plan had it been in effect on such date. At such time as we are subject to the requirements of Section 162(m) of the Internal Revenue Code, the maximum number of shares that may be subject to awards granted under the 2010 Plan to any individual in any calendar year cannot exceed 2,000,000 and the maximum amount that may be paid to a participant in cash during any calendar year with respect to one or more cash based awards under the 2010 Plan is \$2,000,000.

*Awards.* The 2010 Plan provides that our compensation committee (or the board of directors, in the case of awards to non-employee directors) may grant or issue stock options, SARs, restricted stock, restricted stock units, dividend equivalents, performance share awards, performance stock units, stock payments, deferred stock, performance bonus awards, performance-based awards, and other stock-based awards, or any combination thereof. Our compensation committee (or the board of directors, in the case of awards to non-employee directors) will consider each award grant subjectively, considering factors such as the individual performance of the recipient and the anticipated contribution of the recipient to the attainment of our long-term goals. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms and conditions of the award.

Nonqualified stock options, or NQSOs, provide for the right to purchase shares of our common stock at a specified price which may not be less than the fair market value of a share of common stock on the date of grant, and usually will become exercisable (at the discretion of our compensation committee or our board of directors, in the case of awards to non-employee directors) in one or more installments after the grant date, subject to the participant's continued employment or service with us and/or subject to the satisfaction of performance targets established by our compensation committee (or our board of

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**Table of Contents**

directors, in the case of awards to non-employee directors). NQSOs may be granted for any term specified by our compensation committee (or our board of directors, in the case of awards to non-employee directors).

Incentive stock options, or ISOs, are designed to comply with the provisions of the Internal Revenue Code and are subject to specified restrictions contained in the Internal Revenue Code. Among such restrictions, ISOs must have an exercise price of not less than the fair market value of a share of common stock on the date of grant, may only be granted to employees, must expire within a specified period of time following the optionee's termination of employment, and must be exercised within the ten years after the date of grant. In the case of an ISO granted to an individual who owns (or is deemed to own) more than 10% of the total combined voting power of all classes of our capital stock, the 2010 Plan provides that the exercise price must be at least 110% of the fair market value of a share of common stock on the date of grant and the ISO must expire upon the fifth anniversary of the date of its grant.

Restricted stock may be granted to participants and made subject to such restrictions as may be determined by our compensation committee (or our board of directors, in the case of awards to non-employee directors). Typically, restricted stock may be forfeited for no consideration if the conditions or restrictions are not met, and it may not be sold or otherwise transferred to third parties until restrictions are removed or expire. Recipients of restricted stock, unlike recipients of options, may have voting rights and may receive dividends, if any, prior to the time when the restrictions lapse.

Restricted stock units may be awarded to participants, typically without payment of consideration or for a nominal purchase price, but subject to vesting conditions including continued employment or on performance criteria established by our compensation committee (or our board of directors, in the case of awards to non-employee directors). Like restricted stock, restricted stock units may not be sold or otherwise transferred or hypothecated until vesting conditions are removed or expire. Unlike restricted stock, stock underlying restricted stock units will not be issued until the restricted stock units have vested, and recipients of restricted stock units generally will have no voting or dividend rights prior to the time when vesting conditions are satisfied.

SARs granted under the 2010 Plan typically provide for payments to the holder based upon increases in the price of our common stock over the exercise price of the SAR. Except as required by Section 162(m) of the Internal Revenue Code with respect to SARs intended to qualify as performance-based compensation as described in Section 162(m) of the Internal Revenue Code, there are no restrictions specified in the 2010 Plan on the exercise of SARs or the amount of gain realizable therefrom. Our compensation committee (or the board of directors, in the case of awards to non-employee directors) may elect to pay SARs in cash or in common stock or in a combination of both.

Dividend equivalents represent the value of the dividends, if any, per share paid by us, calculated with reference to the number of shares covered by the stock options, SARs or other awards held by the participant.

Performance bonus awards may be granted by our compensation committee on an individual or group basis. Generally, these awards will be based upon the attainment of specific performance goals that are established by our compensation committee and relate to one or more performance criteria on a specified date or dates determined by our compensation committee. Any such cash bonus paid to a covered employee within the meaning of Section 162(m) of the Internal Revenue Code may be, but need not be, qualified performance-based compensation as described below and will be paid in cash.

Stock payments may be authorized by our compensation committee (or our board of directors, in the case of awards to non-employee directors) in the form of common stock or an option or other right to purchase common stock as part of a deferred compensation arrangement, made in lieu of all or any part of compensation, including bonuses, that would otherwise be payable to employees, consultants or members of our board of directors.



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**Table of Contents**

*Qualified Performance-Based Compensation.* The compensation committee may designate employees as covered employees whose compensation for a given fiscal year may be subject to the limit on deductible compensation imposed by Section 162(m) of the Code. The compensation committee may grant to such covered employees restricted stock, dividend equivalents, stock payments, restricted stock units, cash bonuses and other stock-based awards that are paid, vest or become exercisable upon the attainment of company performance criteria which are related to one or more of the following performance criteria as applicable to our performance or the performance of a division, business unit or an individual, measured either in absolute terms, on a same-property basis, as compared to any incremental increase or as compared to results of a peer group: operating or other costs and expenses, improvements in expense levels, cash flow (including, but not limited to, operating cash flow and free cash flow), return on net assets, shareholders' equity, return on shareholders' equity, return on sales, gross or net profit or operating margin, working capital, net earnings (either before or after interest, taxes, depreciation and amortization), gross or net sales or revenue, net income (either before or after taxes), adjusted net income, operating earnings, earnings per share of stock, adjusted earnings per share of stock, price per share of stock, capital raised in financing transactions or other financing milestones, market recognition (including but not limited to awards and analyst ratings), financial ratios, implementation of critical projects, comparisons with various stock market indices, and implementation, completion or attainment of objectively-determinable objectives relating to research, development, regulatory, commercial or strategic milestones or development. These performance criteria may be measured in absolute terms or as compared to performance in an earlier period or as compared to any incremental increase or as compared to results of a peer group.

The compensation committee may provide that one or more objectively determinable adjustments will be made to one or more of the performance goals established for any performance period. Such adjustments may include one or more of the following: items related to a change in accounting principle, items relating to financing activities, expenses for restructuring or productivity initiatives, other non-operating items, items related to acquisitions, items attributable to the business operations of any entity acquired by us during the performance period, items related to the disposal of a business or segment of a business, items related to discontinued operations that do not qualify as a segment of a business under applicable accounting standards, items attributable to any stock dividend, stock split, combination or exchange of shares occurring during the performance period, any other items of significant income or expense which are determined to be appropriate adjustments, items relating to unusual or extraordinary corporate transactions, events or developments, items related to amortization of acquired intangible assets, items that are outside the scope of our core, on-going business activities, items relating to changes in tax laws, items relating to gains and losses for litigation, arbitration or contractual settlements, or items relating to any other unusual or nonrecurring events or changes in applicable laws, accounting principles or business conditions.

*Adjustments.* If there is any stock dividend, stock split, combination or exchange of shares, merger, consolidation or other distribution (other than normal cash dividends) of our assets to stockholders, or any other change affecting the shares of our common stock or the share price of our common stock other than an equity restructuring (as defined in the 2010 Plan), the plan administrator will make such equitable adjustments, if any, as the plan administrator in its discretion may deem appropriate to reflect such change with respect to (1) the aggregate number and type of shares that may be issued under the 2010 Plan (including, but not limited to, adjustments of the number of shares available under the plan and the maximum number of shares which may be subject to one or more awards to a participant pursuant to the plan during any calendar year), (2) the terms and conditions of any outstanding awards (including, without limitation, any applicable performance targets or criteria with respect thereto), and (3) the grant or exercise price per share for any outstanding awards under the plan. If there is any equity restructuring, (1) the number and type of securities subject to each outstanding award and the grant or exercise price per share for each outstanding award, if applicable, will be proportionately adjusted, and (2) the plan administrator will make proportionate adjustments to reflect such equity restructuring with respect to the aggregate number and type of shares that may be issued under the 2010 Plan (including, but not limited to, adjustments of the number of shares available under the plan and the maximum number of shares which may be subject to one or more awards to a participant pursuant to the plan during any calendar year). Adjustments in the event of an equity restructuring will not be discretionary. Any adjustment affecting an award

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**Table of Contents**

intended as qualified performance-based compensation will be made consistent with the requirements of Section 162(m) of the Internal Revenue Code. The plan administrator also has the authority under the 2010 Plan to take certain other actions with respect to outstanding awards in the event of a corporate transaction, including provision for the cash-out, termination, assumption or substitution of such awards.

*Corporate Transactions.* In the event of a change in control where the acquirer does not assume awards granted under the 2010 Plan, awards issued under the 2010 Plan will be subject to accelerated vesting such that 100% of the awards will become vested and exercisable or payable, as applicable. Under the 2010 Plan, a change in control is generally defined as:

a transaction or series of related transactions (other than an offering of our stock to the general public through a registration statement filed with the Securities and Exchange Commission, or SEC) whereby any person or entity or related group of persons or entities (other than us, our subsidiaries, an employee benefit plan maintained by us or any of our subsidiaries or a person or entity that, prior to such transaction, directly or indirectly controls, is controlled by, or is under common control with, us) directly or indirectly acquires beneficial ownership (within the meaning of Rule 13d-3 under the Exchange Act) of more than 50% of the total combined voting power of our securities outstanding immediately after such acquisition;

during any two-year period, individuals who, at the beginning of such period, constitute our board of directors together with any new director(s) whose election by our board of directors or nomination for election by our stockholders was approved by a vote of at least two-thirds of the directors then still in office who either were directors at the beginning of the two-year period or whose election or nomination for election was previously so approved, cease for any reason to constitute a majority of our board of directors; or

our consummation (whether we are directly or indirectly involved through one or more intermediaries) of (x) a merger, consolidation, reorganization, or business combination or (y) the sale, exchange or transfer of all or substantially all of our assets in any single transaction or series of transactions or (z) the acquisition of assets or stock of another entity, in each case other than a transaction:

which results in our voting securities outstanding immediately before the transaction continuing to represent (either by remaining outstanding or by being converted into our voting securities or the voting securities of the person that, as a result of the transaction, controls us, directly or indirectly, or owns, directly or indirectly, all or substantially all of our assets or otherwise succeeds to our business (we or such person being referred to as a successor entity)) directly or indirectly, at least a majority of the combined voting power of the successor entity's outstanding voting securities immediately after the transaction, and

after which no person or group beneficially owns voting securities representing 50% or more of the combined voting power of the successor entity; provided, however, that no person or group is treated as beneficially owning 50% or more of combined voting power of the successor entity solely as a result of the voting power held in us prior to the consummation of the transaction.

*Amendment and Termination of the 2010 Plan.* Our board of directors may terminate, amend or modify the 2010 Plan. However, stockholder approval of any amendment to the 2010 Plan will be obtained to the extent necessary and desirable to comply with any applicable law, regulation or stock exchange rule, or for any amendment to the 2010 Plan that increases the number of shares available under the 2010 Plan. If not terminated earlier by our board of directors, the 2010 Plan will terminate on the tenth anniversary of the date of its initial approval by our board of directors.

*Repricing Permitted.* Our compensation committee (or the board of directors, in the case of awards to non-employee directors) has the authority, without the approval of our stockholders, to authorize the amendment of any outstanding award to reduce its price per share and to provide that an award will be canceled and replaced

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**Table of Contents**

with the grant of an award having a lesser price per share. Our compensation committee (or the board of directors, in the case of awards to non-employee directors) also has the authority, without the approval of our stockholders, to amend any outstanding award to increase the price per share or to cancel and replace an award with the grant of an award having a price per share that is greater than or equal to the price per share of the original award.

*Securities Laws and Federal Income Taxes.* The 2010 Plan is designed to comply with various securities and federal tax laws as follows:

*Securities Laws.* The 2010 Plan is intended to conform to all provisions of the Securities Act of 1933, as amended, or the Securities Act, and the Exchange Act and any and all regulations and rules promulgated by the SEC thereunder, including, without limitation, Rule 16b-3. The 2010 Plan is being administered and will be administered, and awards have been granted and will be granted and have been exercised and may be exercised, only in such a manner as to conform to such laws, rules and regulations.

*Federal Income Tax Consequences.* The federal income tax consequences of the 2010 Plan under current federal income tax law are summarized in the following discussion which deals with the general tax principles applicable to the 2010 Plan and is intended for general information only. The following discussion of federal income tax consequences does not purport to be a complete analysis of all of the potential tax effects of the 2010 Plan. It is based upon laws, regulations, rulings and decisions now in effect, all of which are subject to change. Foreign, state and local tax laws, and employment, estate and gift tax considerations are not discussed, and may vary depending on individual circumstances and from locality to locality.

*Stock Options and Stock Appreciation Rights.* A 2010 Plan participant generally will not recognize taxable income and we generally will not be entitled to a tax deduction upon the grant of a stock option or stock appreciation right. The tax consequences of exercising a stock option and the subsequent disposition of the shares received upon exercise will depend upon whether the option qualifies as an incentive stock option as defined in Section 422 of the Internal Revenue Code. The 2010 Plan permits the grant of options that are intended to qualify as incentive stock options as well as options that are not intended to so qualify; however, incentive stock options generally may be granted only to our employees and employees of our parent or subsidiary corporations, if any. Upon exercising an option that does not qualify as an incentive stock option when the fair market value of our stock is higher than the exercise price of the option, a 2010 Plan participant generally will recognize taxable income at ordinary income tax rates equal to the excess of the fair market value of the stock on the date of exercise over the purchase price, and we (or our subsidiaries, if any) generally will be entitled to a corresponding tax deduction for compensation expense, in the amount equal to the amount by which the fair market value of the shares purchased exceeds the purchase price for the shares. Upon a subsequent sale or other disposition of the option shares, the participant will recognize a short term or long term capital gain or loss in the amount of the difference between the sales price of the shares and the participant's tax basis in the shares.

Upon exercising an incentive stock option, a 2010 Plan participant generally will not recognize taxable income, and we will not be entitled to a tax deduction for compensation expense. However, upon exercise, the amount by which the fair market value of the shares purchased exceeds the purchase price will be an item of adjustment for alternative minimum tax purposes. The participant will recognize taxable income upon a sale or other taxable disposition of the option shares. For federal income tax purposes, dispositions are divided into two categories: qualifying and disqualifying. A qualifying disposition generally occurs if the sale or other disposition is made more than two years after the date the option was granted and more than one year after the date the shares are transferred upon exercise. If the sale or disposition occurs before these two periods are satisfied, then a disqualifying disposition generally will result.

**Table of Contents**

Upon a qualifying disposition of incentive stock option shares, the participant will recognize long term capital gain in an amount equal to the excess of the amount realized upon the sale or other disposition of the shares over their purchase price. If there is a disqualifying disposition of the shares, then the excess of the fair market value of the shares on the exercise date (or, if less, the price at which the shares are sold) over their purchase price will be taxable as ordinary income to the participant. If there is a disqualifying disposition in the same year of exercise, it eliminates the item of adjustment for alternative minimum tax purposes. Any additional gain or loss recognized upon the disposition will be recognized as a capital gain or loss by the participant.

We will not be entitled to any tax deduction if the participant makes a qualifying disposition of incentive stock option shares. If the participant makes a disqualifying disposition of the shares, we should be entitled to a tax deduction for compensation expense in the amount of the ordinary income recognized by the participant.

Upon exercising or settling a stock appreciation right, a 2010 Plan participant will recognize taxable income at ordinary income tax rates, and we should be entitled to a corresponding tax deduction for compensation expense, in the amount paid or value of the shares issued upon exercise or settlement. Payments in shares will be valued at the fair market value of the shares at the time of the payment, and upon the subsequent disposition of the shares the participant will recognize a short term or long term capital gain or loss in the amount of the difference between the sales price of the shares and the participant's tax basis in the shares.

*Restricted Stock and Restricted Stock Units.* A 2010 Plan participant generally will not recognize taxable income at ordinary income tax rates and we generally will not be entitled to a tax deduction upon the grant of restricted stock or restricted stock units. Upon the termination of restrictions on restricted stock or the payment of restricted stock units, the participant will recognize taxable income at ordinary income tax rates, and we should be entitled to a correspond