ZOGENIX, INC.
Form 10-K
March 12, 2012
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

Form 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2011

or

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission file number: 001-34962

Zogenix, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**20-5300780**

(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
12671 High Bluff Drive, Suite 200	
San Diego, California (Address of Principal Executive Offices)	**92130** (Zip Code)

858-259-1165

(Registrant s Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $0.001 per share	The NASDAQ Global Market

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ¨ No x

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). x Yes ¨ No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

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

Large accelerated filer ¨ Accelerated filer ¨ Non-accelerated filer x Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ¨ No x

As of June 30, 2011, the aggregate market value of the registrant s common stock held by non-affiliates of the registrant was approximately $54,202,873, based on the closing price of the registrant s common stock on the Nasdaq Global Market of $4.01 per share.

The number of outstanding shares of the registrant s common stock, par value $0.001 per share, as of March 1, 2012 was 65,368,792.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant s 2012 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant s fiscal year ended December 31, 2011.

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ZOGENIX, INC.

FORM 10-K ANNUAL REPORT

For the Fiscal Year Ended December 31, 2011

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PART I

Forward-Looking Statements and Market Data

This Annual Report on Form 10-K and the information incorporated herein by reference contain forward-looking statements that involve substantial risks and uncertainties. These forward looking statement include, but are not limited to, statements about:

- our ability to maintain and increase market demand for, and sales of, Sumavel DosePro;
- our ability to successfully execute our sales and marketing strategy for the commercialization of Sumavel DosePro;
- the progress and timing of clinical trials for our product candidates;
- the timing of a New Drug Application submission to the U.S. Food and Drug Administration, or 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 Zohydro and our other product candidate;
- the market potential for migraine treatments, and our ability to compete within that market;
- the goals of our development activities and estimates of the potential markets for our product candidates, and our ability to compete within those markets;
- estimates of the capacity of manufacturing and other facilities to support our product and product candidates;
- our ability to ensure adequate and continued supply of Sumavel DosePro to successfully meet anticipated market demand;
- our expected third party research and development costs for Zohydro remaining through our NDA filing with and potential regulatory approval from 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;

the impact of healthcare reform legislation; and

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

The forward-looking statements are contained principally in the sections entitled Risk Factors, 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, potentia 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

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financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. We discuss many of these risks, uncertainties and other factors in this Annual Report on Form 10-K in greater detail under the heading Item 1A Risk Factors.

Given these risks, uncertainties and other factors, we urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. You should read this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. We undertake no obligation to revise or update publicly any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

This Annual Report on Form 10-K 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 Annual Report on Form 10-K is from Wolters Kluwer Pharma Solutions, Source® Pharmaceutical Audit Suite (PHAST) Institution/Prescription, Source® PHAST Prescription, Source® Prescriber or Source® 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.

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

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

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Item 1. 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® 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 (*hydrocodone* bitartrate, formerly ZX002) is a 12-hour extended-release formulation of *hydrocodone* without acetaminophen for the treatment of moderate to severe chronic pain requiring around-the-clock opioid therapy. We completed Phase 3 development of Zohydro in 2011, and we expect to submit the New Drug Application, or NDA, for Zohydro to the FDA early in the second quarter of 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, 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 2011, triptans generated sales of approximately $3.9 billion and *sumatriptan*, including branded and generic forms, represented the largest market share of the seven approved triptans, with sales of approximately $2.3 billion, according to Wolters Kluwer Pharma Solutions (Source® PHAST Institution/Prescription).

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 116 professionals. Our field sales force of approximately 95 representatives has historically been complemented by our collaboration with Astellas and approximately 400 of its sales representatives. The target audience for Astellas sales effort was primarily comprised historically 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 was primarily comprised historically of neurologists and other prescribers of migraine medicines who fall outside the Astellas Segment. In addition, our representatives have historically had the right to call upon a specified number of key prescribers within the Astellas Segment and Astellas representatives historically had the right to call upon a specified number of neurologists.

Our collaboration with Astellas will terminate on March 31, 2012, at which time we will assume full responsibility for the commercialization of Sumavel DosePro. During the fourth quarter of 2011, the Zogenix sales force contributed approximately 73% of our Sumavel DosePro unit demand volume, including jointly called-on physicans, with the remaining unit demand volume derived by Astellas.

We increased our sales force from approximately 80 to approximately 95 professionals in 2011. Based on third-party data, approximately 86% of the prescription demand in the Astellas Segment was concentrated to a population of approximately 500 physicians, which we believe our sales force will be able to support after our transition plan, utilizing our Phase IV data, toolkits and other promotional activities. As such, we do not expect

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that all of the prescription demand contributed by the Astellas sales force will be foregone as a result of the early termination of the co-promotion agreement. However, in the event we are unsuccessful in transitioning the Astellas Segment to our sales force, our net product sales and financial results could be negatively impacted.

We have already begun to assume responsibility from Astellas for marketing Sumavel DosePro to selected high-prescribing primary care physicians and other Astellas-targeted physicians and professionals within the Astellas Segment pursuant to a promotion transition plan. We are currently evaluating potential co-promotion partners who could complement our sales force efforts for the commercial sale of Sumavel DosePro. 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 has demonstrated significant quarterly growth in total prescriptions since its launch in January 2010. For the twelve months ended December 31, 2011, we recognized $30.4 million in net product revenue from sales of Sumavel DosePro, represented by more than 71,779 aggregate dispensed prescriptions (Source® PHAST Prescription, January 2011 December 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 81% since launch (Source® Dynamic Claims January 2011 December 2011).

We believe our lead product candidate, Zohydro, has the potential to be an important therapeutic alternative to existing *hydrocodone* products, including the branded products Vicodin, Norco, Lorcet, 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, Alkermes plc 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. 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 has the potential to 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. We in-licensed exclusive U.S. rights to Zohydro from Alkermes 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 $14.2 billion for the year ended December 2011, based on average wholesale price, on approximately 217 million prescriptions. During the same period, existing *hydrocodone* products, the most commonly prescribed pharmaceutical products in the United States, generated $3.5 billion in sales on approximately 134.6 million prescriptions. (Source® PHAST Prescription). 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

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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 $1.58 billion in 2011 with 72% of net sales outside of the United States, 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 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.

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 through December 31, 2011 was $30.4 million. We continue to leverage our established commercial infrastructure 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. Our co-promotion collaboration with Astellas will terminate in March 2012, and beginning in the second quarter of 2012, we will assume full responsibility for the continued commercialization of Sumavel DosePro, with a focus on headache specialists, neurologists and primary care physicians in the United States. We are currently evaluating potential co-promotion partners who could complement our sales force efforts.

Developing and commercializing Zohydro for the treatment of moderate to severe chronic pain. We completed our Phase 3 clinical program for Zohydro which was 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 top-line results from our pivotal Phase 3 efficacy trial in August 2011 and expect to submit an NDA with the FDA early in the second quarter of 2012. If we receive FDA approval, we intend to consider co-promotion and other partnering opportunities for Zohydro, and an expansion of our sales and marketing infrastructure, including expanding our field sales force to between 170 and 220 representatives, to both launch Zohydro and continue to support Sumavel DosePro.

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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 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.

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.

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 original 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 the National Headache Foundation, more than 29.5 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.

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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_{1B} and 5-HT_{1D} receptors. Triptans presumably exert their antimigrainous effect through binding to vascular 5-HT_1 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 2011.

U.S. Triptan Market

(12 months ended December 2011)

Triptan Form	Sales (millions)	$ Share	Doses (millions)	Dose Share
Oral Tablet	$ 3,032	77.80%	119.4	85.6%
Oral Melt	407	10.4	13.7	9.8
Nasal	118	3.0	2.9	2.1
Injectable	341	8.8	3.5	2.5
Total	$ 3,898	100%	139.5	100%

Source ® PHAST Institution/Prescription.

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 $2.3 billion (60% dollar share of the triptan market). Of that amount, the injectable forms of sumatriptan accounted for $341 million. By comparison, ergotamine agents, another class of drugs used for the acute treatment of migraine, including injectable DHE and Migranal, accounted for $74 million in sales in the United States during the same 12-month period. (Source® PHAST Institution/Prescription). 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.

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

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(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.

T_{max} 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 T_{max}, reaching maximum blood concentration in 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.

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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® PHAST Institution/Prescription, January 2011 December 2011). 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.

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

Due to these limitations, there has historically been a limited prescriber base for injectable delivery forms of *sumatriptan*. Of an aggregate of over 360,000 prescribers of triptans in the United States, only an approximate 69,000 had written a prescription for *sumatriptan* injection (including Sumavel DosePro) in the 12 months ended December 31, 2011 (Wolters Kluwer Pharma Solutions, Source® Prescriber PHAST Prescription, January 2011 December 2011). 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

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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 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 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.

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In support of these strategic objectives, we 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 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 FFDCA, utilizing Imitrex *sumatriptan* injection as the reference listed product. Section 505(b)(2) of the FFDCA 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 *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. In November 2010, Denmark became the first member of the European Union to approve marketing of Sumavel DosePro in that country. Subsequently, Sumavel DosePro has received marketing approval in Germany, Sweden, the United Kingdom, Norway and France.

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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 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 4 mg dosage strength of Sumavel DosePro. We have completed registration batch manufacture, and plan to submit an NDA supplement to the FDA to demonstrate the manufacturability and stability of the new dosage strength by the end of 2012. We anticipate commercializing the 4mg dosage strength in 2013, if approved.

DosePro and Sumavel DosePro Sound Enhancement

In order to further enhance the DosePro technology and Sumavel DosePro, we have completed additional engineering and design work aimed at softening the sound emitted by the DosePro device upon drug delivery. Rather than the current sound, which is similar to the opening of a can of soda, heard upon delivery with the current DosePro device, this enhanced version will sound 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.

DosePro and Sumavel DosePro Clinical Experience

The DosePro drug delivery system has been in development for more than fifteen 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.

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Zohydro for the Treatment of Moderate to Severe Chronic Pain

Our lead product candidate, Zohydro (*hydrocodone* bitartrate), is a 12-hour extended-release formulation of *hydrocodone* without acetominophen for the treatment of moderate to severe chronic pain requiring around-the-clock opioid therapy. We completed Phase 3 development of Zohydro in 2011, and we expect to submit an NDA for Zohydro to the FDA early in the second quarter of 2012. We believe Zohydro has the potential to be an important therapeutic alternative to existing extended-release opioids as well as immediate release *hydrocodone* products, including the branded products Vicodin, Norco, Lorcet, Lortab and their generic equivalents, which contain the analgesic combination ingredient *acetaminophen* and, if taken in high quantities over time, may lead to serious side effects such as liver toxicity. Zohydro utilizes the SODAS Technology, Alkermes 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. 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.

If Zohydro is approved by the FDA, it will be included in a Risk Evaluation and Mitigation Strategies, or REMS, program, compliant with FDA mandates and consistent with other extended release opioids. This program recognizes the abuse potential of opioids and lays out specific education materials to facilitate appropriate prescribing, dispensing and use of extended release opioids.

Zohydro also is expected be designated as a U.S. Drug Enforcement Agency, or DEA, Schedule II product, which will make it more tightly regulated than currently available *hydrocodone* products, all of which are currently designated as Schedule III products. This means that Zohydro will not qualify for automatic refills and prescribers will be required to comply with the REMS program outlined for Zohydro. We believe these restrictions will help facilitate more responsible prescribing of Zohydro in terms of the dose and capsule count should it receive FDA approval.

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, 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

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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 longer 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 and potentially more tolerable. 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 non-opioid analgesics, including *acetaminophen* or an NSAID, which treat the acute inflammatory component of the pain. These non-opioid 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 (5 mg *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 2011, our target market, which we define as prescription non-injectable *codeine*-based and extended-release *morphine*-based pain products, generated sales of approximately $14.2 billion in the United States on approximately 217 million prescriptions. Of the $14.2 billion, *hydrocodone* products, the most commonly prescribed opioid and the most commonly prescribed pharmaceutical products in the United States, generated $3.5 billion in sales on approximately 134.6 million prescriptions. (Source® PHAST Prescription).

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 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.

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Limitations of Current Hydrocodone 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 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.

Widespread use of acetaminophen leading to increased toxicity risk. Even when combination products are carefully prescribed, patients are at risk of *acetaminophen* toxicity due to the prevalence of APAP in many over the counter products and individuals lack of knowledge about the dangers and/or awareness of APAP in other products.

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.

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

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extended relief profile of Zohydro. In addition, there are five other marketed products using SODAS technology that dosed every 24 hours, which we believe helps validate the controlled release technology underlying the formulation 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.

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 also conducted 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 the trial in December 2011. The goal of this trial was to evaluate the safety and tolerability of Zohydro for up to 12 months of treatment. The study further demonstrated that Zohydro was safe and generally well tolerated, and the incidence of adverse events was generally consistent with that seen in our pivotal Phase 3 efficacy trial. The safety and efficacy data from this trial is still being analyzed and will be submitted as part of our NDA to the FDA.

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Based upon feedback from the FDA at our End of Phase 2 meeting and our pre-NDA meetings in the fourth quarter of 2011, with the positive results of our pivotal Phase 3 efficacy trial and the completion of the Phase 3 safety trial, we do not believe that additional Phase 3 safety or efficacy trials will be required to support our NDA submission. We have initiated 2-year carcinogenicity studies in two animal species. We obtained FDA agreement on the protocols for both studies and have agreed with FDA that these studies are an ongoing commitment and are not required for submission or approval of an NDA for Zohydro. We expect to submit an NDA for Zohydro to the FDA early in the second quarter of 2012.

Prior Clinical Development of Zohydro

Our licensor for Zohydro, Alkermes, 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-naive 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.

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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 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 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

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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.

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® PHAST Prescription, January 2011 December 2011). 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 $270 per bi-weekly dose, or more than $500 per month, for the 25mg dosage strength (Source: Gold Standard). Finally, in the United States, prescribers of long-acting antipsychotics are highly concentrated with approximately 15,000 total prescribers of long-acting injectable products, including approximately 8,785 psychiatrists in 2011 (Source® PHAST Prescription, January 2011 December 2011).

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 pre-clinical 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 dilutent, 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

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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 24% of total prescriptions in the twelve months ended December 2011 (Source® PHAST Prescription, January 2011 December 2011).

We intend to initiate clinical studies for Relday in patients with schizophrenia in 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 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 Sates 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 softening the sound emitted by the DosePro device upon drug delivery. Rather than the current sound, which is similar to the opening of a can of soda, heard upon delivery with the current DosePro device, this enhanced version will sound 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.

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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.

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 116 professionals. Our field sales force of approximately 95 representatives has historically promoted 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 13 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 20 years of pharmaceutical industry experience, including an average of nine years of sales management experience. Each of our sales representatives and regional business

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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 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.

In addition, in July 2009, we entered into an exclusive co-promotion agreement with Astellas under which Sumavel DosePro was historically marketed by Astellas in the United States and promoted primarily to primary care physicians (including internal medicine, family practice and general practice), OB/GYNs, emergency medicine physicians and urologists, or collectively the Astellas Segment, by approximately 400 Astellas sales representatives. The target audience for our sales effort was primarily comprised historically of neurologists and other prescribers of migraine medicines who fall outside the Astellas Segment. In addition, our representatives have historically had the right to call upon a specified number of key prescribers within the Astellas Segment and Astellas representatives historically had the right to call upon a specified number of neurologists. This exclusive co-promotion agreement with Astellas will terminate on March 31, 2012, at which time we will assume full responsibility for the commercialization of Sumavel DosePro. We have already begun to assume responsibility from Astellas for marketing Sumavel DosePro to selected high-prescribing primary care physicians and other Astellas-targeted physicians and professionals within the Astellas Segment pursuant to a promotion transition plan. We are currently evaluating potential co-promotion partners who could complement our sales and marketing professionals for the continued marketing of Sumavel DosePro.

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, Sweden and Germany in December 2010 and Norway and France 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.

To build upon our continued success in growing Sumavel DosePro prescriptions, we expanded our sales force in the United States from approximately 80 sales representatives in 2010 to approximately 95 sales representatives at the end of the 2011. We are currently evaluating potential co-promotion partners who could complement our sales and marketing professionals for the continued marketing of Sumavel Dose Pro. For the launch of Zohydro, if approved, we intend to consider co-promotion and other partnering opportunities, and an expansion of our sales and marketing infrastructure, including expanding our field sales force to between 170 and

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220 representatives, to both launch Zohydro 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.

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, we face competition from alternative autoinjector forms of *sumatriptan* injection including *sumatriptan* injection, a needle-based autoinjector which was developed and is manufactured and marketed by Pfizer, and a needle-based generic *sumatriptan* auto-injector from Sun Pharmaceutical Industries Limited. Finally, generic injectable *sumatriptan* in the form of vials and prefilled syringes is available from a number of pharmaceutical companies. 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,

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but are not limited to, Abbott Laboratories, 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 Egalet A/S, Pfizer, Purdue Pharma L.P. and Teva Pharmaceutical Industries Limited. 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 companies listed above, as well and by other pharmaceutical companies such as Alkermes plc, 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 commercialized gas- or spring-driven, multiple-use, patient-filled, needle-free injectors, primarily for injecting human growth hormone or insulin for diabetes. 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 46.0%, 34.9% and 10.9%, respectively, of our total gross sales of Sumavel DosePro for the year ended December 31, 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

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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.

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. If demand exceeds our expectation in 2013 and beyond, we may 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 Alkermes (formerly Elan Drug Delivery, Inc.) under the terms of our license agreement 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.

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 £303,200, or approximately $468,538 (based on the exchange rate as of December 31, 2011), over the remaining term of the agreement, aggregating to £6,670,400, or approximately £10,307,836, over the remaining initial term of the agreement**.** 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

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(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 Munnerstadt, 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. Prior to expiration of the agreement, we intend to extend the commercial manufacturing and supply agreement with MGlas to continue the exclusive supply of the glass capsule. 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 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 chemistry, manufacturing and controls, or CMC, development responsibilities. Durect will be reimbursed by us for its research and development efforts on the product.

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We paid a non-refundable upfront fee to Durect of $2.25 million in July 2011. We are obligated to pay Durect up to $103.0 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. Further, until an NDA for Relday has been filed in the United States, we are obligated to spend no less than $1.0 million in external expenses on the development of Relday in any trailing twelve month period beginning in July 2012. 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 monitory 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). Under the agreement, both Astellas and we were obligated to collaborate and fund the marketing of Sumavel DosePro and to provide annual minimum levels of sales effort directed at Sumavel DosePro. In December 2011, we entered into an amendment to the co-promotion agreement with Astellas, or the amended co-promotion agreement, whereby the agreement will terminate on March 31, 2012. We are responsible for the manufacture, supply, and distribution of commercial product for sale in the United States. In addition, we supply product samples to Astellas, and Astellas pays us for such samples, at an agreed upon transfer price.

The target audience for Astellas sales efforts was primarily comprised historically 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 was primarily comprised historically of neurologists and other prescribers of migraine medicines who fall outside the Astellas Segment. In addition, our representatives have historically had the right to call upon a specified number of key prescribers within the Astellas Segment; conversely Astellas representatives historically had the right to call upon a specified number of neurologists. Under the terms of the amended co-promotion agreement, beginning in the first quarter of 2012, we began to assume responsibility from Astellas for marketing Sumavel DosePro to selected high prescribing primary care physicians and other Astellas-targeted physicians and

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professionals within the Astellas Segment pursuant to a promotion transition plan. We will assume full responsibility for the commercialization of Sumavel DosePro following termination of the agreement in March 2012.

Under the agreement, Astellas has paid us upfront and milestone payments in an aggregate amount of $20.0 million through December 31, 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 in March 2012, we will be required to pay Astellas two additional annual tail payments in July 2013 and July 2014 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 12 months ending March 31, 2012.

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 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.

Alkermes License Agreement (formerly Elan Pharma International Limited)

In November 2007, we entered into a license agreement with Alkermes, which was amended in September 2009. Under the terms of this license agreement, Alkermes granted to us an exclusive license in the United States

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and its possessions and territories, with defined sub-license rights to third parties other than certain technological competitors of Alkermes, to certain Alkermes intellectual property rights related to our Zohydro product candidate. The agreement grants us the exclusive right under certain Alkermes 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. Alkermes has retained the exclusive right to take action in the event of infringement or threatened infringement by a third party of Alkermes intellectual property rights under the agreement. We have the right to pursue an infringement claim against the alleged infringer should Alkermes 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, Alkermes, or an affiliate of Alkermes, will have the sole and exclusive right to manufacture and supply finished commercial product of Zohydro to us under agreed upon financial terms.

Alkermes also granted to us, in the event that Alkermes is unwilling or unable to manufacture or supply commercial product to us, a non-exclusive license to make product under Alkermes 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 Alkermes.

Under the license agreement, we paid an upfront fee to Alkermes of $0.5 million. We paid an additional milestone payment in the amount of $0.8 million to Alkermes 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 Alkermes up to $3.75 million in total future milestone payments with respect to Zohydro depending upon the achievement of various development and regulatory events. These future milestone payments include a payment of $1.0 million upon submission of the first NDA to the FDA, which we currently expect to occur early in the second quarter of 2012, and a payment of $0.8 million upon successful completion of an FDA pre-approval inspection of the manufacturing facility. 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 Alkermes patents covering the product in the United States, or 15 years after commercial launch, if Alkermes 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. Alkermes 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.

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

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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 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 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 February 1, 2012, we have 17 issued U.S. patents, 12 pending U.S. patent applications, 49 issued foreign patents and 22 pending foreign patent applications. Of the above, we have seven issued U.S. patents, three pending U.S. patent applications, 39 issued foreign patents and five 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 activator 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 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 a 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, Canada, Germany, Spain, France, United Kingdom, 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.

We have two U.S. patents 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.

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These patents, and applications if they issue, are expected to expire in 2023. We also have one U.S. patent 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 and five foreign patents (one each in Germany, France, Japan and the United Kingdom) 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 accordingly we are not able to use the patent system to provide for market exclusivity in those countries. 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 Alkermes proprietary SODAS delivery system. Our in-licensed patents from Alkermes 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

With respect to Relday, 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 FFDCA 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.

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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 current good laboratory practice, or CGLP, 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 current good clinical practices, or CGCP, 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;
- submission to the FDA of an NDA;
- satisfactory completion of a potential review by an FDA advisory committee, 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

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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, 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.

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 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

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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.

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

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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.

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 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.

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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 FFDCA, 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.

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 FFDCA. 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 FFDCA, 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

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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.

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.

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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, 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.

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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 approved in Denmark and has received subsequent approvals in Germany, Sweden, the United Kingdom, Norway and France.

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, 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.

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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 $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

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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 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.

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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 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.

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Employees

As of December 31, 2011, we employed 161 full-time employees. Of the full-time employees, 116 were engaged in sales and marketing, nine were engaged in manufacturing operations, 18 were engaged in product development, quality assurance and clinical and regulatory activities and 18 were engaged in general and administrative activities (including business and corporate development). We may expand our sales force in the future through direct hiring or through potential co-promotion partners to support continued sales and marketing of Sumavel DosePro and, if approved, to launch 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.

Research and Development

The Company invested $33.0 million, $28.6 million and $21.4 million in research and development in the years 2011, 2010 and 2009, respectively.

About Zogenix

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.

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 Annual Report on Form 10-K. 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.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended. We make available on our website at www.zogenix.com, free of charge, copies of these reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The public may read or copy any materials we file with the SEC at the SEC s Public Reference Room at 100 F Street NE, Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is http://www.sec.gov. The information in or accessible through the SEC and our website are not incorporated into, and are not considered part of, this filing. Further, our references to the URLs for these websites are intended to be inactive textual references only.

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Item 1A. Risk Factors

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

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, our follow-on public offering completed in September 2011, 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. Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of December 31, 2011, together with estimated future product revenue and borrowings available under our $10.0 million revolving credit facility, will be sufficient to fund our operations into the first quarter of 2013. 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 once our co-promotion agreement with Astellas Pharma US, Inc., or Astellas, terminates in March 2012;
- qualify secondary sources for the manufacturing of Sumavel DosePro;
- fund our operations, submit our NDA for Zohydro, initiate additional 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 Relday and our other product candidates and any other product candidates that we may develop, in-license or acquire;

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

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

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

the effect of competing technological and market developments; and

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

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

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

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, 2011, 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 2012, we obtained a waiver from Oxford and SVB for the breach caused by the receipt of the 2011 audit report from our independent registered public accounting firm which includes a going concern qualification.

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

We anticipate that, for at least the next several years, 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 by expanding our sales force and/or through a new co-promotion partner, if available, as our co-promotion agreement with Astellas will terminate in March 2012;
- obtain greater acceptance of Sumavel DosePro by physicians and patients;
- maintain adequate levels of coverage and reimbursement for Sumavel DosePro from commercial health plans and government health programs, which we refer to collectively as third-party payors, particularly in light of the availability of other branded and generic competitive products;
- maintain compliance with regulatory requirements;
- establish and maintain agreements with wholesalers and distributors on commercially reasonable terms;
- maintain commercial manufacturing arrangements with third-party manufacturers as necessary to meet commercial demand for Sumavel DosePro and continue to manufacture commercial quantities at acceptable cost levels; and
- successfully maintain intellectual property protection for Sumavel DosePro.

We cannot be certain that our continued marketing of Sumavel DosePro will result in increased demand for, and sales of, the product. For example, while we have generally experienced quarterly growth in total prescriptions from the launch of Sumavel DosePro in January 2010 through December 31, 2011, we have at certain times experienced a reduction in total and new prescriptions month over month. Further, if we are unsuccessful in continuing to expand our sales force and/or partnering with a new co-promotion partner once our co-promotion agreement with Astellas terminates in March 2012, we may be unable to successfully maintain or increase sales of Sumavel DosePro. If we fail to successfully maintain and increase sales of Sumavel DosePro, we may be unable to generate sufficient revenues to grow or sustain our business and we may never become profitable, and our business, financial condition and results of operations will be materially adversely affected.

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

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

We have generated substantial net losses and negative cash flow from operations since our inception in 2006. For example, for 2011, 2010 and 2009, we incurred net losses of $83.9 million, $73.6 million and $45.9 million, respectively, our net cash used in operating activities was $80.5 million, $72.0 million, and $32.4 million, respectively, and, at December 31, 2011, our accumulated deficit was $282.0 million. We expect our losses and negative cash flow to continue for at least the next several years as a result of expenses incurred in connection with our planned NDA submission for Zohydro, commercialization activities for Zohydro, any additional clinical development required for Zohydro, the cost of clinical development for Relday and the cost of the sales and marketing expense associated with Sumavel DosePro and, if approved, Zohydro. Our

ability to generate revenues from Sumavel DosePro or any of our product candidates will depend on a number of factors,

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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, including as a result of the termination of our collaboration with Astellas in March 2012, and we may not be able to generate significant revenue.

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

To complement our sales force, we entered into an exclusive co-promotion agreement with Astellas in July 2009 under which Sumavel DosePro has been promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists, or collectively the Astellas Segment, in the United States by approximately 400 Astellas sales representatives. This co-promotion agreement will terminate on March 31, 2012, and beginning in the second quarter of 2012 our sales force will assume full responsibility for the continued promotion of Sumavel DosePro. We expect to expand the focus of our existing sales force to include targeting a portion of the high-prescribing primary care physicians previously part of the Astellas Segment under the co-promotion agreement. Although we believe we have adequately sized our sales force in order to reach our historically targeted audience, our existing sales force may be unable to effectively target these additional primary care physicians. We are also currently evaluating potential co-promotion partners who could complement our sales force efforts for the commercial sale of Sumavel DosePro. We may not be able to enter into co-promotion 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. Further, to the extent that we enter into a new co-promotion agreement, it will take time and resources to train and deploy a new partners sales force, which may strain our managerial resources and may have an adverse affect on our own sales and marketing efforts and revenues. If we are unable to find another partner for the promotion of Sumavel DosePro in the primary care segment in the United States, we may lack the financial and managerial resources to increase the size of our sales and marketing organization to adequately promote and commercialize Sumavel DosePro in this segment and any such expansion could, in any event, substantially increase our expenses and capital requirements. In addition, we may lack the financial and managerial resources to increase the size of our sales and marketing organization to adequately promote and commercialize Sumavel DosePro. For the years ended December 31, 2011 and 2010, the Astellas Segment represented approximately 37.7% and 39.5% of our prescription demand, respectively. Any inability to adequately replace coverage of the Astellas Segment by a new co-promotion partner or through our own sales force may have a material adverse affect on our ability to maintain or increase revenues in the future.

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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, 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 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 political influences, illegal use, overdoses, abuse, diversion, serious injury and death. These events have led to heightened regulatory scrutiny. Controlled substances are classified by the DEA as Schedule I through V substances, with Schedule I substances being prohibited for sale in the United States, Schedule II substances considered to present the highest risk of abuse and Schedule V substances being considered to present the lowest relative risk of abuse. Zohydro 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.

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

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

Despite the implementation of security measures, our internal computer systems and those of our current and any future partners, contractors and consultants are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. For example, we 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 46.0%, 34.9% and 10.9%, respectively, of our total gross sales of Sumavel DosePro for the year ended December 31, 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,

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and may continue to increase, competitive and pricing pressures on pharmaceutical products. In addition, at times, wholesaler purchases may exceed customer demand, resulting in reduced wholesaler purchases in later quarters, which may result in substantial fluctuations in our results of operations from period to period. We cannot assure you that we can manage these pricing pressures or that wholesaler purchases will not decrease as a result of this potential excess buying.

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

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

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

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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 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 Egalet A/S, Pfizer, Purdue Pharma L.P. and Teva Pharmaceutical Industries Limited. 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, Inc, LLC, Intellipharmaceuticals 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 and by other pharmaceutical companies such as Alkermes plc, 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.

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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;
- 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 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 Münnerstadt, 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, Alkermes plc, or Alkermes, 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.

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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;
- 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.

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

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

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 submitted an 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;

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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, Phase 2 clinical trials, and a Phase 3 clinical development program. However, some of these studies and trials were conducted by a third party and, accordingly, we did not directly participate in their design or execution. We initiated the Phase 3 clinical development program for Zohydro in March 2010 and reported positive top-line results from our pivotal Phase 3 efficacy trial, Study 801, in August 2011 and completed our Phase 3 safety trial, Study 802, in December 2011, which showed Zohydro to be safe and generally well tolerated. However, 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. Relday and any of our other product candidates may fail to achieve their specified endpoints in clinical trials. 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.

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

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

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

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products before and after approval. In particular, the FFDCA authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information and require a 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 FFDCA, companies that violate these and other provisions of the law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties.

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

With regard to Zohydro, 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 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 (2%) 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 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 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 or any of our other product candidates are not shown to be safe and effective in clinical trials, the program could be delayed or terminated, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Delays in the commencement or completion of any additional clinical testing for Zohydro, if required, 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 any additional clinical testing for Zohydro, if required, 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. We expect to initiate clinical testing for Relday in patients with schizophrenia in 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;

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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.

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

failure to design appropriate clinical trial protocols;

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

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

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

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

lack of effectiveness of any product candidate during clinical trials;

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

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

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

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

Additionally, changes in applicable regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. All of the above risks will be applicable to Zohydro to the extent we are required by the FDA to conduct any additional clinical trials. If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for Zohydro, 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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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 FFDCA, or Section 505(b)(2). Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. For example, we obtained FDA marketing approval of Sumavel DosePro under Section 505(b)(2), and we 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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We rely on third parties to conduct our pre-clinical and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We conducted our Phase 3 trials for Zohydro under agreements with third-party CROs, and anticipate that we may enter into agreements with third-party CROs in the future regarding Relday or any of our other product candidates. We rely heavily on these parties for the execution of our clinical and pre-clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol. We and our CROs are required to comply with current good clinical practices, or GCPs. The FDA enforces these GCP regulations through periodic inspections of trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCP regulations, the data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon 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 FFDCA. Section 505-1 permits FDA to require a REMS for a drug product to ensure the safe use of the drug. A REMS is a strategic safety program that the FDA requires to ensure that the benefits of a drug outweigh its risks. In determining whether a REMS is necessary, the FDA 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 REMS must include a timetable to assess the strategy at 18 months, three years and seven years after the strategy s approval.

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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, the FDA announced that it had finalized the elements of a class-wide REMS for these products. The central component of the opioid REMS program is an education program for prescribers and patients. Specifically, the REMS for these products must include a Medication Guide available for distribution to patients who are dispensed the drug, as well as a number of elements to assure safe use. These elements include training for prescribers who prescribe the drug; information provided to prescribers that prescribers can use to educate patients in the safe use, storage, and disposal of opioids; and information provided to prescribers of the existence of the REMS and the need to successfully complete the necessary training. 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, the United Kingdom, Norway and France.

Any additional clinical studies Desitin may be required to conduct as part of the regulatory approval process may not corroborate the results of the clinical studies we have conducted or may have adverse results or effects on our ability to maintain regulatory approvals in the United States or obtain them in other countries. In addition, although we believe that the U.S. market represents the largest commercial opportunity for Sumavel DosePro, Desitin may not develop Sumavel DosePro as fast or generate as large of a market as we would like or as the market may expect and Desitin may not seek to develop, obtain approval for or commercialize Sumavel DosePro in countries for which it has exclusive rights, other than in Germany, where Desitin is required to develop, seek approval for and commercialize Sumavel DosePro. Any failure by Desitin to successfully commercialize

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Sumavel DosePro or to successfully obtain applicable foreign regulatory approval for Sumavel DosePro would limit our opportunity to receive revenue from the territories licensed to Desitin. Furthermore, negative developments occurring in those territories controlled by Desitin could have a negative impact on physician and patient impressions of our product in the United States and elsewhere.

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

Major pharmaceutical companies usually employ groups of sales representatives numbering in the thousands to call on the large number of primary care physicians. In connection with the launch of Sumavel DosePro in January 2010 we built a sales and marketing organization to promote Sumavel DosePro in the United States, including a focused sales force currently comprised of approximately 95 representatives primarily targeting neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. In July 2009, we entered into an exclusive agreement with Astellas under which Sumavel DosePro was also being marketed by Astellas in the United States and promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists by approximately 400 Astellas sales representatives. Our Astellas agreement will terminate on March 31, 2012, and in order to maintain and expand the market opportunity for Sumavel DosePro and any additional product candidates that receive regulatory approval into the broader primary care physician audiences, we will need to expand our sales and marketing personnel and commercial infrastructure and/or establish partnerships with pharmaceutical companies or contract sales organizations to co-promote such product and/or product candidates. We currently, and on an ongoing basis will have to, compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. We also face competition in our search for collaborators and potential co-promoters. To the extent we rely on additional third parties to co-promote or otherwise commercialize any product and/or product candidates that may receive regulatory approval, we are likely to receive less revenue than if we commercialized these products ourselves. Further, by entering into strategic partnerships or similar arrangements, we may rely in part on such third parties for financial and commercialization resources. Even if we are able to identify suitable partners to assist in the commercialization of our product and/or product candidates, they may fail to devote the resources necessary to realize the full commercial potential of our products. In addition, we may lack the financial and managerial resources to increase the size of our sales and marketing organization to adequately promote and commercialize Sumavel DosePro and any product candidates that may be approved, and any increase in our sales force would result in an increase in our expenses, which could be significant before we generate revenues from any newly approved product candidate. If we are unable to expand our sales and marketing infrastructure or enter into a third-party arrangement, we would not be able to successfully commercialize any approved products. Even if we are able to expand our sales and marketing personnel or successfully establish partnership arrangements, such sales force and marketing teams may not be successful in commercializing our products, which would adversely affect our ability to generate revenue for such products, which will have a material adverse effect on our business, results of operations, financial condition and prospects.

Our failure to successfully acquire, develop and market additional product candidates or approved products would impair our ability to grow our business. In that regard, our DosePro delivery system 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 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

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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 CMC development responsibilities. As a result, we will be dependent on Durect s successful completion of its responsibilities for Relday. In addition, because our internal research and development capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify and select promising pharmaceutical product candidates and products, negotiate licensing or acquisition agreements with their current owners and finance these arrangements.

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

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including pre-clinical or clinical testing and approval by the FDA and applicable foreign regulatory authorities. We expect to initiate clinical testing for Relday in patients in schizophrenia in 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.

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.

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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 161 as of December 31, 2011. In addition, we have expanded our sales force in the United States from approximately 80 sales representatives to approximately 95 sales representatives at the end of 2011 and we intend to increase our sales force if Zohydro is approved by the FDA. Any such increases in our sales force could substantially increase our expenses. We may need to continue to expand our managerial, operational and other resources in order to grow, manage and fund our existing business. Our management and personnel, systems and facilities currently in place may not be adequate to support this recent and any future growth, and we may be unable to fund the costs and expenses required to increase our necessary headcount and infrastructure. Our need to effectively manage our operations, any future growth and various projects requires that we:

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

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

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

Our success depends on our continued ability to attract, retain and motivate highly qualified management and key clinical development, regulatory, sales and marketing and other personnel. We are highly dependent on the development, regulatory, commercial and financial expertise of our senior management team. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the areas in Southern and Northern California, where we currently operate. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercialization objectives, our ability to raise additional capital and our ability to implement our business strategy. The loss of the services of any members of our senior management team, especially our Chief Executive Officer, Roger L. Hawley, and President and Chief Operating Officer, Stephen J. Farr, Ph.D., could negatively impact the commercialization of Sumavel DosePro and could delay or prevent the development and commercialization of any other product candidates, including Zohydro 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

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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;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

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

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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, 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;

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

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

Our research and development activities and our third-party manufacturers and suppliers activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product and product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous

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

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

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

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

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

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

Payments to our material suppliers and contract manufacturers are denominated in the Euro and U.K. pound sterling. Our reporting currency is the U.S. dollar and to date all of the revenues generated by sales of Sumavel DosePro have been in U.S. dollars. For the year ended December 31, 2011, $31.7 million (based on exchange rates as of December 31, 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 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.

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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 the termination of our partnership with Astellas to co-promote Sumavel DosePro in March 2012. We have financed our operations almost exclusively through the proceeds from the issuance of our common and preferred stock, including the proceeds from our initial public offering completed in November 2010, our follow-on public offering completed in September 2011, and debt, and have incurred losses and negative cash flow from operations in each year since our inception. Our net loss was $83.9 million in 2011, $73.6 million in 2010 and $45.9 million in 2009, and our cash used in operating activities was $80.5 million in 2011, $72.0 million in 2010 and $32.4 million in 2009. As of December 31, 2011, we had an accumulated deficit of $282.0 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 expenses incurred in connection with our regulatory filings for Zohydro, any additional required clinical testing 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 in our cash resources could require that we delay or abandon certain development and commercialization activities and could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

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

As of December 31, 2011, the principal amount of our total indebtedness was approximately $60.2 million. In July 2011, we completed the royalty financing transaction with Cowen Royalty, or the Cowen Financing agreement, which increased our total indebtedness by an additional $30.0 million. We have and expect to

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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, 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 2011 and thereafter not include a going concern qualification. As discussed above, the audit report from our independent registered public accounting firm accompanying our 2011 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,

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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 Financing agreement, 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 Cowen 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 (in the case of co-promotion revenues and license fees) or recorded (in the case of net products sales).

Our obligations under the Cowen 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), 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 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 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 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 Financing agreement at its election in connection with a change of control of our company, as defined in the Cowen 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), or an event of default (which includes the occurrence of a bankruptcy event or other material adverse change in our business), as defined in the Cowen Financing agreement, occurring thereunder. Upon such a termination by Cowen Royalty prior to the maturity date specified in the Cowen 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.

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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 Financing agreement may make us significantly less attractive to potential acquirers, and in the event that we exercised our change of control pay-off option in order to carry out a change of control, the payment of such funds out of our available cash or acquisition proceeds would reduce acquisition proceeds for our stockholders.

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

Our results of operations and liquidity could be materially negatively affected by economic conditions generally, both in the United States and elsewhere around the world. Domestic and international equity and debt markets have experienced and may continue to experience heightened volatility and turmoil based on domestic and international economic conditions and concerns. In the event these economic conditions and concerns continue or worsen and the markets continue to remain volatile, our results of operations and liquidity could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary, and our stock price may decline. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are not federally insured. If economic instability continues, we cannot provide assurance that we will not experience losses on these investments.

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

We may 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 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 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.

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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 performed an additional IRC Section 382 and 383 analysis upon the issuance of common stock in our follow-on public offering in September 2011, and together with the issuance of common stock in our initial public offering and certain other transactions involving our common stock, resulted in an additional ownership change, which further limited the amount of the tax attributes we may use to offset future taxable income, if any. In addition, any future equity financing transactions, private placements and other transactions that occur within the specified three-year period may trigger additional ownership changes, which could further limit our use of such tax attributes. Any such limitations, whether as the result of prior or future offerings of our common stock or sales of common stock by our existing stockholders, could have an adverse effect on our consolidated results of operations in future years.

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

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foreign laws and regulations governing the manufacture of drugs and devices, and any failure by them to comply with those laws and regulations may delay or interrupt supplies of our product.

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

- impose restrictions on the marketing or manufacturing of the product, suspend or withdraw product approvals or revoke necessary licenses;
- issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;
- commence criminal investigations and prosecutions;
- impose injunctions, suspensions or revocations of necessary approvals or other licenses;
- impose fines or other civil or criminal penalties;
- suspend any ongoing clinical trials;
- deny or reduce quota allotments for the raw material for commercial production of our controlled substance products;
- delay or refuse to approve pending applications or supplements to approved applications filed by us;
- refuse to permit drugs or precursor chemicals to be imported or exported to or from the United States;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require us to initiate a product recall.

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

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;

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

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

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

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 FFDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Under this statutory provision, the FDA may rely, for purposes of approving an NDA, on findings of safety and effectiveness based on data not developed by the filer of the NDA. Similar to Sumavel DosePro, we 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

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

Annual DEA quotas on the amount of hydrocodone allowed to be produced in the United States and our specific allocation of hydrocodone by the DEA could significantly limit any additional clinical development of Zohydro, if required, 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

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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. Alkermes, 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 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 and diversion potential and other policy considerations, may choose to set the aggregate *hydrocodone* quota lower than the total amount requested by the companies. Alkermes is permitted to petition the DEA to increase the annual aggregate quota after it is initially established, but there is no guarantee that the DEA would act favorably upon such a petition. Our procurement quota of *hydrocodone* may not be sufficient to meet any future clinical development needs or commercial demand if we receive regulatory approval for Zohydro. Any delay or refusal by the DEA in establishing the procurement quota or a reduction in our quota for *hydrocodone* or a failure to increase it over time as we anticipate could delay or stop any additional clinical development of Zohydro, if required, 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

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elsewhere in this Annual Report on Form 10-K regarding FDA approval in the United States, as well as other risks. For example, legislation analogous to Section 505(b)(2) of the FFDCA in the United States does not exist in other countries. In territories where data is not freely available, we or our partners may not have the ability to commercialize our products without negotiating rights from third parties to refer to their clinical data in our regulatory applications, which could require the expenditure of significant additional funds. We, Desitin, or any potential partner may be unable to obtain rights to the necessary clinical data and may be required to develop our own proprietary safety effectiveness dossiers. Desitin submitted a Marketing Authorization Application for Sumavel DosePro to the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)) in Germany, the reference member state, through the Decentralized Procedure in October 2009, following completion of a European pivotal bioequivalence trial comparing needle-free Sumavel DosePro to a traditional needle-based autoinjector, Imigran-Inject, the European brand of Imitrex STATdose. However, regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others.

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

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;

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

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

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

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

new requirements to report certain financial arrangements with physicians and others, including reporting any transfer of value made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year beginning in 2012, with reporting starting in 2013;

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

a licensure framework for follow-on biologic products;

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

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

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

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

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coverage and reimbursement from third-party payors at the federal, state and private levels. Third-party payors include governmental programs such as Medicare or Medicaid, private insurance plans and managed care plans. These third-party payors may deny coverage or reimbursement for a product or therapy in whole or in part if they determine that the product or therapy was not medically appropriate or necessary. Also, third-party payors have attempted to control costs by limiting coverage through the use of formularies and other cost-containment mechanisms and the amount of reimbursement for particular procedures or drug treatments.

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

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

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

The FDA provides guidelines with respect to appropriate promotion and continuing medical and health education activities. Although we endeavor to follow these guidelines, the FDA or the Office of the Inspector General: 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

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other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

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

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

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

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

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

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

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

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Risks Related to Intellectual Property

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

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

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

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

The patent positions of pharmaceutical, biopharmaceutical and medical device companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in patents in these fields has emerged to date in the United States. There have been recent changes regarding how patent laws are interpreted, and both the

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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;
- 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

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reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If our confidential or proprietary information is divulged to or acquired by third parties, including our competitors, our competitive position in the marketplace will be harmed and our ability to successfully penetrate our target markets could be severely compromised.

If any of our owned or in-licensed patents are found to be invalid or unenforceable, or if we are otherwise unable to adequately protect our rights, it could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Likewise, our patents covering certain technology used in our DosePro device are expected to expire on various dates from 2014 through 2026 and the patents licensed to us by Alkermes are expected to expire in 2019. As of December 31, 2011, our patent portfolio included seven issued U.S. patents, three pending U.S. patent applications, 39 issued foreign patents and five 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 Alkermes or Durect decides not to commence or continue any action relating to the defense of the patents they have licensed to us, they are required to notify us and we have the right to initiate proceedings after receiving their notice. Such proceedings will require the assistance of Alkermes or Durect, as applicable, and we have limited control over the amount or timing of resources Alkermes or Durect devotes on our behalf or the priority they place on enforcing these patent rights.

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

We are a party to a license agreement with Alkermes, pursuant to which we license key intellectual property for Zohydro. 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.

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

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

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

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

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owned or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding declared by the PTO to determine priority of invention in the United States. If another party has reason to assert a substantial new question of patentability against any of our claims in our owned and in-licensed U.S. patents, the third party can request that the PTO reexamine the patent claims, which may result in a loss of scope of some claims or a loss of the entire patent. In addition to potential infringement claims, interference and reexamination proceedings, we may become a party to patent opposition proceedings in the European Patent Office where either our patents are challenged, or we are challenging the patents of others. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if the other party had independently arrived at the same or similar invention prior to our own or, if applicable, our licensor s invention, resulting in a loss of our U.S. patent position with respect to such inventions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our device and/or product candidates and/or proprietary technologies infringe their intellectual property rights. These lawsuits are costly and could adversely affect our results of operations and divert the attention of managerial and technical personnel. There is a risk that a court would decide that we or our commercialization partners are infringing the third party s patents and would order us or our partners to stop the activities covered by the patents. In addition, there is a risk that a court will order us or our partners to pay the other party damages for having violated the other party s patents.

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

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

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management s attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product at issue infringes on or violates the third party s rights, and if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner s attorneys fees;
- a court prohibiting us from selling or licensing the product unless the third party licenses its product rights to us, which it is not required to do;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and/or grant cross-licenses to intellectual property rights for our products; and
- redesigning our products or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

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.

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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, Alkermes is obligated to maintain our in-licensed patents in the United States under our license agreement. Should Alkermes fail to pursue maintenance of our licensed patents and patent applications, Alkermes is obligated to notify us and, at that time, we will be granted an opportunity to maintain the prosecution and avoid withdrawal, cancellation, expiration or abandonment of the licensed U.S. patents and applications. For the patents and patent applications related to Relday, Durect is obligated to maintain certain of our in-licensed patents on a worldwide basis, using commercially reasonable efforts, under our license agreement. Should Durect fail to pursue maintenance of certain of those licensed patents and patent applications, Durect is obligated to notify us and, at that time, we will be granted an opportunity to maintain the prosecution and avoid withdrawal, cancellation, expiration or abandonment of those licensed patents and applications.

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

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

As is common in the device, biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other device, biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that

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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 recently experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. Since the commencement of trading in connection with our initial public offering in November 2010, the publicly traded shares of our common stock have themselves experienced significant price and volume fluctuations. During the year ended December 31, 2011, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price of $1.31 to a high sale price of $6.90. 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:

- our ability to increase the productivity of or expand our sales force and/or partner with a new co-promotion partner once our co-promotion agreement with Astellas terminates in March 2012;
- FDA or international regulatory actions, including whether and when we receive regulatory approval for Zohydro or any of our other product candidates;
- the development status of Relday or any of our other product candidates, including the results from our clinical trials;
- other regulatory developments, including the FDA s potential grant of regulatory exclusivity to a competitor who receives FDA approval before us for an extended-release *hydrocodone* product, which could significantly delay our ability to receive approval for Zohydro;
- 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;

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

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

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

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

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

Our quarterly operating results may fluctuate significantly.

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

fluctuations in the quarterly revenues of Sumavel DosePro, including fluctuations resulting from the termination of our co-promotion agreement with Astellas in March 2012, and from our distributors inventory management practices and buying patterns;

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

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

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

results of clinical trials for Zohydro, Relday or any other of our product candidates;

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

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

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

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

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

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

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. As of December 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.

Our executive officers and directors and their affiliates together control approximately 44.3% of our outstanding common stock, assuming no exercise of outstanding options or warrants. Four of our non-employee directors are, or are representatives designated by, significant stockholders and two of our directors are executive officers. As a result, these stockholders will collectively be able to significantly influence and may be able to control all matters requiring approval of our stockholders, including the election of directors and approval of significant corporate transactions such as mergers, consolidations or the sale of all or substantially all of our assets. The concentration of ownership may delay, prevent or deter a change in control of our company even when such a change may be in the best interests of some stockholders, impede a merger, consolidation, takeover

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or other business combination involving us, or could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might adversely affect the prevailing market price of our common stock.

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

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

Persons who were our stockholders prior to the sale of shares in our initial public offering in November 2010 continue to hold a substantial number of shares of our common stock that they are able to sell in the public market, subject in some cases to certain legal restrictions. Significant portions of these shares are held by a small number of stockholders. If these stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. The perception in the market that these sales may occur could also cause the trading price of our common stock to decline. As of December 31, 2011, we had 65,368,792 shares of common stock outstanding. Of these shares, approximately 36,456,375 are freely tradable, without restriction, in the public market.

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

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

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

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

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by a majority of the total number of authorized directors;

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

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

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

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

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

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

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

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

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the Nasdaq Stock Market, or Nasdaq, that impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and financial condition. In addition, on July 21, 2010, the Dodd-Frank Wall Street Reform and Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation-related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas. The requirements of these rules

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and regulations have increased and will continue to increase our legal and financial compliance costs, make some activities more difficult, time-consuming or costly and may also place considerable strain on our personnel, systems and resources. Our management and other personnel have devoted and will continue to devote a substantial amount of time to these new compliance initiatives. In addition, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. Ensuring that we have adequate internal financial and accounting controls and procedures in place is a costly and time-consuming effort that needs to be re-evaluated frequently. In particular, commencing in fiscal 2011, we performed system and process evaluation and testing of our internal controls over financial reporting which allowed management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act, or Section 404. Our future testing may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. We expect to incur significant expense and devote substantial management effort toward ensuring compliance with Section 404. Pursuant to Section 404(c) of the Sarbanes-Oxley Act, our independent registered public accounting firm will 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.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

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 April 2012. We intend to enter into a new operating lease for office facilities in San Diego in early 2012.

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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.

Item 3. Legal Proceedings

We are not currently a party to any legal proceedings.

Item 4. Mine Safety Disclosures

Not Applicable.

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PART II

Item 5. Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock has been traded on the Nasdaq Global Market since November 23, 2010 under the symbol ZGNX. Prior to such time, there was no public market for our common stock. The following table sets forth the high and low sales price of our common stock, as reported by the Nasdaq Global Market for the period indicated:

	High	Low
Year Ended December 31, 2011		
Fourth Quarter	2.43	1.31
Third Quarter	5.11	1.83
Second Quarter	5.14	3.54
First Quarter	6.90	3.50
Year Ended December 31, 2010		
Fourth Quarter (beginning November 23, 2010)	6.24	3.80
Third Quarter	N/A	N/A
Second Quarter	N/A	N/A
First Quarter	N/A	N/A

Holders of Common Stock

As of March 1, 2012, there were approximately 39 holders of record of our common stock.

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Performance Graph

The following stock performance graph illustrates a comparison of the total cumulative stockholder return on our common stock since November 23, 2010, which is the date our common stock first began trading on the NASDAQ Global Market, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of $100 on November 23, 2010, and that all dividends were reinvested. The comparisons in the graph are required by the Securities and Exchange Commission and are not intended to forecast or be indicative of possible future performance 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 and SVB prohibit us from paying dividends on our common stock.

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Equity Compensation Plan Information

The following table summarizes securities available under our equity compensation plans as of December 31, 2011 (in thousands, except per share data).

	Weighted average per share exercise price of stock options	Shares issuable upon exercise of outstanding stock options	Shares issuable upon vesting of outstanding restricted stock units	Total shares issuable under current outstanding awards	Number of securities available for future issuance
Equity compensation plans approved by security holders:					
2006 Equity Incentive Plan	$ 3.32	1,340,546	0	1,340,546	0
2010 Equity Incentive Plan	$ 4.37	2,176,163	0	2,176,163	1,103,579
Total Equity Incentive Plans		3,516,709	0	3,516,709	1,103,579
2010 Employee Stock Purchase Plan		0	0	0	577,852
Total Equity compensation plans approved by security holders		3,516,709	0	3,516,709	1,681,431
Equity compensation plans not approved by security holders:					

None.

Recent Sales of Unregistered Securities

During the year ending December 31, 2011, we issued and sold the following unregistered securities:

1. In June 2011, as consideration for amending a debt facility, we issued warrants to two lenders exercisable for an aggregate of 26,455 shares of our common stock at an exercise price of $3.78 per share.

2. In July 2011, in connection with the Cowen Financing agreement, we issued and sold an aggregate of 388,601 shares of our common stock at a price of $3.86 per share to a lender. As consideration for entering into the Cowen Financing agreement, we also issued to the lender a warrant exercisable for an aggregate of 225,000 shares of our common stock at an exercise price of $9.00 per share.

3. From January 1, 2011 through December 31, 2011, we granted stock options to purchase 2,200,450 shares of our common stock at a weighted average exercise price of $4.37 per share to our employees, consultants and directors under our 2010 equity incentive plan.

The issuance of securities described above in paragraphs (1) and (2) were exempt from registration under the Securities Act of 1933, as amended, in reliance on Section 4(2) of the Securities Act of 1933, as amended, and Regulation D promulgated thereunder, as transactions by an issuer not involving any public offering. The purchasers of the securities in these transactions represented that they were accredited investors or qualified institutional buyers and they were acquiring the securities for investment only and not with a view toward the public sale or distribution thereof. Such purchasers received written disclosures that the securities had not been registered under the Securities Act of 1933, as amended, and that any resale must be made pursuant to a registration statement or an available exemption from registration. All purchasers either received adequate financial statement or non-financial statement information about the registrant or had adequate access, through their relationship with the registrant, to financial statement or non-financial statement information about the registrant. The sale of these securities was made without general solicitation or advertising.

The issuance of securities described above in paragraph (3) was exempt from registration under the Securities Act of 1933, as amended, in reliance on Rule 701 of the Securities Act of 1933, as amended, pursuant to compensatory benefit plans approved by the registrant s board of

directors.

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All certificates representing the securities issued in these transactions described in this Item included appropriate legends setting forth that the securities had not been offered or sold pursuant to a registration statement and describing the applicable restrictions on transfer of the securities. There were no underwriters employed in connection with any of the transactions set forth above.

Issuer Repurchases of Equity Securities

None.

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Item 6. Selected Financial Data.

The following table summarizes certain of our selected financial data. The selected financial data for the years ended December 31, 2011, 2010, 2009, 2008 and 2007 have been derived from our audited financial statements, of which the consolidated statement of operations data for the three fiscal years ending December 31, 2011, 2010 and 2009 and consolidated balance sheet data as of December 31, 2011 and 2010 are included elsewhere in this Annual Report on Form 10-K. 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 thereto and Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K. Amounts are in thousands, except per share amounts.

	Year Ended December 31,				
	2011	2010	2009	2008	2007
	(In Thousands, Except Per Share Amounts)				
Statement of Operations Data					
Revenue:					
Net product revenue	$ 30,411	$ 19,069	$ 0	$ 0	$ 0
Contract revenue	7,165	4,373	0	0	0
Total revenue	37,576	23,442	0	0	0
Operating expenses:					
Cost of sales	19,293	12,846	0	0	0
Royalty expense	1,205	843	0	0	0
Research and development	33,043	28,643	21,438	33,910	24,329
Selling, general and administrative	60,459	51,270	14,102	11,820	4,725
Total operating expenses	114,000	93,602	35,540	45,730	29,054
Loss from operations	(76,424)	(70,160)	(35,540)	(45,730)	(29,054)
Other income (expense):					
Interest income	37	5	10	696	927
Interest expense	(7,644)	(10,013)	(9,188)	(1,718)	(377)
Change in fair value of warrant liability	445	6,725	(755)	1,119	(107)
Change in fair value of embedded derivatives	(240)	0	0	0	906
Other income (expense)	(86)	(111)	(416)	63	25
Total other income (expense)	(7,488)	(3,394)	(10,349)	160	1,374
Loss before income taxes	(83,912)	(73,554)	(45,889)	(45,570)	(27,680)
Provision for income taxes	9	(10)	0	0	0
Net loss	$ (83,903)	$ (73,564)	$ (45,889)	$ (45,570)	$ (27,680)
Deemed dividend for the beneficial conversion on Series A-1 and Series A-2 convertible preferred stock	0	0	0	0	(18,360)
Net loss applicable to common stockholders	$ (83,903)	$ (73,564)	$ (45,889)	$ (45,570)	$ (46,040)
Net loss per share, basic and diluted (1)	$ (1.96)	$ (17.63)	$ (40.97)	$ (52.68)	$ (80.77)
Weighted-average shares outstanding, basic and diluted (1)	42,712	4,173	1,120	865	570

(1) See Note 2 of Notes to Consolidated Financial Statements for an explanation of the method used to calculate net loss per share and the number of shares used in the computation of the net per share amounts.

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	As of December 31,				
	2011	2010	2009	2008	2007
	(In Thousands)				
Balance Sheet Data:					
Cash and cash equivalents and investment securities, available for sale	$ 56,525	$ 49,172	$ 44,911	$ 14,225	$ 43,255
Working capital	36,532	38,626	42,102	3,032	38,836
Total assets	100,640	94,268	74,568	27,625	53,007
Long-term debt, less current portion	42,070	19,934	8,778	15,336	2,870
Convertible preferred stock warrant liability	0	0	5,041	467	259
Convertible preferred stock	0	0	149,312	76,955	76,955
Accumulated deficit	(282,005)	(198,102)	(124,538)	(78,649)	(33,079)
Total stockholders equity (deficit)	9,312	28,734	(122,300)	(77,534)	(32,926)

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Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations.

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 consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. 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 Item 1A Risk Factors and elsewhere in this Annual Report on Form 10-K.

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 116 professionals. Our field sales force of approximately 95 representatives has historically promoted Sumavel DosePro primarily to neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. Our promotional efforts have been complemented by our collaboration with Astellas and approximately 400 of its sales representatives, who have promoted Sumavel DosePro primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists in the United States. Our collaboration with Astellas will terminate on March 31, 2012, at which time we will assume full responsibility for the commercialization of Sumavel DosePro. We have already begun to assume responsibility from Astellas for marketing Sumavel DosePro to selected high-prescribing primary care physicians and other Astellas-targeted physicians and professionals within the Astellas Segment pursuant to a promotion transition plan. We are currently evaluating potential co-promotion partners who could complement our sales force efforts for the commercial sale of Sumavel DosePro. 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.

Our lead product candidate, Zohydro (*hydrocodone* bitartrate) is a 12-hour extended-release formulation of *hydrocodone* without acetaminophen for the treatment of moderate to severe chronic pain requiring around-the-clock opioid therapy. We completed Phase 3 development of Zohydro in 2011, and we expect to submit a New Drug Application, or NDA, for Zohydro to the U.S. Food and Drug Administration, or FDA, early in the second quarter of 2012. We in-licensed exclusive U.S. rights to Zohydro from Alkermes plc (formerly Elan Pharma International Limited) 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 the new product candidate in patients with schizophrenia in 2012 following filing of an investigational new drug application.

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We have experienced net losses and negative cash flow from operating activities since inception, and as of December 31, 2011, had an accumulated deficit of $282.0 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next several years primarily as a result of the expenses incurred in connection with our regulatory filings for Zohydro, any additional required clinical testing for Zohydro, the initiation of clinical development for Relday and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro. As of December 31, 2011, we had cash and cash equivalents of $56.5 million. In addition, under the terms of our amended and restated loan and security agreement with Oxford Finance LLC and Silicon Valley Bank, or the amended Oxford/SVB loan agreement, we deferred principal repayment to February 1, 2012. In July 2011, we entered into a royalty financing transaction with Cowen Royalty, or the Cowen Financing agreement, resulting in net proceeds of $29.5 million to us. Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of December 31, 2011, estimated future product revenues and borrowings available under our $10.0 million revolving credit facility, will be sufficient to fund our operations into the first quarter of 2013. 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, 2011, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern.

Astellas Co-Promotion Agreement

Under our co-promotion agreement with Astellas that we entered into in July 2009, or the co-promotion agreement, Astellas primarily promoted Sumavel DosePro to primary care physicians (including internal medicine, family practice and general practice), OB/GYNs, emergency medicine physicians and urologists, or collectively, the Astellas Segment, in the United States. Our sales force historically promoted Sumavel DosePro primarily to neurologists and other key prescribers of migraine medications, including headache clinics and headache specialists in the United States. We jointly shared in the cost of advertising, marketing and other promotional activities related to the Sumavel DosePro brand and were required to provide minimum levels of sales effort to promote Sumavel DosePro. In December 2011, we entered into an amendment to the co-promotion agreement with Astellas, or the amended co-promotion agreement, whereby the agreement will terminate on March 31, 2012. Under the co-promotion agreement, we were responsible for the manufacture, supply and distribution of all Sumavel DosePro commercial product and were principally responsible for entering into any contracts and other arrangements with third parties regarding the sale of Sumavel DosePro.

Under the terms of the amended co-promotion agreement, we will be required to make two annual tail payments to Astellas, estimated as a total of $5.3 million, calculated as decreasing fixed percentages (ranging from a mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion. The present value of such tail payments was recorded as a long-term liability on the amendment date and is payable in July 2013 and July 2014. The fair value of the tail payments will be accreted through interest expense on a monthly basis through the date of payment. As of December 31, 2011, the long-term tail payment liability was $4.0 million, net of the discount, and there was an immaterial amount of related interest expense recognized during the year ended December 31, 2011. Additionally, beginning in the second quarter of 2012, our sales force will assume full responsibility for the continued marketing of Sumavel DosePro, expanding our focus to include a portion of the high-prescribing primary care physicians previously covered by Astellas under the co-promotion agreement. We expect to seek another co-promotion partner to compliment our sales to promote Sumavel DosePro, if available.

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. We received the entire $20.0 million in

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license and milestone payments from Astellas through December 31, 2010. These proceeds are reflected as $8.5 million and $15.6 million of deferred revenues on our consolidated balance sheets at December 31, 2011 and December 31, 2010, respectively. Beginning with the launch of Sumavel DosePro in January 2010, we began recognizing these proceeds as contract revenues on a ratable basis over 42 months (the original term of the agreement). Upon amendment of the co-promotion agreement on December 20, 2011, the remaining deferred proceeds will be recognized as contract revenues on a ratable basis over 3.4 months (the remaining term of the amended agreement). This acceleration in the recognition of these contract proceeds resulted in the recognition of an additional $0.9 million of contract revenue during the year ended December 31, 2011.

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 through the date of termination. Astellas pays us 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 years ended December 31, 2011 and 2010, we incurred $6.7 million (excluding the $4.0 million tail payments) and $3.7 million, respectively, in service fee expenses. For the years ended December 31, 2011 and 2010, we recognized shared marketing expense of $1.7 million and $3.9 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. For the years ended December 31, 2011 and 2010, the Astellas Segment represented approximately 37.7% and 39.5%, respectively, of our prescription demand, before consideration of the cost of the service fee payable to Astellas for its sales efforts as described above.

Based on third-party data, approximately 86% of the prescription demand in the Astellas Segment was concentrated to a population of approximately 500 physicians, which we believe our sales force will be able to support after our transition plan utilizing our Phase IV data, toolbox and other promotional activities. As such, we do not expect that all of the prescription demand contributed by the Astellas sales force will be foregone as a result of the early termination of the co-promotion agreement. However, in the event we are unsuccessful in transitioning the Astellas Segment to our sales force, our net product sales and financial results could be negatively impacted.

Durect 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. Further, until an NDA for Relday has been filed in the United States, we are obligated to spend no less than $1.0 million in external expenses on the development of Relday in any trailing twelve month period beginning in July 2012. 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. We have incurred $2.7 million in research and development costs payable to Durect, excluding the upfront fee of $2.25 million, for the twelve months ended December 31, 2011.

Revenues

Through the year ended December 31, 2009, we did not generate any product revenues or recognize any contract revenues. During the year ended December 31, 2010, we began recognizing product revenues from sales

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of Sumavel DosePro and through sales by us to 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 years ended December 31, 2011 and 2010 we recognized $30.4 million and $19.1 million, respectively, in net product revenues. For the years ended December 31, 2011 and 2010 we recognized $7.2 million and $4.4 million, respectively, in contract revenues associated with license and milestone payments made to us by Astellas under the co-promotion agreement.

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

Beginning in the third quarter of 2011, we began recognizing Sumavel DosePro product sales at the time title transfers to our customer, and providing for an estimate of future product returns at that time. We believe that our estimated product return allowances for Sumavel DosePro require a high degree of judgment and are subject to change based on our experience and certain quantitative and qualitative factors. Sumavel DosePro currently has a shelf life of 24 months from the date of manufacture. We accept unused product from our customers that are within six months before and up to one year after its expiration date for a credit at the then-current whole acquisition cost, or WAC, reduced by a nominal fee for processing the return. Our initial product inventories reached expiration in 2011.

We have monitored actual return history on an individual product lot basis since product launch. Actual product return experience in 2011 included a disproportionately high amount of returns from a single retail chain. In addition, we have also experienced a high level of returned product from our initial launch stocking initiatives. We may experience higher levels of returns upon the termination of the co-promotion agreement with Astellas on March 31, 2012 due to fall-off of prescription demand in territories that may no longer be supported with direct promotional efforts. We considered these factors as well as the dating of our product at the time of shipment into the distribution channel, prescription trends and changes in the estimated levels of inventory within the distribution channel to estimate our exposure for returned product. Based on our analysis, we increased the estimate for Sumavel DosePro product returns, resulting in an adjustment of $2.2 million, which decreased net product sales in the fourth quarter of 2011. We recorded a total decrease to net product sales of $4.4 million related to actual product and estimated future product returns for the twelve months ended December 31, 2011. Because of the shelf life of Sumavel DosePro and our return policy of issuing credits on returned product that is within six months before and up to one year after its product expiration date, there may be a significant period of time between when the product is shipped and when we issue credits on returned product. Accordingly, we may have to adjust these estimates, which could have an effect on product sales and earnings in the period of adjustments. A 1% increase or decrease in our returns reserve as a percentage of product shipped would have a cumulative financial statement impact of approximately $0.6 million for the year ended December 31, 2011.

In connection with the change in the timing of recognition of product sales, previously reported deferred product revenues of $0.7 million and deferred cost of sales of $0.2 million as of June 30, 2011 have been recognized as product revenue and cost of sales in 2011.

We permit certain wholesale pharmaceutical distributors to purchase limited quantities of product after the announcement of an increase to the WAC of our product and prior to the effectiveness of the increase. In turn, WAC price increases can result in accelerated purchases by wholesalers relative to anticipated retail and prescription demand. The timing of purchases made by wholesale distributors and retail pharmacies are subject to

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fluctuations for these reasons among others. Absent accelerated purchasing by wholesalers or other periodic changes in buying patterns, the wholesale channel has historically contained two to three weeks of product on hand. As of December 31, 2011, wholesale distributors reported approximately three weeks of our product on hand.

In November 2010, Desitin received regulatory approval to market Sumavel DosePro in Denmark and subsequently received approvals in Germany, Sweden, the United Kingdom, Norway and France. 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 maintains 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 Corporation. As such, we recognize revenues for product sales to Desitin upon acceptance of product by Desitin (generally at point of shipment). For the years ended December 31, 2011 and 2010 we recognized $0 and $0.4 million, respectively, in revenue for sales to Desitin. We recognized an immaterial amount of royalty revenues related to the Desitin agreement for the year ended December 31, 2011, and no royalty revenues related to the Desitin agreement for the year ended December 31, 2010.

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 years ended December 31, 2011 and 2010 was $19.3 million and $12.8 million, respectively. Our product gross margin for the years ended December 31, 2011 and 2010 was 36.6% and 32.6%, respectively. Prior to the change in timing of our revenue recognition in the third quarter of 2011, the cost of sales associated with the deferred product revenues were recorded as deferred costs, which were included in inventory, until such time the deferred revenue was recognized. Deferred cost of sales totaled $0 and $1.3 million at December 31, 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 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 years ended December 31, 2011 and 2010, we incurred $1.2 million and $0.8 million, respectively, in royalty expense to Aradigm.

Research and Development Expenses

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

- payments made to Durect for the license to and further development of Relday;
- milestone payments made to Alkermes in connection with development and regulatory milestones of Zohdyro;
- payments made to third-party contract research organizations, or CROs, and investigational sites, which conduct our trials on our behalf, and consultants;
- expenses associated with regulatory submissions, pre-clinical development and clinical trials;

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

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

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

facility, maintenance, depreciation and other related expenses.

We expense all research and development costs as incurred.

In March 2010, we initiated our Phase 3 clinical development program for Zohydro. 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 years ended December 31, 2011 and 2010, we incurred $20.5 million and $20.2 million in third party research and development costs related to Zohydro, respectively.

Relday is currently in the pre-clinical development phase and we plan to initiate clinical development of Relday in 2012. We recognize the costs of pre-clinical work as it is performed. Under the Relday license agreement, Durect is responsible for non-clinical, formulation, chemistry, and manufacturing and controls development for Relday. We paid a non-refundable upfront fee to Durect of $2.25 million in July 2011. In addition, we incurred $2.7 million in research and development costs payable to Durect during the twelve months ended December 31, 2011.

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

	Year Ended December 31,		
	2011	2010	2009
		(In Thousands)	
Research and development expenses:			
Zohydro	$ 20,461	$ 20,174	$ 1,728
Relday	5,066	761	1,150
Sumavel DosePro	1,129	1,672	13,772
Other (1)	6,387	6,036	4,788
Total	$ 33,043	$ 28,643	$ 21,438

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

We expect our research and development costs for 2012 to decrease over amounts incurred in 2011 as we completed the Phase 3 clinical trials for Zohydro in December 2011. In addition, in August 2011 we paid

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Alkermes, from whom we in-licensed exclusive rights to Zohydro in November 2007, a milestone payment in the amount of $0.8 million 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 Alkermes up to $3.75 million in total future milestone payments with respect to Zohydro depending upon the achievement of various development and regulatory events. These future milestone payments include a payment of $1.0 million upon submission of the first NDA to the FDA, which we expect to occur early in the second quarter of 2012, and a payment of $0.8 million upon successful completion of an FDA pre-approval inspection of our manufacturing facility. 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.

While we expect to submit an NDA for Zohydro with the FDA early in the second quarter of 2012, 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 regulatory review of Zohydro;
- the costs, timing and outcome of any additional pre-clinical studies and clinical trials for Zohydro, if required;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the potential for future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development and commercialization plans and capital requirements;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the emergence of competing technologies and products and other adverse marketing developments;
- the effect on our product development activities of actions taken by the FDA or other regulatory authorities; and
- our degree of success in commercializing Zohydro, 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 clinical studies for our early-stage product candidates and manufacturing development for our DosePro technology. We expect to incur research and development costs of approximately $3.0 million to $4.0 million in 2012 for initial clinical studies planned for Relday. We also expect to incur research and development costs of approximately $0.1 million to $0.3 million in 2012 for the development of the Sumavel DosePro 4 mg line extension and sound enhancement of the DosePro technology.

Selling, General and Administrative Expenses

During the years ended December 31, 2011 and 2010, our selling expenses, which includes sales and marketing costs, including salaries and benefits of sales and marketing management and sales representatives,

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shared marketing and advertising costs under our co-promotion agreement with Astellas, sample product costs, and consulting fees. During the year ended December 31, 2009, prior to our product launch, our selling expenses consisted primarily of salaries, benefits, consulting fees, costs of obtaining prescription and market data and market research studies related to preparation for the launch of Sumavel DosePro, including shared marketing and advertising costs under our co-promotion agreement with Astellas. Our selling expenses may further increase in connection with a new co-promotion agreement with another third party.

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

Interest Income

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

Interest Expense

Interest expense consists of interest or revenue interest payments incurred in connection with our $30.0 million Cowen Financing agreement, our $25.0 million loan and security agreement and $10.0 million revolving credit facility with Oxford and SVB, the $4.5 million borrowed under our loan and security agreement with General Electric Capital Corporation, or GE Capital, and non-cash interest expense associated with amortization of debt discount and debt issuance costs and the estimated cost of revenue interest payments calculated under the effective interest method. The outstanding principal balance of the GE Capital agreement was repaid in full on June 30, 2011.

As a result of a full year of borrowing under our $30.0 million Cowen Financing agreement that we entered into in July 2011, and the recognition of imputed interest from the two annual tail payments to Astellas related to the termination of our co-promotion agreement, we expect that interest expense related to debt service will increase over 2011 levels.

Change in Fair Value of Warrant Liability

Change in fair value of warrant liability represents non-cash (expense) income associated with changes in the fair value of the warrants issued to purchase common and/or preferred stock.

In connection with our initial public offering in November 2010, the liability reflected on our consolidated balance sheet on December 31, 2009 for convertible preferred stock warrants has been 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.

Change in fair value of warrant liability for the year ended December 31, 2011 represents non-cash income associated with the changes in the fair value of the warrants to purchase common stock issued in connection with our Cowen Financing agreement.

Change in Fair Value of Embedded Derivatives

Change in fair value of embedded derivatives represents non-cash expense from changes in the fair value of the embedded derivatives associated with the Cowen Financing agreement.

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. pounds sterling and the Euro.

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Provision for Income Taxes

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

Net Operating Loss and Tax Credit Carryforwards

As of December 31, 2011, we had available federal and state net operating loss carryforwards of approximately $93.0 million and $117.4 million, respectively. If not utilized, the net operating loss carryforwards will begin expiring in 2026 for federal tax purposes and 2020 for state tax purposes. As of December 31, 2011, we had federal and state research and development tax credit carryforwards of approximately $0.3 million and $1.7 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 that could be utilized annually in the future to offset taxable income. 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. Any such annual limitation may significantly reduce the utilization of the net operating loss carryforwards before they expire.

We completed an analysis under Internal Revenue Service Code, or IRC, Sections 382 and 383 to determine if our net operating loss carryforwards and research and development credits are limited due to a change in ownership. We determined that as of December 31, 2010 we had one ownership change, which occurred in August 2006 upon the issuance of the Series A-1 convertible preferred stock. As a result of this ownership change, we reduced our net operating loss carryforwards by $1.9 million and research and development income tax credits by $8,000. We determined that as of December 31, 2011, we had a second ownership change, as defined by IRC Section 382 and 383, which occurred in September 2011 upon the issuance of stock. As a result of this second ownership change, we reduced our federal and state net operating loss carryforwards as of December 31, 2010 by $83.5 million and $46.2 million, respectively, and research and development income tax credits as of December 31, 2010 by $2.2 million. Pursuant to IRC Section 382 and 383, use of the our net operating loss and research and development income tax credit carryforwards may be limited in the event of a future cumulative change in ownership of more than 50% within a three-year period. Any such limitations, whether as the result of prior or future offerings of our common stock or sales of common stock by our existing stockholders, could have an adverse effect on our consolidated results of operations in future years. 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.

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 is required to deliver a report that assesses the effectiveness of our internal control over financial reporting. Pursuant to Section 404(c) of the Sarbanes-Oxley Act, our independent registered public accounting firm will 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.

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

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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 Annual Report on Form 10-K, 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 revenue from the sale of Sumavel DosePro and from license fees and milestones earned on collaborative arrangements. Revenue is recognized when: (i) persuasive evidence that an arrangement exists, (ii) delivery has occurred and title has passed, (iii) the price is fixed or determinable and (iv) collectability is reasonably assured. Revenue from sales transactions where the buyer has the right to return the product is recognized at the time of sale only if (i) our price to the buyer is substantially fixed or determinable at the date of sale, (ii) the buyer has paid us, or the buyer is obligated to pay us and the obligation is not contingent on resale of the product, (iii) the buyer s obligation to us would not be changed in the event of theft or physical destruction or damage of the product, (iv) the buyer acquiring the product for resale has economic substance apart from that provided by us, (v) we do not have significant obligations for future performance to directly bring about resale of the product by the buyer, and (vi) the amount of future returns can be reasonably estimated.

Product Revenue

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

Beginning in the third quarter of 2011, we began recognizing Sumavel DosePro product sales at the time title transfers to our customer, and providing for an estimate of future product returns at that time. We believe that our estimated product return allowances for Sumavel DosePro require a high degree of judgment and are subject to change based on our experience and certain quantitative and qualitative factors. Sumavel DosePro currently has a shelf life of 24 months from the date of manufacture. We accept unused product from our customers that are within six months before and up to one year after its expiration date for a credit at the then-current WAC, reduced by a nominal fee for processing the return. Our initial product inventories reached expiration in 2011.

We have monitored actual return history on an individual product lot basis since product launch. Actual product return experience in 2011 included a disproportionately high amount of returns from a single retail chain. In addition, we have also experienced a high level of returned product from our initial launch stocking initiatives. We may experience higher levels of returns upon the termination of the co-promotion agreement with Astellas on March 31, 2012 due to fall-off of prescription demand in territories that may no longer be supported with direct promotional efforts. We considered these factors as well as the dating of our product at the time of shipment into the distribution channel, prescription trends and changes in the estimated levels of inventory within the distribution channel to estimate our exposure for returned product. Based on our analysis, we increased the estimate for Sumavel DosePro product returns resulting in an adjustment of $2.2 million, which decreased net product sales in the fourth quarter of 2011. We recorded a total decrease to net product sales of $4.4 million

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related to actual product returns and estimated future product returns for the twelve months ended December 31, 2011. Because of the shelf life of Sumavel DosePro and our return policy of issuing credits on returned product that is within six months before and up to one year after its product expiration date, there may be a significant period of time between when the product is shipped and when we issue credits on returned product. Accordingly, we may have to adjust these estimates, which could have an effect on product sales and earnings in the period of adjustments. A 1% increase or decrease in our returns reserve as a percentage of product shipped would have a cumulative financial statement impact of approximately $0.6 million for the year ended December 31, 2011.

In connection with the change in the timing of recognition of product sales, previously reported deferred product revenues of $0.7 million and deferred cost of sales of $0.2 million as of June 30, 2011 have been recognized as product revenue and cost of sales in 2011.

We permit certain wholesale pharmaceutical distributors to purchase limited quantities of product after the announcement of an increase to the WAC of our product and prior to the effectiveness of the increase. In turn, WAC price increases can result in accelerated purchases by wholesalers relative to anticipated retail and prescription demand. The timing of purchases made by wholesale distributors and retail pharmacies are subject to fluctuations for these reasons among others. Absent accelerated purchasing by wholesalers or other periodic changes in buying patterns, the wholesale channel has historically contained two to three weeks of product on hand. As of December 31, 2011, wholesale distributors reported approximately three weeks of our product on hand.

Sumavel DosePro is also sold to third parties that license the rights to market and sell the product in territories outside of the United States. Under these arrangements, Sumavel DosePro is sold at a specified transfer price with the right of return available for damaged goods upon receipt or in the event of a recall. All risk for retail and wholesaler fees and discounts, collectability of customer receivables, customer returns and expiration of the product remain with the licensee. As such, we recognize revenues for product sales under license arrangements upon acceptance of the product (generally at point of shipment). We also receive royalties on net sales of Sumavel DosePro at a predetermined rate as a pass through of royalties payable to Aradigm. For the years ended December 31, 2011 and 2010 we recognized $0 and $0.4 million, respectively, in revenue for sales to third parties that license the rights to market and sell the product in territories outside of the Unites States. We recognized an immaterial amount of royalty revenues related to these third party sales for the year ended December 31, 2011, and no royalty revenues for the year ended December 31, 2010.

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.

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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.

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 $0.5 million at December 31, 2011 and $0.4 million at December 31, 2010. We recognized $2.9 million and $1.4 million in reductions to product revenues related to these discounts for the year ended December 31, 2011 and 2010, respectively. 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 $1.7 million at December 31, 2011 and $0.5 million at December 31, 2010. We recognized $5.0 million and $1.0 million in reductions to product revenues related to these sales allowances for the years ended December 31, 2011 and 2010, respectively. 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

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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 product sales, based on operating results for the year ended December 31, 2011, would have resulted in an increase or decrease to net product sales for that period of approximately $2.1 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.

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 sales under license arrangements have no right of return).

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. We received payments for the entire $20.0 million from Astellas through December 31, 2010.

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 on the date of termination. 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 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 co-promotion agreement. 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.

In December 2011, we amended our co-promotion agreement with Astellas. Under the terms of the amendment, the co-promotion agreement will terminate in March 2012, and beginning in the second quarter of

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2012, we will assume full responsibility for the continued commercialization of Sumavel DosePro. In accordance with accounting guidance for revenue arrangements with multiple deliverables, we determined that there was no change in the deliverables or units of accounting identified in the co-promotion agreement upon amendment. We further concluded that the remaining deferred revenue balance of $9.6 million (as of the date of the amendment) requires recognition ratably over the amended term of the co-promotion agreement which is the date of amendment through termination on March 31, 2012. This acceleration in the recognition of the deferred contract revenue resulted in the recognition of an additional $0.9 million of contract revenue during the twelve months ended December 31, 2011.

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.

Warrants for Common Stock and/or Convertible Preferred Stock

We classify common stock warrants and convertible preferred stock warrants that contain covenants where compliance with such covenants may be outside of our control as short-term liabilities on the consolidated balance sheet. We record the warrant liability at fair value and adjust the carrying value of these common and/or convertible preferred stock warrants to their estimated fair value at each reporting date with the increases or decreases in the fair value of such warrants recorded as change in fair value of warrant liability in the consolidated statement of operations.

Embedded Derivatives

Embedded derivatives are recorded in the consolidated balance sheet at fair value. We adjust the carrying value of the embedded derivatives to their estimated fair value at each reporting date with the increases or decreases in the fair value of such embedded derivatives recorded as change in fair value of embedded derivatives in the consolidated statement of operations. We measure the fair value of the embedded derivatives using various discounted cash flow valuation models.

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-

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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 years ended December 31, 2011, 2010 and 2009.

Results of Operations

Comparison of year ended December 31, 2011 and 2010

Revenue. Revenue for the year ended December 31, 2011 was $37.6 million and $23.4 million for the year ended December 31, 2010. Product revenue for the years ended December 31, 2011 and 2010 was $30.4 million and $19.1 million, respectively. During the third quarter of 2011, we began to recognize net product sales upon the shipment of product to wholesale pharmaceutical distributors and retail pharmacies because we had developed sufficient historical experience and data to reasonably estimate future returns of Sumavel DosePro. Prior to the third quarter of 2011, we recognized product revenue based on product dispensed to patients as estimated by independent third party data providers, which amounts were recorded net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs, as applicable. As a result, product revenue for the first six months of 2011 and for the twelve months ended 2010 represents product revenue based on product dispensed to patients net of product-related discounts and allowances, as applicable, with the six months ended December 31, 2011 consisting of Sumavel DosePro shipped to wholesale distributors and retail pharmacies, net of product-related discounts, allowances and product returns, as applicable.

The aggregate $11.3 million, or 59%, increase in net product revenue is primarily due to an increase in prescription demand from the initial launch of Sumavel DosePro in late January 2010, offset by the establishment of a product returns reserve. Net product revenues are impacted by the volume of product sold to our customers and the average selling price of those sales. While prescription volume increased in 2011 over 2010, the increases were offset by a decrease in our average selling price of Sumavel DosePro of 3%. This decrease in our average selling price in 2011 over 2010 was driven by an increase of $5.5 million in product sales allowances through increased third-party payor contracting/rebates and patient incentives. In addition, net product revenues were negatively impacted by $4.4 million in charges related to actual and estimated returned product. In addition, previously reported deferred product revenues of $0.7 million were recognized within net product sales in 2011.

Contract revenue for the years ended December 31, 2011 and 2010 consists of $7.2 million and $4.4 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 2010 reflects a pro-rata amount of amortization of license fees and milestones as compared to the contract revenues in 2011, which reflects the full amortization of all license fees and milestone payments. On December 20, 2011 we amended our co-promotion agreement with Astellas whereby the agreement will terminate on March 31, 2012, rather than the initial termination date of June 30, 2013. Based upon this revised termination date, all deferred contract revenue will be recognized ratably on an accelerated basis, from the date of the amendment through March 31, 2012. This acceleration resulted in the recognition of an additional $0.9 million of contract revenue during the year ended December 31, 2011.

Cost of Sales. Cost of sales for the year ended December 31, 2011 was $19.3 million and $12.8 million for the year ended December 31, 2010. Product gross margin for the year ended December 31, 2011 was 36.6% compared to 32.6% for the year ended December 31, 2010. Cost of sales represents the cost of Sumavel DosePro units recognized as net product revenues in the period and the impact of underutilized production capacity and other manufacturing variances. The improvement in product gross margin of 4.0% was primarily a result of 59% increased volume of Sumavel DosePro product sales in 2011 as compared to 2010. This improvement was offset by a decrease in the production requirements in 2011 resulting in an increase in excess capacity charges based on

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an average 64% utilization level of our contract manufacturing organizations as compared to an average 72% utilization level in 2010. In 2010, we produced product to meet estimated demand requirements, sample initiatives and for the establishment of certain safety stock levels of Sumavel DosePro on hand, which resulted in higher utilization of our contract manufacturing facilities. We maintain certain lead times ranging from six to nine months for our production activities and therefore we may not be able to make significant near-term adjustments to production levels in response to changes in product demand.

Our current production capacity supports current levels of sample and prescription demand to ensure adequate safety 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 underutilize our production capacity. In addition, as we periodically adjust production levels to manage our inventory levels, we may incur excess capacity charges which will negatively impact our gross margins.

Royalty Expense. Royalty expense increased to $1.2 million for the year ended December 31, 2011 from $0.8 million for the year ended December 31, 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 $0.4 million increase in royalty expense is primarily due to the increase in sales.

Research and Development Expenses. Research and development expenses increased to $33.0 million for the year ended December 31, 2011 compared to $28.6 million for the year ended December 31, 2010. This increase of $4.4 million primarily was due to:

- an increase of $2.0 million as a result of the one-time non-refundable upfront license fee paid to Durect in July 2011 upon execution of the Relday license agreement;
- an increase of $2.1 million in research and development costs related to the pre-clinical studies and formulation and stability testing for Relday;
- an increase of $0.8 million as a result of a milestone payment to Alkermes in connection with the completion of Study 801 of the Zohydro Phase 3 clinical trials;
- an increase of $0.8 million in manufacturing development expenses related to the Sumavel DosePro 4 mg line extension and sound enhancement projects for the DosePro technology; and
- an increase of $0.2 million in other development expenses primarily related to the development of our other product candidates and costs related to our employee and infrastructure resources that are not tracked on a program-by-program basis; offset by
- a decrease of $1.2 million in research and development costs primarily resulting from the completion of the Phase 4 open-label study for Sumavel DosePro in 2010; and
- a decrease of $0.5 million in third party research and development costs related to the Phase 3 clinical trials for Zohydro, which were initiated in March 2010 and completed in December 2011.

Selling, General and Administrative Expenses. Selling, general and administrative expenses increased to $60.5 million for the year ended December 31, 2011 compared to $51.3 million for the year ended December 31, 2010. Selling expenses were $47.7 million for the year ended December 31, 2011 compared to $42.3 million for the year ended December 31, 2010. General and administrative expenses were $12.8 million for the year ended December 31, 2011 compared to $9.0 million for the year ended December 31, 2010. The increase of $9.2 million in selling, general and administrative expenses primarily was due to:

an increase of $5.4 million in sales and marketing expense primarily as a result of $3.0 million in increased service fees payable to Astellas from higher product revenues and an additional $4.0 million

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in accrued tail payments associated with the termination of the co-promotion agreement, $1.0 million increase in sales force costs due to an increase in the average number of sales representatives, $0.7 million increase in advertising and promotional efforts, offset by a $3.3 million decrease in sampling efforts; and

an increase of $3.8 million of general and administrative expenses primarily as a result of a $2.5 million increase in professional service related costs, such as legal, accounting and advisory services, insurance premiums, investor relations services and directors fees that we incur for operating as a public company. In addition, we experienced an increase of $1.2 million in non-cash stock-based compensation charges.

Interest Income. Interest income increased to $37,000 for the year ended December 31, 2011 compared to $5,000 for the year ended December 31, 2010. This increase of $32,000 was due primarily to the increase in average cash and cash equivalent balances.

Interest Expense. Interest expense decreased to $7.6 million for the year ended December 31, 2011 compared to $10.0 million for the year ended December 31, 2010. The decrease of $2.4 million primarily was due to:

a decrease of $4.7 million related to a non-cash gain from conditional Series B warrants that expired unexercised upon the completion of our initial public offering in November 2010;

a decrease of $0.6 million in the non-cash amortization of debt issuance and debt discount costs in connection with the $25.0 million amended Oxford/SVB loan agreement; and

a decrease of $0.3 million in interest expense related to 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; offset by

an increase of $1.2 million in revenue interest payments related to the $30.0 million borrowed from Cowen Royalty and $1.4 million in accrued non-cash interest expense based on our estimate of future revenue interest payments on this facility; and

an increase of $0.6 million in interest expense due to higher debt balances associated with the amended Oxford/SVB loan agreement.

Change in Fair Value of Warrant Liability. Change in fair value of warrant liability resulted in $0.4 million of non-cash income during the year ended December 31, 2011 compared to $6.7 million of non-cash income for the year ended December 31, 2010. The income recognized in 2011 related to the change in fair value of warrant liability established in connection with the Cowen Financing agreement in July 2011. The change in fair value of warrant liability in 2010 was due to the decrease in the fair value of the preferred stock warrants upon their conversion to warrants of common stock in connection with the initial public offering in November 2010.

Change in Fair Value of Embedded Derivatives. Change in fair value of embedded derivatives resulted in $0.2 million of expense during the year ended December 31, 2011, which was due to the change in fair value of the embedded derivatives associated with the Cowen Financing agreement in July 2011.

Other Income (Expense). Other income (expense) was $0.1 million of expense for each of the years ended December 31, 2011 and 2010. Any changes in other income (expense) were primarily related to foreign currency transaction gains and 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

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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, the United Kingdom, Norway and France. 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 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 a 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 $35.0 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,

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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 $2.2 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:

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

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; offset by

an increase of $4.7 million in amortization of debt discount costs in connection with the issuance of $15.0 million of convertible promissory notes 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 entered into in June 2008 and amended in July and October 2010;

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 amended in July and October 2010; and

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.

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 change in fair value of the Series A-1, Series A-2 and Series B convertible preferred stock. This change 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 the initial public offering. 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. pounds sterling.

Liquidity and Capital Resources

We have experienced net losses and negative cash flow from operations since inception, and as of December 31, 2011, had an accumulated deficit of $282.0 million, and we expect our losses to continue for at least the next several years as a result of the expenses incurred in connection with our regulatory filings for Zohydro, any additional required clinical testing for Zohydro, the initiation of clinical development for Relday and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro.

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As of December 31, 2011, we had cash and cash equivalents of $56.5 million. 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 the Cowen Financing agreement, 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. Further, in September 2011, we issued and sold a total of 30,000,000 shares of common stock in a follow-on public offering, with 711,566 additional shares issued upon the exercise of the underwriters option to purchase shares in October 2011, for aggregate net proceeds of $57.9 million.

Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of December 31, 2011, together with estimated future product revenue and borrowings available under our $10.0 million revolving credit facility, will be sufficient to fund our operations into the first quarter of 2013. We will need to obtain additional capital to finance our operations beyond that point or possibly earlier. We intend to raise additional capital through public or private equity offerings, debt financings, receivables financings or through collaborations or partnerships with other companies. If we are unsuccessful in raising additional required funds, we may be required to significantly delay, reduce the scope of or eliminate one or more of our development programs or our commercialization efforts, or cease operating as a going concern. We also may be required to relinquish, license or otherwise dispose of rights to product candidates or products that we would otherwise seek to develop or commercialize ourselves on terms that are less favorable than might otherwise be available.

In its report on our consolidated financial statements for the year ended December 31, 2011, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern. A going concern opinion means, in general, that our independent registered public accounting firm has substantial doubt about our ability to continue our operations without continuing infusions of capital from external sources and this opinion could impair our ability to finance our operations through the sale of debt or equity securities or commercial bank loans. 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 December 31, 2011, we received aggregate net cash proceeds of approximately $274.8 million from the sale of shares of our preferred and common stock, including the following recent financing transactions:

- 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;
- 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 overallotment option, for aggregate net proceeds of $51.7 million;
- in July 2011, we entered into the Cowen Financing agreement pursuant to which we sold 388,601 shares of our common stock, resulting in $1.4 million of net proceeds; and
- in September 2011 and October 2011, we issued and sold a total of 30,711,566 shares of common stock in a follow-on public offering, including shares issued upon the exercise of the underwriters option to purchase shares, for aggregate net proceeds of $57.9 million.

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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. We amended and restated the Oxford loan agreement in July and again in October 2010, and as described below, we entered into an amendment to the Oxford loan agreement in June 2011.

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 Agreement consists of a $25.0 million term loan and a $10.0 million revolving credit facility. The obligations under the amended Oxford/SVB loan agreement are collateralized by our intellectual property (including among other things, copyrights, patents, patent applications, trademarks, service marks and trade secret rights) and personal property (including, among other things, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash).

The 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 not include a going concern qualification in addition to other limitations as defined in the agreement. In March 2012, we obtained a waiver from Oxford and SVB for the breach caused by the receipt of the 2011 audit report from our independent registered public accounting firm, which includes a modification of their standard report for the going concern uncertainty. The agreement also provides that an event of default will occur if, among other customary events of default as defined in the agreement, 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.

The $25.0 million term loan bears an interest rate of 12.06% per annum. Payments consist of monthly interest only payments for the first 18 months followed by principal and interest payments for the subsequent 30 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 January 1, 2014. We have the option to prepay the outstanding balance of the term loan in full subject to certain fees 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 nominal final payment is depending upon when the termination occurs.

On July 18, 2011, we closed the Cowen Financing agreement. Under the terms of the Cowen 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, or collectively, revenue interest, that we may 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 Cowen Financing agreement, our royalty rate will increase to 5.75% in April 2012 in connection with the early termination of the co-promotion agreement with Astellas, with a reversion back to 5% 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.

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

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

Cowen Royalty has the option to terminate the Cowen Financing agreement at its election in connection with a change of control of our company (which includes the sale, transfer, assignment or licensing of our rights in the United States to either Sumavel DosePro or Zohydro), or an event of default (which includes the occurrence of a bankruptcy event or other material adverse change in our business), as defined in the Cowen Financing agreement. Upon such 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 Revenue Interest and principal payments received by Cowen Royalty up to the date of prepayment.

Unless terminated earlier as discussed above, the Cowen Financing agreement terminates on March 31, 2018.

In connection with the Cowen 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 a warrant to purchase 225,000 shares of our common stock at an exercise price of $9.00 per share. We received total net proceeds, after expenses, of $29.5 million from the borrowings under the Cowen Financing agreement and the sale of common stock to Cowen Royalty.

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. Cowen Royalty exercised this right and purchased $1.5 million of shares of our common stock at $2.00 per share in our follow-on public offering completed in September 2011.

We depend in part upon borrowings available under the revolving credit facility provided under the amended Oxford/SVB loan agreement. Any termination of our debt agreements, or any requirement that we repay any of our outstanding term loans or the borrowed amount under the Cowen 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 $56.5 million and $49.2 million at December 31, 2011 and December 31, 2010, respectively.

The following table summarizes our cash flows from (used in) operating, investing and financing activities for the years ended December 31, 2011, 2010 and 2009:

	Year Ended December 31,		
	2011	2010	2009
		(In Thousands)	
Statement of Cash Flows Data:			
Total cash provided by (used in):			
Operating activities	$ (80,471)	$ (71,952)	$ (32,361)
Investing activities	(617)	(3,442)	(2,057)
Financing activities	88,441	79,655	65,104
Increase in cash and cash equivalents	$ 7,353	$ 4,261	$ 30,686

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Operating Activities. Net cash used in operating activities was $80.5 million, $72.0 million and $32.4 million for the years ended December 31, 2011, 2010 and 2009, respectively. Net cash used for the year ended December 31, 2011 primarily reflects the use of $75.9 million for operations (excluding non-cash items), which includes personnel-related costs, research and development costs for Zohydro and Relday, sales and marketing expenses for Sumavel DosePro, and other professional services. Net cash used for the year ended December 31, 2011 also includes $4.6 million used for other working capital purposes. Net cash used for the year ended December 31, 2010 primarily reflects expenditures relating to the commercial sale of Sumavel DosePro, personnel-related costs, third-party supplier expenses and professional fees. 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.

Investing Activities. Net cash used in investing activities was $0.6 million, $3.4 million, and $2.1 million for the years ended December 31, 2011, 2010 and 2009, respectively. These amounts are the result of the purchase of property and equipment primarily for use in manufacturing Sumavel DosePro.

We expect to incur capital expenditures of approximately $0.5 million to $1.0 million in 2012. These planned capital expenditures primarily relate to further investments in our manufacturing operations in support of the sound enhancement version of the DosePro technology expected to be commercially available in 2013 and toward enhancing our existing manufacturing technology and equipment.

Financing Activities. Net cash provided by financing activities was $88.4 million, $79.7 million and $65.1 million for the years ended December 31, 2011, 2010 and 2009, respectively. Net cash provided by financing activities for the year ended December 31, 2011 relates to net proceeds received from the issuance of common stock in our follow-on public offering of $57.9 million, the net proceeds received in connection with our Cowen Financing agreement of $28.1 million, net proceeds received from our $10.0 million revolving credit facility of $1.5 million, net proceeds from the issuance of common stock in connection with our Cowen Financing agreement of $1.4 million, proceeds from the issuance of common stock purchased through our Employee Stock Purchase Plan of $0.3 million, offset by payments on borrowings of debt of $0.8 million. 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 $18.1 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.

Our sources of liquidity include our cash balances, cash receipts from the sale of Sumavel DosePro and our debt facilities. As of December 31, 2011, we had $56.5 million in cash and cash equivalents. Other potential sources of near-term liquidity include (i) entering into a co-promotion agreement for Sumavel DosePro; (ii) entering into a commercialization agreement for Zohydro or a licensing arrangement on our DosePro technology, (iii) equity, debt or other financing or (iv) 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 December 31, 2011, we received aggregate net cash proceeds of approximately $274.8 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 loan with Oxford and SVB and our Cowen Financing agreement, 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.

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

As described above, under our amended Oxford/SVB loan agreement, we are subject to financial covenants and 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 Cowen Financing agreement 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 Cowen Financing agreement 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, 2011 and 2012 we were required to obtain amendments or waivers under our credit facilities.

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

Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of December 31, 2011, together with estimated future product revenue and borrowings available under our $10.0 million revolving credit facility, will be sufficient to fund our operations into the first quarter of 2013. 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 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.

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Contractual Obligations and Commitments

The following table describes our long-term contractual obligations and commitments as of December 31, 2011:

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	4-5 Years	More than 5 Years
			(In Thousands)		
Debt obligations (1)	$ 60,151	$ 15,868	$ 14,283	$ 20,000	$ 10,000
Debt interest (2)	4,712	2,487	2,225	0	0
Operating lease obligations (3)	3,422	1,448	1,561	413	0
Co-Promotion marketing & promotional expenses (4)	103	103	0	0	0
Co-Promotion tail payments (5)	5,291	0	5,291	0	0
Purchase obligations (6)	20,608	10,279	7,329	2,000	1,000
Total	$ 94,287	$ 30,185	$ 30,689	$ 22,413	$ 11,000

(1) Represents principal payments due in each period on our loan and security agreement with Oxford and SVB and outstanding balances under our revolving credit facility with Oxford and SVB. Also includes annual payments under the Cowen Financing agreement, which occur on January 1 of 2015, 2016 and 2017.

(2) Includes the interest on regular scheduled debt payments to Oxford and SVB 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 joint promotional efforts for Sumavel DosePro through March 31, 2012, which is the termination date of the agreement.

(5) Represents the two annual tail payments due to Astellas for the termination of our co-promotion agreement in March 2012, which occur in July 2013 and July 2014.

(6) Primarily represents non-cancellable purchase orders for the production of key components of Sumavel DosePro, a minimum manufacturing fee payable to Patheon UK Limited, our contract manufacturing organization, and a minimum annual spend in external expenses for the development of Relday.

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.

Under our license agreement with Alkermes 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. These future milestone payments include a payment of $1.0M upon submission of the first NDA to the FDA, and a payment of $0.8 million upon successful completion of FDA pre-approval inspection of the manufacturing facility. 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.

Under our licensing agreement with Durect we are obligated to pay Durect up to $103.0 million in total future milestone payments with respect to the product subject to and upon the achievement of various development, regulatory and sales milestones. In addition, we are required to pay Durect a mid single-digit to

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low double-digit percentage patent royalty on annual net sales of the product determined on a jurisdiction-by-jurisdiction basis, and we are also required to pay to Durect a tiered percentage of fees received in connection with any sublicense of the licensed rights. Further, until an NDA for Relday has been filed in the US, we are obligated to spend no less than $1.0 million in external expenses on the development of Relday in any trailing twelve month period beginning in July 2012.

Under our Cowen Financing agreement we are obligated to pay to Cowen Royalty revenue interest on product sales between 5% and 0.5%, depending upon the level of product sales made. Upon termination of our co-promotion agreement with Astellas on March 31, 2012, the revenue interest rate will increase to 5.75%, with a reversion back to 5% 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 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 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. The adoption of this guidance did not have a material impact on our results of operations for the year ended December 31, 2011.

In March 2010, the FASB Emerging Issues Task Force, or 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 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.

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In May 2011, the FASB issued accounting guidance related to fair value measurements and disclosures to achieve common fair value measurements and disclosures between GAAP and International Financial Reporting Standards. This guidance clarifies the application of certain existing fair value measurement guidance and expands the disclosures for fair value measurements that are estimated using significant unobservable (Level 3) inputs. This guidance is effective on a prospective basis for annual and interim reporting periods beginning on or after December 15, 2011. The adoption of this updated standard is not expected to have a material effect 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.

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Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

Our cash and cash equivalents as of December 31, 2011 consisted of cash and money market funds. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. The primary objective of our investment activities is to preserve principal. Instruments that meet this objective include commercial paper, money market funds and government and non-government debt securities. Some of the investment securities available-for-sale that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the value of the investment securities available-for-sale to fluctuate. To minimize this risk, we intend to continue to maintain our portfolio of cash and money market funds. Due to the short-term nature of our investments and our ability to hold them to maturity, we believe that there is no material exposure to interest rate risk.

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 December 31, 2011, we had $5.1 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. pounds sterling, thereby increasing our exposure to exchange rate gains and losses on non-U.S. currency transactions. Foreign currency gains and losses associated with these expenditures have not been significant to date. However, fluctuations in the rate of exchange between the U.S. dollar and these or other foreign currencies could adversely affect our financial results in the future, particularly to the extent we increase production to support Sumavel DosePro sales demands. For the twelve months ended December 31, 2011, approximately $31.7 million (based on exchange rates as of December 31, 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 twelve months ended December 31, 2011 would have resulted in approximately $1.5 million or $1.7 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.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements and the reports of our independent registered public accounting firm are included in this report on pages F-1 through F-36.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

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

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As required by Securities and Exchange Commission Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as of the end of the period covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2011 at the reasonable assurance level.

Management s Annual Report on Internal Control Over Financial Reporting

Internal control over financial reporting refers to the process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that: (1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company s assets that could have a material effect on the financial statements.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting. Management has used the framework set forth in the report entitled *Internal Control Integrated Framework* published by the Committee of Sponsoring Organizations of the Treadway Commission to evaluate the effectiveness of our internal control over financial reporting. Based on its evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2011, the end of our most recent fiscal year. 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.

Changes in Internal Control Over Financial Reporting

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

Item 9B. Other Information

None.

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PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information required by this item will be contained in our Definitive Proxy Statement, or the Definitive Proxy Statement, to be filed with the Securities and Exchange Commission in connection with our 2012 Annual Meeting of Stockholders, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2011, under the headings Election of Directors, Corporate Governance and Other Matters , Executive Officers, and Section 16(a) Beneficial Ownership Reporting Compliance, and is incorporated herein by reference .

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our internet website at www.zogenix.com. The Code of Business Conduct and Ethics contains general guidelines for conducting the business of our company consistent with the highest standards of business ethics, and is intended to qualify as a code of ethics within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

Item 11. Executive Compensation

Information required by this item will be contained in our Definitive Proxy Statement under the heading Executive Compensation and Other Information and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Information required by this item will be contained in our Definitive Proxy Statement under the headings Security Ownership of Certain Beneficial Owners and Management and is incorporated herein by reference.

Item 13. Certain Relationships, Related Transactions and Director Independence

Information required by this item will be contained in our Definitive Proxy Statement under the headings Certain Relationships and Related Party Transactions and Independence of the Board of Directors and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

Information required by this item will be contained in our Definitive Proxy Statement under the heading Independent Registered Public Accounting Firm s Fees and is incorporated herein by reference.

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PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) *Documents filed as part of this report.*

1. *Financial Statements.* The following consolidated financial statements of Zogenix, Inc., together with the report thereon of Ernst & Young LLP, an independent registered public accounting firm, are included in this Annual Report on Form 10-K:

2. *Financial Statement Schedules.*

Schedule II. Valuation and Qualifying Accounts Years ended December 31, 2011, 2010 and 2009. All other schedules are omitted as the required information is inapplicable, or the information is presented in the consolidated financial statements or related notes.

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Zogenix, Inc.

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Zogenix, Inc.

We have audited the accompanying consolidated balance sheets of Zogenix, Inc. as of December 31, 2011 and 2010, and the related consolidated statements of operations, convertible preferred stock and stockholders equity (deficit), and cash flows for each of the three years in the period ended December 31, 2011. Our audits also included the financial statement schedule listed in the Index at Item 15(a)(2).These consolidated financial statements and schedule are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements and schedule based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company s internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Zogenix, Inc. at December 31, 2011 and 2010, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2011, in conformity with U.S. generally accepted accounting principles. Also, in our opinion, the related financial statement schedule, when considered in relation to the basic financial statements taken as a whole, presents fairly in all material respects the information set forth therein.

As discussed in Note 1 to the financial statements, the Company s recurring losses from operations and lack of sufficient working capital raise substantial doubt about its ability to continue as a going concern. Management s plans as to these matters also are described in Note 1. The December 31, 2011 financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ Ernst & Young LLP

San Diego, California

March 12, 2012

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Zogenix, Inc.

Consolidated Balance Sheets

(In Thousands, except Par Value)

	December 31, 2011	December 31, 2010
Assets		
Current assets:		
Cash and cash equivalents	$ 56,525	$ 49,172
Trade accounts receivable, net	4,913	4,474
Inventory, net	16,251	18,293
Prepaid expenses and other current assets	2,210	2,251
Total current assets	79,899	74,190
Property and equipment, net	14,590	15,434
Other assets	6,151	4,644
Total assets	$ 100,640	$ 94,268
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	$ 5,168	$ 5,580
Accrued expenses	11,093	9,439
Accrued compensation	3,805	3,604
Revolving credit facility	5,081	3,449
Long-term debt, current portion	9,758	3,519
Deferred revenue, current portion	8,462	9,973
Total current liabilities	43,367	35,564
Long-term debt, less current portion	42,070	19,934
Deferred revenue, less current portion	0	9,376
Other long-term liabilities	5,891	660
Commitments and contingencies		
Stockholders equity:		
Common stock, $0.001 par value; 100,000 shares authorized at December 31, 2011 and 2010, respectively; 65,369 and 34,017 shares issued and outstanding at December 31, 2011 and 2010, respectively.	65	34
Additional paid-in capital	291,252	226,802
Accumulated deficit	(282,005)	(198,102)
Total stockholders equity	9,312	28,734
Total liabilities and stockholders equity	$ 100,640	$ 94,268

See accompanying notes.

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Zogenix, Inc.

Consolidated Statements of Operations

(In Thousands, except Per Share Amounts)

	Year Ended December 31,		
	2011	**2010**	**2009**
Revenue:			
Net product revenue	$ 30,411	$ 19,069	$ 0
Contract revenue	7,165	4,373	0
Total revenue	37,576	23,442	0
Operating expenses:			
Cost of sales	19,293	12,846	0
Royalty expense	1,205	843	0
Research and development	33,043	28,643	21,438
Selling, general and administrative	60,459	51,270	14,102
Total operating expenses	114,000	93,602	35,540
Loss from operations	(76,424)	(70,160)	(35,540)
Other income (expense):			
Interest income	37	5	10
Interest expense	(7,644)	(10,013)	(9,188)
Change in fair value of warrant liability	445	6,725	(755)
Change in fair value of embedded derivatives	(240)	0	0
Other expense	(86)	(111)	(416)
Total other income (expense)	(7,488)	(3,394)	(10,349)
Loss before income taxes	(83,912)	(73,554)	(45,889)
Provision for income tax benefit (expense)	9	(10)	0
Net loss	$ (83,903)	$ (73,564)	$ (45,889)
Net loss per share, basic and diluted	$ (1.96)	$ (17.63)	$ (40.97)
Weighted average shares outstanding, basic and diluted	42,712	4,173	1,120

See accompanying notes.

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Zogenix, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders Equity (Deficit)

(In Thousands, except Per Share Amounts)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2008	77,891	$ 76,955	0	$ 0	1,346	$ 1	$ 1114	$ (78,649)	$ (77,534)
Net loss and comprehensive loss	0	0	0	0	0	0	0	(45,889)	(45,889)
Issuance of Series B convertible preferred stock for cash at $1.10 per share, net of issuance costs of $774	0	0	50,636	54,930	0	0	0	0	0
Issuance of Series B convertible preferred stock from conversion of convertible notes, net of issuance costs of $30	0	0	13,871	15,228	0	0	0	0	0
Beneficial conversion feature from issuance of convertible notes	0	0	0	3,009	0	0	0	0	0
Issuance of warrants for Series B convertible preferred stock	0	0	0	(810)	0	0	0	0	0
Issuance of common stock in conjunction with exercise of stock options	0	0	0	0	98	0	97	0	97
Stock-based compensation	0	0	0	0	0	0	1,026	0	1,026
Balance at December 31, 2009	77,891	76,955	64,507	72,357	1,444	1	2,237	(124,538)	(122,300)
Net loss and comprehensive loss	0	0	0	0	0	0	0	(73,564)	(73,564)
Issuance of common stock from initial public offering, net of issuance costs of $6,013	0	0	0	0	14,436	14	51,719	0	51,733
Conversion of convertible preferred stock to common stock at initial public offering	(77,891)	(76,955)	(64,507)	(72,357)	14,240	14	149,298	0	149,312
Issuance of common stock from conversion of convertible notes, net of issuance costs of $18	0	0	0	0	3,874	5	15,472	0	15,477
Beneficial conversion feature from issuance of convertible notes	0	0	0	0	0	0	4,696	0	4,696
Conversion of warrants from warrants for preferred stock to warrants for common stock	0	0	0	0	0	0	743	0	743
Issuance of common stock in conjunction with exercise of stock options	0	0	0	0	0	0	71	0	71
Vesting of early exercised stock options	0	0	0	0	23	0	59	0	59
Stock-based compensation	0	0	0	0	0	0	2,507	0	2,507
Balance at December 31, 2010	0	0	0	0	34,017	34	226,802	(198,102)	28,734
Net loss and comprehensive loss	0	0	0	0	0	0	0	(83,903)	(83,903)
Issuance of common stock from secondary offering, net of issuance costs of $3,564	0	0	0	0	30,712	31	57,828	0	57,859
Issuance of common stock from financing agreement at $3.86 per share, net of issuance costs of $96	0	0	0	0	389	0	1,404	0	1,404
Issuance of common stock in conjunction with exercise of stock	0	0	0	0	67	0	92	0	92

options									
Issuance of common stock from ESPP purchase	0	0	0	0	172	0	263	0	263
Issuance of common stock warrants	0	0	0	0	0	0	39	0	39
Release of restricted stock units	0	0	0	0	12	0	0	0	0
Vesting of early exercised stock options	0	0	0	0	0	0	15	0	15
Stock-based compensation	0	0	0	0	0	0	4,809	0	4,809
Balance at December 31, 2011	0	$ 0	0	$ 0	65,369	$ 65	$ 291,252	$ (282,005)	$ 9,312

See accompanying notes.

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Zogenix, Inc.

Consolidated Statements of Cash Flows

(In Thousands)

	Year Ended December 31,		
	2011	**2010**	**2009**
Operating activities			
Net loss	$ (83,903)	$ (73,564)	$ (45,889)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	4,809	2,507	1,026
Depreciation and amortization	1,584	1,428	1,017
Amortization of debt issuance costs and non-cash interest	1,793	1,582	4,297
Change in fair value of warrant liability	(445)	(6,725)	755
Change in fair value of embedded derivatives	240	0	0
Beneficial conversion feature from issuance of convertible notes	0	4,696	3,009
Loss on disposal and impairment of property and equipment	0	2	11
Changes in operating assets and liabilities:			
Trade accounts receivable	(439)	(4,474)	0
Inventory	2,042	(5,133)	(13,160)
Prepaid expenses and other current assets	24	537	(1,769)
Other assets	(187)	(3,976)	(176)
Accounts payable and accrued expenses	4,955	10,866	(396)
Deferred rent	(57)	(48)	(86)
Deferred revenue	(10,887)	350	19,000
Net cash used in operating activities	(80,471)	(71,952)	(32,361)
Investing activities:			
Purchases of property and equipment	(617)	(3,442)	(2,057)
Net cash used in investing activities	(617)	(3,442)	(2,057)
Financing activities:			
Proceeds from issuance of common stock, net of issuance costs	59,527	51,733	0
Proceeds from issuance of convertible preferred stock, net of issuance costs	0	0	54,930
Proceeds from convertible notes, net of issuance costs	0	14,957	14,770
Proceeds from borrowings of debt and revolving credit facility, net of issuance costs	39,124	31,072	0
Payments on borrowings of debt	(825)	(18,178)	(4,691)
Payments on revolving credit facility	(9,477)	0	0
Proceeds from exercise of common stock options	92	71	95
Net cash provided by financing activities	88,441	79,655	65,104
Net increase in cash and cash equivalents	7,353	4,261	30,686
Cash and cash equivalents at beginning of period	49,172	44,911	14,225
Cash and cash equivalents at end of period	$ 56,525	$ 49,172	$ 44,911
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 4,186	$ 2,403	$ 1,894
Noncash investing and financing activities:			
Warrants issued in connection with debt	$ 866	$ 0	$ 0
Embedded derivatives related to debt	$ 605	$ 0	$ 0
Purchase of property and equipment in accounts payable	$ 123	$ 126	$ 213

Vesting of early exercised stock options	$ 15	$ 59	$ 54
Conversion of convertible preferred stock to common stock at initial public offering	$ 0	$ 149,312	$ 0
Conversion of convertible notes and related interest to common stock, net of issuance costs	$ 0	$ 15,477	$ 0
Reclassification of convertible preferred stock warrants to common stock warrants	$ 0	$ 743	$ 0
Acquisition of leasehold paid by landlord	$ 0	$ 305	$ 0
Conversion of convertible notes and related interest to convertible preferred stock, net of issuance costs	$ 0	$ 0	$ 15,258
Warrants issued in connection with debt and convertible preferred stock	$ 0	$ 0	$ 3,819

See accompanying notes.

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Zogenix, Inc.

Notes to Consolidated Financial Statements

1. Organization and Basis of Presentation

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

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

The Company has incurred significant net losses since inception and has relied on its ability to fund its operations through equity financings, debt financings, revenues from the sale of its product Sumavel DosePro and proceeds from business collaborations. As the Company continues to incur losses, successful transition to profitability is dependent upon achieving a level of revenues adequate to support the Company s cost structure. This may not occur and, unless and until it does, the Company will continue to need to raise additional cash. These conditions raise substantial doubt about the Company s ability to continue as a going concern. The accompanying financial statements have been prepared assuming that the Company will continue as a going concern and do not include any adjustments that might result from the outcome of this uncertainty. This basis of accounting contemplates the recovery of the Company s assets and the satisfaction of liabilities in the normal course of business.

Management expects operating losses and negative cash flows to continue for at least the next several years as the Company continues to incur costs related to the continued development of its product candidates and commercialization of its approved product. Management may pursue opportunities to raise additional capital through public or private equity offerings, debt financings, receivables financings or through collaborations or partnerships with other companies. There can be no assurance that the Company will be able to obtain any source of financing on acceptable terms, or at all. If the Company is unsuccessful in raising additional required funds, it may be required to significantly delay, reduce the scope of or eliminate one or more of its development programs or its commercialization efforts, or cease operating as a going concern. The Company also may be required to relinquish, license or otherwise dispose of rights to product candidates or products that it would otherwise seek to develop or commercialize itself on terms that are less favorable than might otherwise be available.

On June 30, 2011, the Company amended certain terms of its loan agreement with Oxford Finance LLC, as successor in interest to Oxford Finance Corporation (Oxford), and Silicon Valley Bank (SVB) including the deferral of principal repayment to commence on February 1, 2012 (see note 6). Concurrent to the amendment of the Oxford and SVB loan agreement, the Company entered into equity and royalty financing agreements with Cowen Healthcare Royalty Partners II, L.P. (Cowen Royalty) pursuant to which the Company committed to borrow $30,000,000 from Cowen Royalty and to sell $1,500,000 of its common stock for $29,484,000 in net proceeds. The Cowen Royalty equity and royalty financing closed on July 18, 2011 (see note 6).

On September 21, 2011, the Company completed a follow-on public offering (Offering) of common stock pursuant to a Registration Statement that was declared effective on September 15, 2011. In the Offering, the Company sold 30,000,000 shares of its common stock, at a price of $2.00 per share. The underwriters were granted an option to purchase up to 4,500,000 additional shares of common stock at $2.00 per share. A total of 711,566 shares were sold pursuant to the option to purchase additional shares on October 4, 2011. As a result of the Offering, the Company raised a total of $57,859,000 in net proceeds after deducting underwriting discounts and commissions of $2,586,000 and offering expenses of $978,000. These costs have been recorded as a reduction of the proceeds received in arriving at the amount recorded in additional paid-in capital.

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Initial Public Offering

On November 29, 2010, the Company completed its Initial Public Offering (IPO) of common stock pursuant to a Registration Statement that was declared effective on November 22, 2010. In the IPO, the Company sold 14,000,000 shares of its common stock, at a price of $4.00 per share. The underwriters had an option to sell up to an additional 2,100,000 shares at $4.00 per share pursuant to an over-allotment option granted. A total of 436,493 shares were sold pursuant to the overallotment option on December 27, 2010. As a result of the IPO, the Company raised a total of $51,733,000 in net proceeds after deducting underwriting discounts and commissions of $2,743,000 and offering expenses of $3,270,000. These costs have been recorded as a reduction of the proceeds received in arriving at the amount recorded in additional paid-in capital.

Upon the closing of the IPO, all outstanding convertible preferred stock converted into 14,239,797 shares of common stock. Also upon the closing of the IPO, $15,495,000 of unsecured convertible notes (including accrued interest thereon) converted into 3,873,756 shares of the Company s common stock. Certain warrants to purchase convertible preferred stock were terminated unexercised at the completion of the offering and the remaining warrants to purchase convertible preferred stock converted into warrants to purchase common stock. The preferred stock warrant liability was reclassified to additional paid-in capital upon the conversion of warrants to purchase preferred stock into warrants to purchase common stock.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of consolidated financial statements in conformity with accounting principles generally accepted in the United States (GAAP) requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results may differ from those estimates.

Principles of Consolidation

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

Cash and Cash Equivalents

The Company considers cash equivalents to be only those investments which are highly liquid, readily convertible to cash and have an original maturity of three months or less when purchased.

Restricted Cash

In December 2009, the Company issued a letter of credit for $200,000 in connection with another operating lease. The letter of credit is collateralized by a certificate of deposit in the same amount. Restricted cash of $200,000 at December 31, 2011 and 2010 is included in other assets on the consolidated balance sheet.

Accounts Receivable

Trade accounts receivable are recorded at the invoice amount net of allowances for cash discounts for prompt payment. The Company evaluates the collectability of its accounts receivable based on a variety of factors including the length of time the receivables are past due, the financial health of the customer and historical experience. Based upon the review of these factors, the Company recorded an allowance of $127,000 at December 31, 2011. The Company did not record an allowance for doubtful accounts at December 31, 2010. The need for bad debt allowance is evaluated each reporting period.

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Fair Value Measurements

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

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

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

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

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

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We classify our cash equivalents within Level 1 of the fair value hierarchy because we value our cash equivalents using quoted market prices. We classify our common stock warrant liability and embedded derivative liabilities within Level 3 of the fair value hierarchy because they are valued using valuation models with significant unobservable inputs. Assets and liabilities measured at fair value on a recurring basis at December 31, 2011 and December 31, 2010 are as follows (in thousands):

	Fair Value Measurements at Reporting Date Using			
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
At December 31, 2011				
Assets				
Money market fund shares (1)	$ 49,752	0	0	$ 49,752
Liabilities				
Common stock warrant liability (2)	$ 0	0	345	$ 345
Embedded derivative liabilities (3)	$ 0	0	845	$ 845
At December 31, 2010				
Assets				
Money market fund shares (1)	$ 42,615	0	0	$ 42,615

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

(2) Common stock warrants measured at fair value using the Black-Scholes option pricing valuation model are included as a component of accrued expenses on the consolidated balance sheet. The assumptions used in the Black-Scholes option pricing valuation model were: (a) a risk-free interest rate based on the rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the remaining contractual term of the warrants; (b) an assumed dividend yield of zero based on the Company s expectation to not pay dividends in the foreseeable future; (c) an expected term based on the remaining contractual term of the warrants; and (d) given the Company s lack of relevant historical data due to the Company s limited historical experience, an expected volatility based upon the historical volatility of comparable companies whose share prices have been publicly available for a sufficient period of time.

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

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The following table provides a reconciliation of liabilities measured at fair value using significant observable inputs (Level 3) for the years ended December 2011 and 2010 (in thousands):

	Convertiable Preferred Stock Warrant Liability	Common Stock Warrant Liability	Embedded Derivative Liabilities
Balance at December 31, 2009	$ 5,041	$ 0	$ 0
Issuance	2,427	0	0
Reclassification of convertible preferred stock warrants to common stock warrants	(743)	0	0
Changes in fair value	(6,725)	0	0
Balance at December 31, 2010	0	0	0
Issuance	0	790	605
Changes in fair value	0	(445)	240
Balance at December 31, 2011	$ 0	$ 345	$ 845

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

Concentration of Credit Risk, Sources of Supply and Significant Customers

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents and trade accounts receivable. The Company maintains accounts in federally insured financial institutions in excess of federally insured limits. The Company also maintains investments in money market funds and that are not federally insured. However, management believes the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which these deposits are held and of the money market funds and other entities in which these investments are made. Additionally, the Company has established guidelines regarding the diversification of its investments and their maturities, which are designed to maintain safety and liquidity.

The Company sells its products primarily to established wholesale distributors and retailers in the pharmaceutical industry. Three wholesale pharmaceutical distributors individually comprised 46.0%, 34.9% and 10.9% of the Company s total gross sales of Sumavel DosePro for the year ended December 31, 2011. Approximately 89.5% of the trade accounts receivable balance as of December 31, 2011 represents amounts due from these three wholesale distributors. Credit is extended based on an evaluation of the customer s financial condition, and collateral is not required. The Company evaluates the collectability of its accounts receivable based on a variety of factors including the length of time the receivables are past due, the financial health of the customer and historical experience. Based upon the review of these factors, the Company recorded an allowance of doubtful accounts of $127,000 at December 31, 2011. The Company did not record an allowance for doubtful accounts at December 31, 2010.

The Company relies on third-party manufacturers for the production of Sumavel DosePro and single source third-party suppliers to manufacture several key components of Sumavel DosePro. If the Company s third-party manufacturers are unable to continue manufacturing Sumavel DosePro, or if the Company lost one or more of its single source suppliers used in the manufacturing process, the Company may not be able to meet market demand for its product.

Astellas Pharma US, Inc. (Astellas) provides a significant amount of funding for the advertising and promotional costs for Sumavel DosePro and co-promotes the product in the United States. See Note 3 for more detailed information regarding this collaboration and its upcoming termination on March 31, 2012.

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Inventory

Inventory is stated at the lower of cost or market. Cost, which includes amounts related to materials, labor and overhead, is determined in a manner which approximates the first-in, first-out (FIFO) method. The Company provides reserves for potentially excess, dated or obsolete inventories based on an analysis of inventory on hand and on firm purchase commitments compared to forecasts of future sales.

Property and Equipment, Net

Property and equipment is recorded at cost, net of accumulated depreciation and amortization. Depreciation is calculated on a straight-line basis over the estimated useful lives of the respective assets, as follows:

Computer equipment and software	3 years
Furniture and fixtures	3-7 years
Manufacturing equipment and tooling	3-15 years
Leasehold improvements	Shorter of estimated useful life or lease term

Impairment of Long-Lived Assets

The Company reviews its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. There were immaterial charges as a result of impairment losses through December 31, 2011.

Warrants for Common Stock and/or Convertible Preferred Stock

In accordance with accounting guidance for warrants for shares in redeemable securities or warrants that could be settled for cash, the Company classifies warrants for common stock and/or convertible preferred stock as liabilities on the consolidated balance sheet. The Company adjusts the carrying value of these stock warrants to their estimated fair value at each reporting date with the increases or decreases in the fair value of such warrants recorded as change in fair value of warrant liability in the consolidated statement of operations.

Revenue Recognition

The Company recognizes revenue from the sale of Sumavel DosePro and from license fees and milestones earned on collaborative arrangements. Revenue is recognized when (i) persuasive evidence of an arrangement exists, (ii) delivery has occurred and title has passed, (iii) the price is fixed or determinable and (iv) collectability is reasonably assured. Revenue from sales transactions where the buyer has the right to return the product is recognized at the time of sale only if (i) the Company s price to the buyer is substantially fixed or determinable at the date of sale, (ii) the buyer has paid the Company, or the buyer is obligated to pay the Company and the obligation is not contingent on resale of the product, (iii) the buyer s obligation to the Company would not be changed in the event of theft or physical destruction or damage of the product, (iv) the buyer acquiring the product for resale has economic substance apart from that provided by the Company, (v) the Company does not have significant obligations for future performance to directly bring about resale of the product by the buyer, and (vi) the amount of future returns can be reasonably estimated.

Product Revenue

The Company sells Sumavel DosePro product in the United States to wholesale pharmaceutical distributors and retail pharmacies, or collectively the Company s customers, subject to rights of return. Prior to the third quarter of 2011, Sumavel DosePro had a limited sales history, and the Company could not reliably estimate expected returns of the product at the time of shipment. Accordingly, the Company deferred recognition of

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revenue on product shipments of Sumavel DosePro until the right of return no longer existed, which occurred at the earlier of the time Sumavel DosePro units were dispensed through patient prescriptions or expiration of the right of return. Units dispensed are generally not subject to return, except in the rare cases where the product malfunctions or the product is damaged in transit. The Company estimates patient prescriptions dispensed using an analysis of third-party information, including third-party market research data.

Beginning in the third quarter of 2011, the Company began recognizing Sumavel DosePro product sales at the time title transfers to its customer, and providing for an estimate of future product returns at that time. The Company believes that its estimated product return allowances for Sumavel DosePro require a high degree of judgment and are subject to change based on the Company s experience and certain quantitative and qualitative factors. Sumavel DosePro currently has a shelf life of 24 months from the date of manufacture. The Company accepts unused product from their customers that are within six months before and up to one year after its expiration date for a credit at the then-current wholesaler acquisition cost (WAC), reduced by a nominal fee for processing the return. The Company s initial product inventories reached expiration in 2011.

The Company has monitored actual return history on an individual product lot basis since product launch. Actual product return experience in 2011 included a disproportionately high amount of returns from a single retail chain. In addition, the Company has also experienced a high level of returned product from the Company s initial launch stocking initiatives. The Company may experience higher levels of returns upon the termination of the co-promotion agreement with Astellas on March 31, 2012 due to fall-off of prescription demand in territories that may no longer be supported with direct promotional efforts. The Company considered these factors as well as the dating of product at the time of shipment into the distribution channel, prescription trends and changes in the estimated levels of inventory within the distribution channel to estimate its exposure for returned product. Based on the Company s analysis, the Company increased the estimate for Sumavel DosePro product returns resulting in an adjustment of $2,180,000, which decreased net product sales in the fourth quarter of 2011. The Company recorded a total decrease to net product sales of $4,394,000 related to actual product returns and estimated future product returns for the twelve months ended December 31, 2011. Because of the shelf life of Sumavel DosePro and the Company s return policy of issuing credits on returned product that is within six months before and up to one year after its product expiration date, there may be a significant period of time between when the product is shipped and when the Company issues credits on returned product. Accordingly, the Company may have to adjust these estimates, which could have an effect on product sales and earnings in the period of adjustments.

In connection with the change in the timing of recognition of product sales, previously reported deferred product revenues of $729,000 and deferred cost of sales of $237,000 as of June 30, 2011 have been recognized as product revenue and cost of sales in 2011.

The Company permits certain wholesale pharmaceutical distributors to purchase limited quantities of product after the announcement of an increase to the WAC of the Company s product and prior to the effectiveness of the increase. In turn, WAC price increases can result in accelerated purchases by wholesalers relative to anticipated retail and prescription demand. The timing of purchases made by wholesale distributors and retail pharmacies are subject to fluctuations for these reasons among others. Absent accelerated purchasing by wholesalers or other periodic changes in buying patterns, the wholesale channel has historically contained two to three weeks of product on hand. As of December 31, 2011, wholesale distributors reported approximately three weeks of our product on hand.

The Company recognized $30,411,000 and $19,069,000 in Sumavel DosePro product revenue for the years ended December 31, 2011 and 2010, respectively, which was net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates, patient discount programs and product returns, as applicable. The Company had a deferred product revenue balance of $0 and $3,722,000 at

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December 31, 2011 and December 31, 2010, respectively, for Sumavel DosePro product shipments, which was net of estimated wholesaler and retail pharmacy discounts, stocking allowances, prompt pay discounts, chargebacks, rebates and patient discount programs.

Sumavel DosePro is also sold to third parties that license the rights to market and sell the product in territories outside of the United States. Under these arrangements, Sumavel DosePro is sold at a specified transfer price with the right of return available for damaged goods upon receipt or in the event of a recall. All risk for retail and wholesaler fees and discounts, collectability of customer receivables, customer returns and expiration of the product remain with the licensee. As such, the Company recognizes revenues for product sales under license arrangements upon acceptance of the product (generally at point of shipment). The Company also receives royalties on net sales of Sumavel DosePro at a predetermined rate as a pass through of royalties payable to Aradigm. For the years ended December 31, 2011 and 2010 the Company recognized $0 and $422,000, respectively, in revenue for sales to third parties that license the rights to market and sell the product in territories outside of the Unites States. The Company recognized an immaterial amount of royalty revenues related to these third party sales for the year ended December 31, 2011, and no royalty revenues for the year ended December 31, 2010.

Product Sales Allowances

The Company recognizes product 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 the Company s 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, the Company recognizes the cost of patient discounts as a reduction of revenue based on estimated utilization. If actual future results vary, the Company may need to adjust these estimates, which could have an effect on product revenue in the period of adjustment. The Company s product sales allowances include:

Wholesaler and Retail Pharmacy Discounts. The Company offers discounts to certain wholesale distributors and retail pharmacies based on contractually determined rates. The Company accrues the discount on shipment to the respective wholesale distributors and retail pharmacies and recognizes the discount as a reduction of revenue in the same period the related revenue is recognized.

Prompt Pay Discounts. The Company offers cash discounts to its customers, generally 2% of the sales price, as an incentive for prompt payment. The Company accounts for cash discounts by reducing accounts receivable by the prompt pay discount amount and recognizes the discount as a reduction of revenue in the same period the related revenue is recognized.

Chargebacks. The Company provides discounts primarily to authorized users of the Federal Supply Schedule (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 the Company the difference between the current retail price and the price the entity paid for the product. The Company estimates and accrues chargebacks based on estimated wholesaler inventory levels, current contract prices and historical chargeback activity. Chargebacks are recognized as a reduction of revenue in the same period the related revenue is recognized.

Rebates. The Company participates in certain rebate programs, which provide discounted prescriptions to qualified insured patients. Under these rebate programs, the Company pays 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. The Company estimates and accrues for 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 same period the related revenue is recognized.

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Patient Discount Programs. The Company offers discount card programs to patients for Sumavel DosePro in which patients receive discounts on their prescriptions that are reimbursed by the Company. The Company estimates the total amount that will be redeemed based on levels of inventory in the distribution and retail channels and recognizes the discount as a reduction of revenue in the same period the related revenue is recognized.

Stocking Allowances. The Company 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. The Company accrues the discount on shipment to the respective wholesale distributors and retail pharmacies and recognizes the discount as a reduction of revenue in the same period the related revenue is recognized.

Contract Revenue

The Company recognizes revenues related to license fees and milestone payments received under its Co-Promotion Agreement with Astellas entered into in July 2009 (Co-Promotion Agreement). Revenue arrangements with multiple deliverables are divided into separate units of accounting if certain criteria are met, including whether the deliverable has stand-alone value to the customer, 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. The selling price for each deliverable is determined using: (i) vendor-specific objective evidence of selling price (VSOE), if it exists, (ii) third-party evidence of selling price (TPE) if VSOE does not exist, and (iii) the Company s best estimate of the selling price if neither VSOE nor TPE exists. For transactions entered into prior to January 1, 2011, revenue is recognized for each deliverable based upon the applicable revenue recognition criteria discussed above and upon acceptance of goods or performance of service. Effective January 1, 2011, for new or significantly modified transactions, the Company allocates revenue consideration, excluding contingent consideration, based on the relative selling prices of the separate units of accounting contained within an arrangement containing multiple deliverables.

Collaborative Arrangements

Effective January 1, 2009, the Company implemented new authoritative guidance related to accounting for collaborative arrangements. The new guidance requires that certain transactions between collaborators be recorded in the consolidated statement of operations on either a gross or net basis within revenues or operating expenses, depending on the characteristics of the collaboration relationship, and provides for enhanced disclosure of collaborative relationships. The Company evaluates its collaborative agreements for proper classification of shared expenses, license fees, milestone payments and any reimbursed costs within the consolidated statement of operations based on the nature of the underlying activity. If payments to and from collaborative partners are not within the scope of other authoritative accounting literature, the statement of operations classification for the payments is based on a reasonable, rational analogy to authoritative accounting literature that is applied in a consistent manner. For collaborations relating to commercialized products, if the Company acts as the principal in the sale of goods or services, the Company records revenue and the corresponding operating costs in its respective line items within the consolidated statement of operations based on the nature of the shared expenses. Per authoritative accounting guidance, the principal is the party who is responsible for delivering the product to the customer, has latitude with establishing price and has the risks and rewards of providing product to the customer, including inventory and credit risk. Effective January 1, 2011, for collaborations relating to research or development arrangements, the Company will recognize revenue for a payment that is contingent upon the achievement of a substantive milestone in its entirety in the period in which the milestone is achieved.

Research and Development Expenses

All costs of research and development are expensed in the period incurred. Research and development costs primarily consist of salaries and related expenses for personnel, stock-based compensation expense, outside

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service providers, facilities costs, fees paid to consultants, milestone payments, license fees, professional services, travel costs, dues and subscriptions, depreciation and materials used in clinical trials and research and development. The Company expenses costs relating to the purchase and production of pre-approval inventories as research and development expense in the period incurred until FDA approval. The Company received FDA approval for Sumavel DosePro in July 2009, after which it began capitalizing costs as inventory related to the production of Sumavel DosePro, including the cost of materials, third-party manufacturing costs, freight and indirect personnel and other overhead costs.

The Company reviews and accrues expenses related to clinical trials based on work performed, which relies on estimates of total costs incurred based on completion of patient studies and other events. The Company follows this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical development costs are subject to revisions as trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revision become known.

Advertising Expense

The Company records the cost of its advertising efforts when services are performed or goods are delivered. The Company incurred approximately $4,559,000, $4,308,000 and $1,072,000 in advertising costs for the years ended December 31, 2011, 2010 and 2009, respectively. At December 31, 2011 and 2010, the Company capitalized advertising costs of $26,000 and $93,000 in prepaid and other current assets, respectively.

Income Taxes

Deferred tax assets and liabilities are determined based on the differences between the financial reporting and tax basis of assets and liabilities using enacted tax rates which will be in effect when the differences reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax asset will be realized. The Company recognizes the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities based on the technical merits of the position.

Foreign Currency Transactions

Gains or losses resulting from transactions denominated in foreign currencies are included in other expense in the consolidated statements of operations. The Company recorded losses from foreign currency transactions in other expense of $86,000, $111,000 and $416,000 for the years ended December 31, 2011, 2010 and 2009, respectively.

Stock-Based Compensation

Stock-based compensation cost 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 on a straight-line basis. As of December 31, 2011, there were no outstanding equity awards with market or performance conditions. Equity awards issued to non-employees are recorded at their fair value on the measurement date and are re-measured at each reporting date as the underlying awards vest unless the instruments are fully vested, immediately exercisable and nonforfeitable on the date of grant.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period reduced by weighted average shares subject to repurchase, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common share equivalents outstanding for the period determined using the

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treasury-stock method and as-if converted method, as applicable. For purposes of this calculation, preferred stock, stock options and warrants are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

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

	Year Ended December 31,		
	2011	2010	2009
Numerator			
Net loss	$ (83,903)	$ (73,564)	$ (45,889)
Denominator			
Weighted average common shares outstanding	42,715	4,267	1,359
Weighted average shares subject to repurchase	(3)	(94)	(239)
Weighted average shares outstanding, basic and diluted	42,712	4,173	1,120
Basic and diluted net loss per share	$ (1.96)	$ (17.63)	$ (40.97)

Potentially dilutive securities not included in the calculation of diluted net loss per share because to do so would be anti-dilutive are as follows (in thousands, of common equivalent shares):

	Year Ended December 31,		
	2011	2010	2009
Convertible preferred stock	0	0	14,240
Convertible preferred stock warrants	0	0	1,389
Common stock warrants	508	257	0
Common stock subject to repurchase	0	15	190
Common stock options and restricted stock units	3,517	1,479	808
	4,025	1,751	16,627

Segment Reporting

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

Recent Accounting Pronouncements

In October 2009, the Financial Accounting Standards Board (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 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. The Company 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. The Company will now allocate revenue consideration, excluding contingent consideration, based on the relative selling prices of the separate units of accounting

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contained within an arrangement containing multiple deliverables. Selling prices are determined using fair value, when available, or the Company s estimate of selling price when fair value is not available for a given unit of accounting. The adoption of this guidance did not have a material impact on the Company s results of operations for the year ended December 31, 2011.

In March 2010, the FASB Emerging Issues Task Force (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 the Company. The Company 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 retrospectively for all periods presented. The Company adopted this guidance on January 1, 2011 on a prospective basis. Adoption of this guidance did not have a material impact on the Company s results of operations.

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

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

3. Collaboration, License and Purchase Agreements

Durect Development and License Agreement

On July 11, 2011, the Company entered into a development and license agreement with Durect Corporation (the License Agreement). Under the License Agreement, the Company is 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 the Company s DosePro® needle-free, subcutaneous drug delivery system. Durect is responsible for non-clinical, formulation and chemistry, manufacturing and controls development. Durect will be reimbursed by the Company for its research and development efforts on the product.

The Company paid a non-refundable upfront fee to Durect of $2,250,000, which was recorded as research and development expenses in the consolidated statement of operations during the year ended December 31, 2011.

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The Company is obligated to pay Durect up to $103,000,000 in total future milestone payments with respect to the product subject to and upon the achievement of various development, regulatory and sales milestones. The Company is 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. Further, until an NDA for Relday has been filed in the US, we are obligated to spend no less than $1,000,000 in external expenses on the development of Relday in any trailing twelve month period beginning in July 2012. 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, the Company will continue to pay royalties on annual net sales of the product at a reduced rate for so long as the Company continues to sell the product in the jurisdiction. The Company is also required to pay to Durect a tiered percentage of fees received in connection with any sublicense of the licensed rights.

Durect granted to the Company 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 the Company s Phase 3 clinical trial and commercial product requirements on the terms set forth in the License Agreement.

Durect retains the right to terminate the License Agreement with respect to specific countries if the Company fails to advance the development of the product in such country within a specified period, either directly or through a sublicensee. In addition, either party may terminate the License 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 impairing such other party s relevant intellectual property rights. The Company may terminate the License 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 monitory board or other similar body alleging significant concern regarding a patient safety issue and, as a result, the Company believes the long-term viability of the product would be seriously impacted. The Company may also terminate the License Agreement with or without cause, at any time upon prior written notice.

Astellas Pharma US, Inc. Co-Promotion Agreement

In July 2009, the Company entered into the Co-Promotion Agreement with Astellas. Under the terms of the agreement, the Company granted Astellas the co-exclusive right (with the Company) to market and sell Sumavel DosePro in the United States (excluding Puerto Rico and the other territories and possessions of the United States) until June 30, 2013. Under the agreement, both Astellas and the Company were obligated to collaborate and fund the marketing of Sumavel DosePro and to provide annual minimum levels of sales effort directed at Sumavel DosePro during the term. In December 2010, the Company entered into an amendment to the Co-Promotion agreement with Astellas, or the amended Co-Promotion agreement, whereby the agreement will terminate on March 31, 2012. The Company is responsible for the manufacture, supply, and distribution of commercial product for sale in the United States. In addition, the Company will supply product samples to Astellas, and Astellas pays the Company for such samples, at an agreed upon transfer price.

In connection with the execution of the Co-Promotion Agreement, Astellas made a non-refundable up-front payment of $2,000,000 and agreed to make an additional $18,000,000 of payments to the Company upon the achievement of a series of milestones. Through December 31, 2010, Astellas paid a total of $20,000,000 in proceeds to the Company. In consideration for Astellas performance of its commercial efforts, the Company is 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 primary care physicians, OB/GYNs, emergency medicine physicians, and

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urologists in the United States (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, in March 2012, the Company will be required to pay Astellas two additional annual tail payments in July 2013 and July 2014 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 twelve months ending March 31, 2012.

In accordance with accounting guidance for revenue arrangements with multiple deliverables, the Company identified the deliverables in the Co-Promotion Agreement and divided them into separate units of accounting as follows: (i) co-exclusive right to promote Sumavel DosePro combined with the manufacturing and supply of commercial and sample product and (ii) sales support of Sumavel DosePro. The Company concluded both units of accounting require recognition ratably through the term of the Co-Promotion Agreement beginning with the date of the launch of Sumavel DosePro (January 2010) through June 30, 2013. Consequently, the Company initially recorded the $20,000,000 in upfront and milestone payments received from Astellas as deferred revenue. Beginning with the launch of Sumavel DosePro in January 2010, the Company began amortizing the upfront and milestone payments as contract revenue in the consolidated statement of operations over the term of the Co-Promotion Agreement. For the years ended December 31, 2011 and 2010, the Company recognized $7,165,000 and $4,373,000, respectively, of contract revenue. As of December 31, 2011 and December 31, 2010, the remaining balance of these payments in deferred revenue was $8,462,000 and $15,627,000, respectively.

On December 20, 2011, the Company amended the Co-Promotion Agreement with Astellas to terminate the agreement on March 31, 2012. The Company will be required to make two annual tail payments to Astellas, estimated as a total of $5,291,000, calculated as decreasing fixed percentages (ranging from mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion**.** The present value of such tail payments was recorded as a long-term liability on the amendment date. The fair value of the tail payments will be accreted through interest expense through the dates of payment in July 2013 and July 2014. As of December 31, 2011, tail payment liability was $4,016,000. An immaterial amount of related interest expense was recognized during the year ended December 31, 2011.

In accordance with accounting guidance for revenue arrangements with multiple deliverables, the Company determined that there was no change in the deliverables or units of accounting identified in the Co-Promotion Agreement upon amendment in December 2011. The Company further concluded that the remaining deferred revenue balance of $9,561,000 should be recognized ratably through the amended term of the Co-Promotion Agreement. This acceleration in the recognition of these contract proceeds resulted in the recognition of an additional $914,000 of contract revenue during the year ended December 31, 2011.

Further, under the terms of the amended Co-Promotion Agreement, Astellas will contribute its agreed portion of marketing expenses through March 31, 2012, and will continue to earn a service fee based on product sales to the Astellas Segment during that period. The Company will no longer pay service fees to Astellas for sales of Sumavel DosePro beginning in the second quarter of 2012. Additionally, beginning in the second quarter of 2012, the Company s sales force will assume full responsibility for the commercialization and the continued marketing of Sumavel DosePro, expanding their focus to include headache specialists, neurologists and primary care physicians in the United States.

Amounts received from Astellas for shared marketing costs and sample product are reflected as a reduction of selling, general and administrative expenses, and amounts payable to Astellas for shared marketing expenses and service fees are reflected as selling, general and administrative expenses, inclusive of the estimated cost of the tail payments owed upon the termination of the agreement.

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For the years ended December 31, 2011, 2010 and 2009, the Company recognized shared marketing expense of $1,663,000, $3,853,000, and $2,213,000, respectively, under the Co-Promotion Agreement. For the years ended December 31, 2011, 2010 and 2009, the Company incurred $6,657,000 (excluding the $4,016,000 tail payments), $3,660,000 and $0 in service fee expenses.

Desitin Arzneimittel GmbH Licensing and Distribution Agreement

In March 2008, the Company entered into a licensing and distribution agreement with Desitin Arzneimittel GmbH (Desitin), a private German pharmaceutical company focused on the development, manufacturing and distribution of products for the treatment of central nervous system disorders. Under the terms of the agreement, the Company 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. The Company has agreed to manufacture and supply the product to Desitin for commercial sale. Desitin has agreed to pay the Company a specified transfer price for commercial product and a low single-digit percentage royalty on net sales of the product. In November 2010, Desitin received regulatory approval for the commercialization of Sumavel DosePro in Denmark. It received subsequent approvals in Germany, Sweden, the United Kingdom, Norway and France. In connection with such approvals and in anticipation of launch in those markets,

the Company recognized $0 and $422,000 in revenue for sales to Desitin for the years ended December 31, 2011 and 2010, respectively. Under the terms of the agreement, Desitin does not have the right to return product that it has purchased.

Alkermes License Agreement (formerly Elan Pharma International Limited)

In November 2007, the Company entered into a License Agreement with Alkermes Plc, or Alkermes, which was amended in September 2009. Under the terms of this License Agreement, Alkermes granted the Company 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 Alkermes, to certain Alkermes intellectual property rights related to the Company s Zohydro product candidate. The License Agreement grants the Company the exclusive right under certain Alkermes 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 the Company to exclusively develop and sell Zohydro in the United States. Alkermes has retained the exclusive right to take action in the event of infringement or threatened infringement by a third party of Alkermes intellectual property rights under the License Agreement. The Company has the right to pursue an infringement claim against the alleged infringer should Alkermes decline to take or continue an action.

Under the terms of the License Agreement, the Company and Alkermes agreed that, subject to the future negotiation of a commercial manufacture and supply agreement, Alkermes, or an affiliate of Alkermes, will have the sole and exclusive right to manufacture and supply finished commercial product of Zohydro to the Company under agreed upon financial terms.

Alkermes also granted to the Company, in the event that Alkermes is unwilling or unable to manufacture or supply commercial product to the Company, a non-exclusive license to make product under Alkermes 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 Alkermes.

Under the License Agreement, the Company paid an upfront fee of $500,000 to Alkermes, which was recorded as research and development expense. The Company paid an additional payment in the amount of $750,000 to Alkermes in August 2011 in connection with the completion of the treatment phase of the

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Company s pivotal efficacy Phase 3 clinical trial, Study 801, which was recorded as research and development expense. The Company may be obligated to pay Alkermes up to $3,750,000 in total future milestone payments with respect to Zohydro depending upon the achievement of various development and regulatory events. These future milestone payments include a payment of $1,000,000 upon submission of the first NDA to the FDA, which we expect to occur early in the second quarter of 2012, and a payment of $750,000 upon successful completion of an FDA pre-approval inspection of the Company s manufacturing facility. In addition, if Zohydro is approved, the Company 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.

The Company is 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 Alkermes patents covering the product in the United States, or 15 years after commercial launch, if Alkermes 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 the Company will continue to pay royalties to Alkermes 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 License 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. Alkermes may terminate the License Agreement in the event that the Company fails to meet specified development and commercialization milestones within specified time periods. The Company may terminate the License Agreement if the sale of Zohydro is prohibited by regulatory authorities, or if, despite commercially reasonable efforts, the Company is unable to obtain regulatory approval for Zohydro. The Company may also terminate the License 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.

Aradigm Corporation Asset Purchase Agreement

On August 25, 2006, the Company entered into an asset purchase agreement with Aradigm Corporation (Aradigm). Under the terms of the agreement, Aradigm assigned and transferred to the Company 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 the Company 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 the Company granted Aradigm a license under other intellectual property rights solely for use in the pulmonary field.

The Company paid Aradigm $4,000,000 at the closing of the asset purchase and was required to make an additional $4,000,000 milestone payment to Aradigm upon the U.S. commercialization of Sumavel DosePro (which payment was made in February 2010). The Company is also required to pay a 3% royalty on global net sales of Sumavel DosePro, by the Company or one of the Company s future 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. The Company has recorded the second milestone payment as other assets in the consolidated balance sheet and is amortizing the milestone over the estimated life of the technology. For the years ended December 31, 2011 and 2010, the Company recorded $1,205,000 and $843,000, respectively, of expense related to the amortization of the milestone and royalties from net sales of Sumavel DosePro. The Company expects to

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record annual amortization expense of $286,000 during the years ended December 2012 through 2016, and $2,000,000 in amortization expense thereafter related to the amortization of the milestone.

In addition, in the event the Company or one of its future licensees, if any, commercializes a non-*sumatriptan* product in the DosePro delivery system, the Company will be required to pay Aradigm, at the Company s 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 the Company 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 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 the Company, 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.

4. Consolidated Balance Sheet Details

Inventory, Net (in thousands)

	December 31,	
	2011	**2010**
Raw materials	$ 5,260	$ 5,727
Work in process	7,338	6,454
Finished goods	3,653	4,861
Deferred costs	0	1,251
	$ 16,251	$ 18,293

Deferred costs represent the costs of product shipped for which recognition of revenue has been deferred.

Property and Equipment, Net (in thousands)

	December 31,	
	2010	**2010**
Machinery, equipment and tooling	$ 11,902	$ 9,919
Construction in progress	5,416	6,735
Computer equipment and software	1,122	1,051
Furniture and fixtures	562	557
Leasehold improvements	780	780
Property and equipment, at cost	19,782	19,042
Less accumulated depreciation	(5,192)	(3,608)
	$ 14,590	$ 15,434

Depreciation expense for the years ended December 31, 2011, 2010 and 2009 was $1,584,000, $1,428,000 and $1,017,000, respectively.

Other Assets (in thousands)

	December 31,

	2011	2010
Prepaid Aradigm royalty expense	$ 3,429	$ 3,714
Debt acquisition costs	1,432	113
Deposits	1,090	617
Restricted cash	200	200
	$ 6,151	$ 4,644

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Accrued Expenses (in thousands)

	December 31,	
	2011	2010
Accrued product returns	$ 2,446	0
Accrued discounts and allowances	2,153	813
Accrued interest expense	1,924	265
Accrued co-promotion service fee	1,615	1,190
Accrued clinical expense	945	3,629
Warrant liability	345	0
Accrued royalty expenses	303	286
Accrued sales and marketing expenses	153	286
Value added tax payable	0	989
Other accrued expenses	1,209	1,981
	$ 11,093	$ 9,439

Other Long-Term Liabilities (in thousands)

	December 31,	
	2011	2010
Astellas tail payments	$ 4,016	$ 0
Embedded derivatives	845	0
Term loan final payment	642	203
Deferred Rent	303	360
Other long-term liabilities	85	97
	$ 5,891	$ 660

5. Commitments

Operating Leases

In August 2008, the Company entered into a 20-month operating lease for office facilities in San Diego, California commencing on September 1, 2008. Monthly rental payments are adjusted on an annual basis, and the office lease expires, as extended, in April 2012. This space is used for general and administrative and sales and marketing operations and personnel.

The Company also leases office space for its supply chain and inventory management and research and product development operations in Emeryville, California under a non-cancelable operating lease that expires in November 2011. The base rent is subject to a 3.0% increase each year for the duration of the lease. Under the terms of the lease, as amended, the Company received an option to expand into additional space. The Company also received free rent for two months and a tenant improvement allowance of $305,000.

In August 2009, the Company entered an operating lease agreement to lease up to 95 vehicles. Each vehicle has a lease term of 36 months with a fixed monthly rental payment. As security for the vehicle leases, the lessor required a letter of credit for $200,000, which is collateralized by a certificate of deposit in the same amount.

The Company recognizes rent expense on a straight-line basis over the non-cancelable term of its operating leases. Rent expense for the years ended December 31, 2011, 2010 and 2009 was $826,000, $839,000 and $799,000, respectively.

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Future minimum lease payments as of December 31, 2011 are as follows (in thousands):

2012	$ 1,448
2013	834
2014	727
2015	413
2016 and thereafter	0
Total	$ 3,422

Manufacturing and Supply Agreements

The Company has a manufacturing services agreement with Patheon UK Limited (Patheon) for the aseptic capsule assembly, filling and inspection, final device assembly and purchasing of Sumavel DosePro, as well as other manufacturing and support services, which agreement expires on October 31, 2013. The Company has manufacturing and supply agreements with several third-party suppliers for the production of key components of Sumavel DosePro, which expire on various dates between 2012 and 2020. As of December 31, 2011, the Company has non-cancellable purchase orders for 2012 totaling approximately $3,656,000 under these arrangements. In addition, the Company is required to pay Patheon a monthly manufacturing fee of £303,200 or approximately $469,538 (based on the exchange rate as of December 31, 2011). As of December 31, 2011, the Company was committed to pay Patheon a total manufacturing fee of £6,670,400, or approximately $10,307,836 (based on the exchange rate as of December 31, 2011), which is payable monthly over the remaining 23 months of the Patheon manufacturing services agreement.

6. Debt

Bridge Loans

In July 2010, the Company entered into a Note Purchase Agreement, pursuant to which the Company borrowed an aggregate of $15,000,000 from certain existing investors. Outstanding balances under the Note Purchase Agreement accrued interest at a rate of 8% per annum. The principal amount of the 2010 Notes and accrued interest thereon automatically converted into 3,873,756 shares of the Company s common stock upon completion of the Company s IPO at a conversion price equal to the Company s IPO price of $4.00 per share.

The holders of the 2010 Notes received the benefit of a deemed conversion price of the 2010 Notes that was below the estimated fair value of the Series B convertible preferred stock at the time of their issuance. The fair value of this beneficial conversion feature was estimated to be $8,182,000. The fair value of this beneficial conversion feature was recorded to debt discount and amortized to interest expense using the effective interest method over the term of the 2010 Notes. The Company recorded $4,696,000 of interest expense related to the beneficial conversion feature during the year ended December 31, 2010.

Term Debt

In June 2008, the Company entered into and borrowed $18,000,000 under the Loan and Security Agreement with Oxford and CIT Healthcare LLC (the Oxford Agreement). The obligations under the Oxford Agreement were collateralized by personal property excluding certain intellectual property and all equipment pledged to secure the equipment financing described below. In July and October 2010, the Company amended and restated

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the Oxford Agreement, and Oxford and SVB became party to the amended agreement. In June 2011, the Company entered into an amendment to the second amended and restated Oxford/SVB agreement (the Amended Oxford/SVB Agreement), which provided among other things, the addition of intellectual property to the collateral securing the Oxford/SVB loan and the deferral of principal repayment to commence on February 1, 2012. In connection with entering into the Amended Oxford/SVB Agreement, the Company issued to Oxford and SVB warrants exercisable into an aggregate of 26,455 shares of the Company s 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 Agreement consists of a $25,000,000 term loan and a $10,000,000 revolving credit facility. The obligations under the Amended Oxford/SVB Agreement are collateralized by the Company s intellectual property and personal property (including, among other things, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash).

The Amended Oxford/SVB Agreement includes financial covenants requiring that the Company 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 the Company s projected revenue as provided to Oxford and SVB in the event the Company fails 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 Amended Oxford/SVB Agreement also includes a covenant that the audit report accompanying the Company s year-end consolidated financial statements for fiscal year 2010 and thereafter not include a going concern qualification. In March 2012, the Company obtained a waiver from Oxford and SVB for the breach caused by the receipt of the 2011 audit report from our independent registered public accounting firm, which includes a modification of their standard report for the going concern uncertainty. The Amended Oxford/SVB Agreement also provides that an event of default will occur if, amoung other customary events of default as defined in the Amended Oxford/SVB Agreement, there is a material adverse change in the Company s business, operations or condition (financial or otherwise) or material impairment in the prospects of the Company repaying any portion of its obligations under the Amended Oxford/SVB Agreement.

The $25,000,000 term loan bears an interest rate of 12.06% per annum. The monthly repayment schedule includes 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 $1,200,000, in addition to principal repayments, at the loan maturity date, which is January 1, 2014. The Company has the option to prepay the outstanding balance of the term loan in full, subject to the $1,200,000 final payment and a prepayment fee of either 2% or 3% of the principal amount prepaid depending upon when the prepayment occurs. The outstanding principal balance of the term loan as of December 31, 2011and 2010 is $25,000,000.

Under the terms of the revolving credit facility, the Company may borrow up to $10,000,000 based on eligible accounts receivable and inventory balances, as defined within the Amended Oxford/SVB 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, the Company pays 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 nominal final payment is due depending upon when the termination occurs.

As of December 31, 2011 and 2010, the Company had $5,151,000 and $3,585,000, respectively, of outstanding principal under the revolving credit facility, and $4,849,000 and $6,415,000, respectively, was available for future borrowings to the extent of available borrowing base. As of December 31, 2011 and 2010, $5,081,000 and $3,449,000, respectively, is reflected on the consolidated balance sheet net of debt discounts related to the fees and warrants issued in connection with the Amended Oxford/SVB Agreement.

Equipment Financing

In March 2007, the Company entered into a $10,000,000 master loan and security agreement (GE Agreement) with GE Capital Corporation (GE Capital) for the purpose of financing capital equipment purchases. Each borrowing is under a promissory note repayable in 48 monthly installments based upon a monthly

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repayment schedule bearing interest at an annual rate determined on the date of borrowing. The first promissory note was executed in March 2007 for $3,500,000 with an interest rate of 10.08%. A second promissory note was executed in December 2007 for $1,000,000 with an interest rate of 9.91%. The Company s ability to make further borrowing under the GE Agreement expired on December 21, 2007.

The Company had the option to prepay the outstanding balance of the promissory notes in full, subject to a prepayment fee as defined in the GE Agreement. 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.

Cowen Royalty Financing Agreement

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

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

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

- 5% of the first $75,000,000 of Revenue Interest recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year (or 5.75% after the co-promotion agreement with Astellas is terminated on March 31, 2012, with a reversion back to 5% 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);

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

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

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

The obligation of the Company to make the Revenue Interest payments during the term of the Financing Agreement are secured under a security agreement by a second priority security interest (junior to the security interest of Oxford and SVB under the Amended Oxford /SVB Agreement) in all assets of the Company,

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including intellectual property and other rights of the Company to the extent necessary or used to commercialize the Company products. The security interest will be extinguished at the end of the term or once the aggregate payments made by the Company to Cowen Royalty equal $75,000,000, whichever is sooner. Cowen Royalty, Oxford and SVB entered into an intercreditor agreement which governs their respective rights as secured creditors. The Company has agreed to specified positive and negative covenants in connection with the Financing Agreement.

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

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

The rights of the Company and Cowen Royalty to early terminate the Financing Agreement, as well the potential change in the Revenue Interest rate from 5% to 5.75% in connection with the early termination of the Astellas co-promotion agreement, met the definition of an embedded derivative at the closing of the Financing Agreement. As a result, the Company carved out these embedded derivatives from the Financing Agreement and determined the fair value of each derivative using various discounted cash flow valuation models taking into account the probability of these events occurring and various scenarios surrounding the potential Revenue Interest payments that would be made if these events occurred (see Note 2). The aggregate fair value of the embedded derivatives was $605,000 at issuance and was included in other long-term liabilities.

As of December 31, 2011, the rights of the Company and Cowen Royalty to early terminate the Financing Agreement meet the definition of an embedded derivative. As the Company executed the amendment to co-promotion agreement with Astellas, which will terminate the agreement on March 31, 2012, the related embedded derivative has been derecognized, resulting in a $417,000 adjustment to the fair value of embedded derivatives for the year ended December 31, 2011. The Company determined the fair value of each derivative as of December 31, 2011 using various discounted cash flow valuation models, which resulted in a derivative liability of $845,000. The change in fair value of the embedded derivatives during the twelve months ended December 31, 2011 of $240,000 was included in other expenses.

The Company received aggregate net proceeds of $29,485,000 from the Financing Agreement (including the purchase of common stock). The discounts, which are being amortized using the effective interest method over the term of the arrangement within interest expense, include the fair value of the common stock warrants issued to Cowen Royalty of $790,000, fees payable to Cowen Royalty in connection with the execution of the arrangement of $476,000 and the fair value of embedded derivatives of $605,000. The Company has recognized other income (expense) in relation to the change in the fair value of the common stock warrant and embedded derivatives of $445,000 and $(240,000), respectively, for the year ended December 31, 2011in the statement of operations.

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The following is a summary of all debt obligations recorded in current and long-term debt on the balance sheet at December 31, 2011 (in thousands):

	Revolver	Oxford /SVB	Cowen Royalty
Long-term debt, current portion	$ 5,151	$ 10,717	$ 0
Debt discount	(70)	(959)	0
Total long-term debt, current portion	$ 5,081	$ 9,758	$ 0
Long-term debt, less current portion	$ 0	$ 14,283	$ 30,000
Debt discount	0	(451)	(1,762)
Total long-term debt, less current portion	$ 0	$ 13,832	$ 28,238

Maturities of long-term debt as of December 31, 2011, are as follows (in thousands):

2012	$ 18,355
2013	14,130
2014	2,378
2015	10,000
2016	10,000
2017	10,000
Total minimum payments	64,863
Less amount representing interest	(4,712)
Present value of net minimum payments	60,151
Less unamortized discount	(3,242)
Total long-term debt	56,909
Less current portion	(14,839)
Long-term portion	$ 42,070

Interest expense related to long-term debt for the years ended December 31, 2011, 2010 and 2009 was $5,562,000, $4,727,000 and $2,712,000, respectively.

7. Convertible Preferred Stock and Stockholders Equity

Convertible Preferred Stock

As of December 31, 2011 and 2010, there were no shares of convertible preferred stock issued or outstanding as all shares totaling 142,398,142 of preferred stock converted to 14,239,797 shares of common stock on a 10 for 1 basis upon completion of the IPO.

Under the Company s amended and restated certificate of incorporation, as of December 31, 2011 and 2010, the Company is authorized to issue 10,000,000 shares of preferred stock with a $0.001 par value.

Common Stock

Under the Company s amended and restated certificate of incorporation, as of December 31, 2011 and 2010, the Company is authorized to issue 100,000,000 shares of common stock with a $0.001 par value. Each share of common stock is entitled to one vote. The holders of common stock are also entitled to receive dividends whenever funds are legally available, when declared by the board of directors and with the consent of Oxford/SVB as required under the Amended Oxford/SVB Agreement (only if dividends are not paid soley in capital stock), subject to the prior rights of holders of convertible preferred stock.

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Common stock reserved for future issuance is as follows (in thousands):

	December 31,	
	2011	2010
Stock options and restricted stock units outstanding	3,517	1,479
Warrants to purchase common stock	508	257
Shares authorized for future issuance under equity and purchase plans	1,681	2,721
	5,706	4,457

Common Stock Warrants

In June 2011, and in connection with entering into the Amended Oxford/SVB Agreement (see Note 6), the Company issued to Oxford and SVB warrants exercisable into an aggregate of 26,455 shares of common stock. The warrants are exercisable at $3.78 per share of common stock and have a term of 7 years. The value of the warrants of approximately $76,000 was recorded as debt discount and additional paid in capital in the consolidated balance sheet as of December 31, 2011.

In July 2011, upon the closing of and in connection with the Financing Agreement (see Note 6), the Company issued to Cowen Royalty a warrant exercisable into 225,000 shares of common stock. The warrant is exercisable at $9.00 per share of common stock and has a term of 10 years. As the warrant contains covenants where compliance with such covenants may be outside of the Company s control, the warrant was recorded as a current liability and is marked to market at each reporting date. The fair value of the warrant was approximately $345,000 as of December 31, 2011.

Convertible Preferred Stock Warrants

In connection with the execution of the Amended Oxford Agreement in July 2010, which was subsequently amended in October 2010, the Company issued warrants to Oxford and Silicon Valley Bank to purchase 1,145,455 and 445,455 shares, respectively, of Series B convertible preferred stock at an exercise price of $1.10 per share. The warrants expire in November 2015. In connection with the Company s initial public offering in November 2010, these warrants were converted to 159,090 warrants for common stock at an exercise price of $11.00 per share.

In accordance with accounting guidance for warrants for shares in redeemable securities, the Company classified warrants for convertible preferred stock as liabilities on the consolidated balance sheet based on fair value and increases or decreases in the fair value of such warrants were recorded as other income (expense) in the consolidated statement of operations. Upon the closing of the IPO on November 29, 2010, all preferred stock converted into common stock. The warrants were converted into warrants to purchase common stock and reclassed from a liability to equity.

8. Stock-Based Compensation

Stock Option Plans

During 2006, the Company adopted the 2006 Equity Incentive Award Plan (as amended, the 2006 Plan) under which 1,134,000 shares of common stock were reserved for issuance to employees, directors and consultants of the Company at December 31, 2011 and 2010. The 2006 Plan provides for the grant of incentive stock options, non-qualified stock options and rights to purchase restricted stock to eligible recipients. Recipients of stock options are eligible to purchase shares of the Company s common stock at an exercise price equal to no less than the estimated fair market value of such stock on the date of grant. The maximum term of options granted under the 2006 Plan is ten years.

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Options granted pursuant to the 2006 Plan generally vest over four years and vest at a rate of 25% upon the first anniversary of the vesting commencement date and 1/48th per month thereafter. The 2006 Plan allows the option holders to exercise their options early and acquire option shares, which are then subject to repurchase by the Company at the original exercise price of such options. At December 31, 2011 and 2010 there were zero and 15,000, respectively, of unvested shares of common stock issued to employees of the Company in connection with the early exercise of stock option grants which the Company has recorded as a liability in the accompanying consolidated balance sheets.

During 2010, the Company adopted the 2010 Equity Incentive Award Plan (the 2010 Plan). The 2010 Plan became effective immediately prior to the completion of the IPO. An initial 2,243,668 shares are reserved for issuance to employees, directors and consultants of the Company under the 2010 plan. The number of shares initially reserved were subsequently increased by the number of shares of common stock related to awards granted under the 2006 Plan that are repurchased, forfeited, expired or are cancelled on or after the effective date of the 2010 Plan. The 2010 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock units and rights to purchase restricted stock to eligible recipients. Recipients of stock options are eligible to purchase shares of the Company s common stock at an exercise price equal to no less than the estimated fair market value of such stock on the date of grant. The maximum term of options granted under the 2010 Plan is ten years.

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 is equal to the lower of:

4% of the Company s outstanding common stock on the applicable January 1;

1,000,000 shares; or

A lesser number of shares as determined by the board of directors.

At December 31, 2011 and 2010, 1,103,579 and 2,220,717 shares of common stock were available for future issuance under the 2010 Plan, respectively.

Options granted pursuant to the 2010 Plan generally vest over four years and vest at a rate of 25% upon the first anniversary of the vesting commencement date and 1/48th per month thereafter. Restricted stock units granted pursuant to the 2010 Plan vest on the first anniversary of the vesting commencement date.

The 2006 and 2010 Plans are intended to encourage ownership of stock by employees, consultants and non-employee directors of the Company and to provide additional incentives for them to promote the success of the Company s business. The board of directors is responsible for determining the individuals to receive equity grants, the number of shares subject to each grant, the exercise price per share and the exercise period of each option. The Company satisfies option exercises through issuance of new shares.

During 2010, the Company adopted the 2010 Employee Stock Purchase Plan (The Purchase Plan), which allows employees to purchase shares of the Company s common stock during a specified offering period. The purchase price is 85% of the lower of the closing price of the stock on the first day of the offering period or the closing price of the stock on the date of purchase. Eligible employees may elect to withhold up to 20% of their compensation during any offering period for the purchase of stock up to a maximum of 20,000 shares per purchase period. At December 31, 2011 and 2010, a total of 577,852 and 500,000 shares of common stock are reserved for issuance under the Purchase Plan, respectively. The length of the offering period is determined by the compensation committee and may be up to 27 months long. The first offering period under the Purchase Plan is from June 1, 2011 through May 31, 2012 with two purchase periods of six months each. A total of 172,148 shares were purchased under the Purchase Plan in November 2011.

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Information with respect to the number and weighted average exercise price of stock options and restricted stock units under the 2006 and 2010 Plans is summarized as follows (number of shares in thousands):

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2010	1,479	$ 3.35		
Granted	2,200	$ 4.36		
Exercised	(79)	$ 1.37		
Canceled/Forfeited	(83)	$ 4.25		
Outstanding at December 31, 2011	3,517	$ 4.01	9	$ 127
Exercisable at December 31, 2011 (1)	1,246	$ 3.58	8	$ 91
Vested at December 31, 2011	3,356	$ 4.00	9	$ 124

(1) Includes awards with early exercise provisions that permit optionee to exercise unvested options.

The intrinsic values above represent the aggregate value of the total pre-tax intrinsic value based upon a common stock price of $2.22 and $5.67 at December 31, 2011 and 2010, respectively, and the contractual exercise prices. At December 31, 2011, the weighted average fair value of options outstanding was $4.01 per share.

	Years Ended December 31,		
	2011	2010	2009
Weighted-average grant date fair value	$ 2.88	$ 11.52	$ 3.30
Aggregate intrinsic value of options exercised	$ 226,000	$ 61,000	$ 256,000
Total fair value of shares vested	$ 2,340,000	$ 660,000	$ 414,000

Stock-Based Compensation

The Company uses the Black-Scholes option-pricing model for determining the estimated fair value and 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:

	Year Ended December 31,		
	2011	2010	2009
Stock Options			
Risk free interest rate	1.2% to 2.6%	1.7% to 2.3%	2.3% to 2.8%
Expected term	5.1 to 6.1 years	5.0 to 6.1 years	5.0 to 6.1 years
Expected volatility	72.3% to 89.7%	90.8% to 96.0%	105.6% to 107.6%
Expected dividend yield	0.0%	0.0%	0.0%
Employee Stock Purchase Plan			
Risk free interest rate	0.05% to 0.11%	N/A	N/A
Expected term	0.5 to 1.0 years	N/A	N/A
Expected volatility	75.2% to 77.1%	N/A	N/A
Expected dividend yield	0.0%	N/A	N/A

The risk-free interest rate assumption was based on the rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the award being valued. The assumed dividend yield was based on the Company s expectation of not paying dividends in the foreseeable future. The weighted average

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expected term of options was calculated using the simplified method as prescribed by accounting guidance for stock-based compensation. This decision was based on the lack of relevant historical data due to the Company s limited historical experience. In addition, due to the Company s limited historical data, the estimated volatility was calculated based upon the historical volatility of comparable companies whose share prices are publicly available.

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

	Year Ended December 31,		
	2011	2010	2009
Cost of sales	$ 137	$ 105	$ 0
Research and development	768	393	310
Selling, general and administrative	3,904	2,009	716
Total	$ 4,809	$ 2,507	$ 1,026

As of December 31, 2011, there was approximately $10,345,000 of total unrecognized compensation costs related to outstanding options, which is expected to be recognized over a weighted average period of 2.92 years.

At December 31, 2011, all stock options outstanding to consultants were vested. In accordance with accounting guidance for stock-based compensation, the Company re-measured the fair value of stock option grants to non-employees at each reporting date and recognized the related income or expense during their vesting period. Expense recognized for stock options to consultants was immaterial for the years ended December 31, 2011, 2010 and 2009, respectively. Stock option expense for awards issued to consultants is included within research and development expense in the consolidated statement of operations.

9. Employee Benefit Plan

Effective February 1, 2007, the Company has established a defined contribution 401(k) plan (the Plan) for all employees who are at least 21 years of age. Employees are eligible to participate in the Plan beginning on the first day of the month following one month of employment. Under the terms of the Plan, employees may make voluntary contributions as a percentage of compensation. The Company s contributions to the Plan are discretionary, and no contributions have been made by the Company to date.

10. Income Taxes

The Company only recognizes tax benefits if it is more-likely-than-not to be sustained upon audit by the relevant taxing authority based upon its technical merits. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained.

The following table summarizes the activity related to the Company s unrecognized tax benefits (in thousands):

	December 31,	
	2011	2010
Beginning balance of unrecognized tax benefits	$ 562	0
Gross increases based on tax positions related to current year	116	85
Gross increases based on tax positions related to prior year	0	477
Settlements with taxing authorities	0	0
Expiration of statute of limitations	0	0
Ending balance of unrecognized tax benefits	$ 678	$ 562

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The Company s policy is to recognize interest and/or penalties related to income tax matters in income tax expense. The Company had no accrued interest or penalties on the consolidated balance sheets at December 31, 2011 and 2010 and has recognized no interest and/or penalties in the consolidated statements of operations through the year ended December 31, 2011.

The Company is subject to taxation in the U.S. and state jurisdictions. The Company s tax years for 2006 and forward can be subject to examination by the United States and state tax authorities due to the carry forward of net operating losses.

At December 31, 2011, the Company had available federal and state income tax net operating loss carryforwards of approximately $93,009,000 and $117,385,000, respectively. The federal tax loss carryforwards will begin expiring in 2026 unless previously utilized, and the state tax loss carryforwards will begin expiring in 2021 unless previously utilized. In addition, the Company has federal and California research and development income tax credit carryforwards of $310,000 and $1,687,000, 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.

The Company has completed an analysis under Internal Revenue Service Code (IRC) Sections 382 and 383 to determine if the Company s net operating loss carryforwards and research and development credits are limited due to a change in ownership. The Company has determined that as of December 31, 2011 the Company had two ownership changes. The first ownership change occurred in August 2006 upon the issuance of the Series A-1 convertible preferred. As a result of this ownership change, the Company has reduced its net operating loss carryforwards by $1,900,000 and research and development income tax credits by $8,000. The Company has determined that as of December 31, 2011, the Company had a second ownership change as defined by IRC Sections 382 and 383, which occurred in September 2011 upon the issuance of common stock in its follow-on offering. As a result of the second ownership change, the Company has reduced its federal net operating loss carryforwards as of December 31, 2010 by $83,503,000 and research and development income tax credits as of December 31, 2010 by $2,203,000. The Company also reduced its California net operating loss carryforwards as of December 31, 2010 by $46,243,000 as a result of the second ownership change. Pursuant to IRC Section 382 and 383, use of the Company s net operating loss and research and development income tax credit carryforwards may be limited in the event of a future cumulative change in ownership of more than 50% within a three-year period.

The reconciliation of income tax computed at the Federal statutory tax rate to the expense (benefit) for income taxes is as follows:

	December 31,		
	2011	2010	2009
Tax at statutory rate	$ (28,530)	$ (25,008)	$ (16,825)
State taxes, net of federal benefit	(2,780)	(2,953)	(1,965)
Change in valuation allowance	(16,807)	27,968	15,055
Section 382 limitation	45,728	0	0
Permanent Interest Disallowed	(70)	526	3,811
Credits and other	2,450	(523)	(76)
	$ (9)	$ 10	$ 0

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Significant components of the Company s deferred tax assets as of December 31, 2011 and 2010 are listed below. A valuation allowance of $58,359,000 and $75,166,000 for the years ended December 31, 2011 and 2010, respectively, has been established to offset the deferred tax assets as realization of such assets is uncertain. The components of the deferred tax assets are as follows (in thousands):

	December 31,	
	2011	2010
Deferred tax assets:		
Net operating losses	$ 38,357	$ 62,364
Capitalized research and development	7,901	0
Accrued expenses	3,728	2,358
Deferred Revenue	3,169	6,684
Research and development	1,078	2,241
Inventory reserve and UNICAP	983	914
Allowance for doubtful accounts	964	0
Depreciation and amortizaiton	824	101
Other, net	1,355	504
Total deferred tax assets	58,359	75,166
Less valuation allowance	(58,359)	(75,166)
Net deferred tax assets	$ 0	$ 0

The Company received a benefit of $9,000 in income tax expense for the year ended December 31, 2011 related to taxable income generated by its wholly-owned subsidiary Zogenix Europe Limited.

11. Summarized Quarterly Data (Unaudited)

The following financial information reflects all adjustments, which include only normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the consolidated financial results of the interim periods. Summarized quarterly data for the years ended December 31, 2011 and 2010 are as follows:

	Fiscal 2011 Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
	(in thousands, except per share amounts)			
Revenue	$ 9,040	$ 10,237	$ 10,398	$ 7,901
Cost of Sales	$ 4,875	$ 3,975	$ 5,482	$ 4,961
Gross Profit	$ 4,165	$ 6,262	$ 4,916	$ 2,940
Net loss	$ (18,983)	$ (19,177)	$ (22,038)	$ (23,705)
Net loss per share, basic and diluted	$ (0.56)	$ (0.56)	$ (0.59)	$ (0.36)
Weighted-average shares outstanding, basic and diluted	33,973	34,018	37,320	65,215

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	Fiscal 2010 Quarter Ended (1)			
	March 31,	June 30,	September 30,	December 31,
	(in thousands, except per share amounts)			
Revenue	$ 2,444	$ 5,135	$ 7,059	$ 8,804
Cost of Sales	$ 2,092	$ 3,210	$ 2,932	$ 4,612
Gross Profit	$ 352	$ 1,925	$ 4,127	$ 4,192
Net loss	$ (21,466)	$ (27,839)	$ (22,124)	$ (2,135)
Net loss per share, basic and diluted	$ (16.69)	$ (20.65)	$ (16.00)	$ (0.17)
Weighted-average shares outstanding, basic and diluted	1,286	1,348	1,383	12,584

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SCHEDULE II VALUATION AND QUALIFYING ACCOUNTS (in thousands):

	Balance at Beginning of Year	Additions Charged to Expense	(Deductions)	Balance at End of Year
Inventory reserves:				
2011	$ 1,681	$ 1,887	$ (1,909)	$ 1,659
2010	$ 2,497	$ 1,401	$ (2,217)	$ 1,681

3. *Exhibits.*

See Item 15(b) below.

(b) Exhibits:

(c) Financial Schedules:

See Item 15(a)(2) above.

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SIGNATURES

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

ZOGENIX, INC.

Date: March 12, 2012 By: /s/ Roger L. Hawley
Chief Executive Officer

Date: March 12, 2012 By: /s/ Ann D. Rhoads
Executive Vice President, Chief Financial Officer, Treasurer and Secretary

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Roger L. Hawley **Roger L. Hawley**	Chief Executive Officer and Director (Principal Executive Officer)	March 12, 2012
/s/ Ann D. Rhoads **Ann D. Rhoads**	Executive Vice President, Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer)	March 12, 2012
/s/ Cam L. Garner **Cam L. Garner**	Chairman of the Board	March 12, 2012
/s/ James C. Blair, Ph.D. **James C. Blair, Ph.D.**	Director	March 12, 2012
/s/ Louis C. Bock **Louis C. Bock**	Director	March 12, 2012
/s/ Stephen J. Farr, Ph.D. **Stephen J. Farr, Ph.D.**	President, Chief Operating Officer and Director	March 12, 2012
/s/ Mark Wiggins **Mark Wiggins**	Director	March 12, 2012
/s/ Erle T. Mast **Erle T. Mast**	Director	March 12, 2012

/s/ Arda M. Minocherhomjee, Ph.D. **Arda M. Minocherhomjee, Ph.D.**	Director	March 12, 2012
/s/ Kurt C. Wheeler **Kurt C. Wheeler**	Director	March 12, 2012

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EXHIBIT INDEX

Exhibit Number	Description
3.1(3)	Fifth Amended and Restated Certificate of Incorporation of the Registrant
3.2(3)	Amended and Restated Bylaws of the Registrant
4.1(4)	Form of the Registrant s Common Stock Certificate
4.2(1)	Third Amended and Restated Investors Rights Agreement dated December 2, 2009
4.3(1)	Amendment to Third Amended and Restated Investors Rights Agreement dated July 1, 2010
4.4(5)	Second Amendment to Third Amended and Restated Investors Rights Agreement dated June 30, 2011
4.5(1)	Warrant dated March 5, 2007 issued by the Registrant to General Electric Capital Corporation
4.6(1)	Warrant dated June 30, 2008 issued by the Registrant to Oxford Finance Corporation
4.7(1)	Warrant dated June 30, 2008 issued by the Registrant to CIT Healthcare LLC (subsequently transferred to The CIT Group/Equity Investments, Inc.)
4.8(1)	Transfer of Warrant dated March 24, 2009 from CIT Healthcare LLC to The CIT Group/Equity Investments, Inc.
4.9(1)	Warrant dated July 1, 2010 issued by the Registrant to Oxford Finance Corporation
4.10(1)	Warrant dated July 1, 2010 issued by the Registrant to Silicon Valley Bank
4.11(5)	Warrant dated June 30, 2011 issued by the Registrant to Oxford Finance LLC
4.12(5)	Warrant dated June 30, 2011 issued by the Registrant to Silicon Valley Bank
4.13(5)	Warrant dated July 18, 2011 issued by the Registrant to Cowen Healthcare Royalty Partners II, L.P.
10.1(3)	Form of Director and Executive Officer Indemnification Agreement
10.2#(1)	Form of Executive Officer Employment Agreement
10.3#(1)	2006 Equity Incentive Plan, as amended, and forms of option agreements thereunder
10.4#(3)	Independent Director Compensation Policy
10.5#(3)	2010 Equity Incentive Award Plan and forms of option and restricted stock agreements thereunder
10.6#(3)	2010 Employee Stock Purchase Plan and form of Offering document thereunder
10.7#(1)	Executive Officer Employment Agreement dated March 1, 2010 by and between the Registrant and Ann D. Rhoads
10.8 (1)	Supply Agreement dated September 29, 2004 by and between the Registrant and Dr. Reddy s Laboratories, Inc.
10.9 (1)	Asset Purchase Agreement dated August 25, 2006 by and between the Registrant and Aradigm Corporation
10.10(1)	Lease dated October 31, 2006 by and between the Registrant and Emery Station Joint Venture, LLC
10.11(1)	First Amendment to Lease dated July 10, 2007 by and between the Registrant and Emery Station Joint Venture, LLC
10.12(1)	Second Amendment to Lease dated October 20, 2009 by and between the Registrant and Emery Station Joint Venture, LLC
10.13(1)	Consent to Assignment Agreement dated August 29, 2008 by and among the Registrant, R.B. Income Properties and Verus Pharmaceuticals, Inc. and related Lease dated February 2, 2005 by and between R.B. Income Properties and Verus Pharmaceuticals, Inc.
10.14 (1)	License Agreement dated November 27, 2007 by and between the Registrant and Elan Pharma International Limited

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Exhibit Number	Description
10.15 (1)	First Amendment to License Agreement dated September 28, 2009 by and between the Registrant and Elan Pharma International Limited
10.16 (3)	Licensing and Distribution Agreement dated March 14, 2008 by and between the Registrant and Desitin Arzneimittel GmbH
10.17 (3)	Manufacturing Services Agreement dated November 1, 2008 by and between the Registrant and Patheon U.K. Ltd.
10.18 (1)	Commercial Manufacturing and Supply Agreement dated April 1, 2009 by and between the Registrant and MGlas AG
10.19 (3)	Co-Promotion Agreement dated July 31, 2009 by and between the Registrant and Astellas Pharma US, Inc.
10.20#(2)	General Release of Claims dated August 13, 2010 by and between the Registrant and Jennifer D. Haldeman
10.21 (2)	Second Amended and Restated Loan and Security Agreement dated October 8, 2010 by and among the Registrant, Oxford Finance Corporation and Silicon Valley Bank
10.22 (5)	First Amendment to Second Amended and Restated Loan and Security Agreement dated June 30, 2011 by and among the Registrant, Oxford Finance LLC and Silicon Valley Bank
10.23 (5)	Financing Agreement dated June 30, 2011 by and between the Registrant and Cowen Royalty Healthcare Partners II, L.P.
10.24(5)	Stock and Warrant Purchase Agreement dated June 30, 2011 by and between the Registrant and Cowen Royalty Healthcare Partners II, L.P.
10.25 (5)	Development and License Agreement dated July 11, 2011 by and between the Registrant and Durect Corporation
10.26#(5)	2011 Annual Incentive Plan
10.27	Amendment to Co-Promotion Agreement dated December 20, 2011 by and between the Registrant and Astellas Pharma US, Inc.
21.1(6)	Subsidiaries of the Registrant.
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm
24.1	Power of Attorney (reference is made to the signature page of this report)
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
32.1	Certification of Chief Executive Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
32.2	Certification of Chief Financial Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
101	The following financial statements from Zogenix, Inc. s Annual Report on Form 10-K for the year ended December 31, 2011, filed on March 12, 2012, formatted in XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statements of Cash Flows, and (iv) the Notes to Consolidated Financial Statements, tagged as blocks of text.

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(1) Filed with the Registrant s Registration Statement on Form S-1 on September 3, 2010 (Registration No. 333-169210).
(2) Filed with Amendment No. 1 to Registrant s Registration Statement on Form S-1 on October 12, 2010 (Registration No. 333-169210).
(3) Filed with Amendment No. 2 to Registrant s Registration Statement on Form S-1 on October 27, 2010 (Registration No. 333-169210).
(4) Filed with Amendment No. 3 to the Registrant s Registration Statement on Form S-1 on November 4, 2010 (Registration No. 333-169210).
(5) Filed with the Registrant s Quarterly Report on Form 10-Q on August 11, 2011.
(6) Filed with the Registrant s Annual Report on Form 10-K on March 4, 2011.
Confidential treatment has been granted for portions of this exhibit. These portions have been omitted from the Registration Statement and filed separately with the Securities and Exchange Commission
Confidential treatment has been requested for portions of this exhibit. These portions have been omitted and submitted separately to the Securities and Exchange Commission.
# Indicates management contract or compensatory plan.

(b) Financial Statement Schedules

Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.