ZOGENIX, INC.
Form 10-K
March 15, 2013
Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

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Form 10-K

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(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, 2012

or

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

For the transition period from to

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Commission file number: 001-34962

Zogenix, Inc.
(Exact Name of Registrant as Specified in its Charter)

| | |
|---|---|
| Delaware | 20-5300780 |
| (State or Other Jurisdiction of Incorporation or Organization) | (I.R.S. Employer Identification No.) |
| 12400 High Bluff Drive, Suite 650<br>San Diego, California | 92130 |
| (Address of Principal Executive Offices) | (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 x Non-accelerated filer o 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, 2012, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $90,904,936, based on the closing price of the registrant's common stock on the Nasdaq Global Market of $2.48 per share.

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of March 1, 2013 was 100,808,601.

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 2013 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, 2012.

Table of Contents

ZOGENIX, INC.
FORM 10-K — ANNUAL REPORT
For the Fiscal Year Ended December 31, 2012
Table of Contents

Table of Contents

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 statements include, but are not limited to, statements about:

- our ability to maintain and increase market demand for, and sales of, Sumavel DosePro;
- our ability to successfully execute our sales and marketing strategy for the commercialization of Sumavel DosePro;
- the progress and timing of clinical trials for our product candidates;
- the potential for the FDA to approve the NDA for Zohydro ER despite the advisory committee's recommendation against approval;
- the timing of submissions to, and decisions made by, the FDA and other regulatory agencies, including foreign regulatory agencies, and demonstrating the safety and efficacy of Zohydro ER or any other product candidates to the satisfaction of the FDA and such other agencies;
- adverse side effects or inadequate therapeutic efficacy of Sumavel DosePro that could result in product recalls, market withdrawals or product liability claims;
- the safety and efficacy of Zohydro ER and our other product 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 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,” “p “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “ongoing” or the negative of these terms or otl comparable terminology, although not all forward-looking statements contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. We discuss many of these risks, uncertainties and other factors in this 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 ER, 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

Table of Contents

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 Source Healthcare Analytics, 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 ER™ 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.

Table of Contents

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. We commercialize Sumavel DosePro through our internal sales and marketing organization and in collaboration with Mallinckrodt LLC, our co-promotion partner.

Our lead product candidate, Zohydro™ ER (hydrocodone bitartrate, formerly ZX002) is a 12-hour extended-release formulation of hydrocodone without acetaminophen for the treatment of moderate to severe chronic pain requiring around-the-clock opioid therapy. We completed Phase 3 development of Zohydro ER in 2011, and we submitted the New Drug Application, or NDA, for Zohydro ER to the FDA in May 2012. In July 2012, the FDA accepted our NDA as being sufficiently complete for a full review and assigned a Prescription Drug User Fee Act, or PDUFA, target action date of March 1, 2013. In December 2012, an advisory committee convened by the FDA voted 2-11 (with 1 abstention) against the approval of Zohydro ER. The advisory committee provides the FDA with independent expert advice and recommendations; however, the final decision regarding approval is made by the FDA. In February 2013, the FDA informed us that we were unlikely to receive an action letter for our NDA for Zohydro ER by the PDUFA target action date of March 1, 2013. The FDA has not provided us with information as to the reason for the delay, but has indicated that the delay would likely be brief and may last only several weeks. We have not been informed of any deficiencies in the NDA for Zohydro ER during the review process to date.

Sumavel DosePro and Zohydro ER, if approved, 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 serves 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 over 29.5 million people in the United States, according to the National Headache Foundation, or NHF, website. Triptans are the class of drugs most often prescribed for treating migraines. In the United States in the 12 months ended December 2012, triptans generated sales of approximately $4.4 billion and sumatriptan, including branded and generic forms, represented the largest market share of the seven approved triptans, with sales of approximately $2.6 billion, according to Source Healthcare Analytics (Source® PHAST Institutional Prescription January 2012 - December 2012).

We launched the commercial sale of Sumavel DosePro in the United States in January 2010 with our original co-promotion partner, Astellas Pharma US, Inc., or Astellas. Our collaboration with Astellas terminated on March 31, 2012, at which time we assumed full responsibility for the commercialization of Sumavel DosePro. In August 2012, Mallinckrodt began promoting Sumavel DosePro to a mutually agreed prescriber audience in the United States under our co-promotion agreement, pursuant to which we granted to Mallinckrodt a co-exclusive right (with us) to promote Sumavel DosePro to a mutually agreed prescriber audience in the United States. Mallinckrodt has committed to a minimum number of sales representatives for the initial term of the co-promotion agreement.

Sumavel DosePro has demonstrated quarterly growth in total prescriptions since its launch in January 2010. For the twelve months ended December 31, 2012, we recognized $35.9 million in net product revenue from sales of Sumavel DosePro, represented by more than 83,000 aggregate dispensed prescriptions (Source® PHAST Prescription, January 2012 — December 2012). 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 82% since launch (Source® Dynamic Claims January 2010 — December 2012).

Table of Contents

We believe our lead product candidate, Zohydro ER, 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 ER 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 ER. 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 ER 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 ER from Alkermes in 2007.

The Institute of Medicine Report from the Committee on Advancing Pain Research, Care, and Education reported in 2011 that an estimated 116 million people in the United States are burdened with chronic pain, at a national economic cost of $560 to $635 billion annually. Chronic pain can be treated with both immediate-release and extended-release opioids. We define our target market for Zohydro ER as prescription, non-injectable codeine-based and extended-release morphine-based pain products. This market generated U.S. sales of approximately $14.0 billion for the year ended December 2012, based on average wholesale price, on approximately 216 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 131 million prescriptions. (Source® PHAST Prescription January 2012 - December 2012).

We are also developing Relday™, a proprietary, long-acting injectable formulation of risperidone using Durect's SABER™ controlled-release formulation technology through a development and license agreement with Durect Corporation. Risperidone is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. If successfully developed and approved, we believe Relday may be the first subcutaneous antipsychotic product that allows for once-monthly dosing. The existing long-acting injectable risperidone product achieved global net sales of $1.43 billion in 2012 with 69% 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 Durect's SABER controlled-release technology will allow Relday to be delivered subcutaneously 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. In May 2012, we filed an investigational new drug, or IND, application with the FDA. In July 2012, we initiated our first IND clinical trial for Relday. This Phase 1 clinical trial was a single-center, open-label, safety and pharmacokinetic trial of 30 patients with chronic, stable schizophrenia or schizoaffective disorder. We announced positive single-dose pharmacokinetic results from the Phase 1 clinical trial in January 2013. Adverse events in the Phase 1 trial in patients diagnosed with schizophrenia were generally mild to moderate and consistent with other risperidone products. Based on the favorable safety and pharmacokinetic profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, we extended the study to include an additional cohort of 10 patients at a 100 mg dose of the same formulation. The addition of this 100 mg dose to the study will enable evaluation of dose proportionality across the full dose range that would be anticipated to be used in clinical practice. Positive results from this study extension would better position us to begin a multi-dose clinical trial, which would provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies. We expect to complete the extension of the Phase 1 clinical trial during the second quarter of 2013. The development of Relday will first focus on its delivery by conventional needle and syringe in order to allow the administration of different volumes of the same formulation of Relday by a healthcare professional. We anticipate that the introduction of our DosePro needle-free technology for administration of Relday can occur later in development or as part of life cycle management after further work involving formulation development, technology enhancements and applicable regulatory approvals.

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. 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

Table of Contents

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 from launch through December 31, 2012 was $84.5 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 terminated in March 2012, and beginning in the second quarter of 2012, we assumed full responsibility for the continued commercialization of Sumavel DosePro, with a focus on headache specialists, neurologists and primary care physicians in the United States. In June 2012, we entered into the co-promotion agreement with Mallinckrodt to complement the efforts of our internal sales force, with Mallinckrodt beginning promotion efforts in August 2012.
- Developing and commercializing Zohydro ER for the treatment of moderate to severe chronic pain. If approved, Zohydro ER could be the first hydrocodone product to offer the benefit of less frequent dosing and the ability to treat chronic pain patients without the risk of liver injury associated with the use of acetaminophen in high dosages or over long periods of time. We completed our Phase 3 clinical program for Zohydro ER in 2011, 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 results from our pivotal Phase 3 efficacy trial in August 2011 and submitted the NDA for Zohydro ER to the FDA in May 2012. In July 2012, the FDA accepted our NDA as being sufficiently complete for a full review and assigned a PDUFA target action date of March 1, 2013. While there is a delay in the FDA providing an action letter for our NDA, the FDA indicated that the delay would likely be brief and may last only several weeks after the PDUFA target action date of March 1, 2013. If we receive FDA approval, we intend to explore commercial strategies including co-promotion and other partnering opportunities for Zohydro ER, and a staged expansion of our sales force to support broader reach to pain specialists for both Zohydro ER and Sumavel DosePro, and neurologists for Sumavel DosePro.
- Developing Relday for the treatment of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. We filed an IND application for Relday with the FDA in May 2012. In January 2012, we announced positive single-dose pharmacokinetic results from a Phase 1 clinical trial. Based on the favorable safety and pharmacokinetic profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, we extended the study to include an additional cohort of 10 patients at a 100 mg dose of the same formulation. The addition of this 100 mg dose to the study will enable evaluation of dose proportionality across the full dose range that would be anticipated to be used in clinical practice. We expect to complete the extension of the Phase 1 clinical trial during the second quarter of 2013. Our development of Relday will first focus on its delivery by conventional needle and syringe in order to allow the administration of different volumes of the same formulation of Relday by a healthcare professional. We anticipate that the introduction of our DosePro needle-free technology for administration of Relday can occur later in development or as part of life cycle management after further work involving formulation development, technology enhancements, and applicable regulatory approvals.
- Expanding our product pipeline in CNS disorders and/or pain. We are utilizing our proprietary DosePro technology to add to our internal product pipeline. We are 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 seeking and evaluating opportunities to capitalize on our DosePro needle-free drug delivery technology by out-licensing it to potential partners enabling them to enhance, differentiate or extend the life-cycle of their injectable products. In March 2012, we entered into a co-marketing and option agreement with Battelle Memorial Institute, or Battelle, pursuant to which we granted to Battelle the exclusive right to co-market our DosePro drug delivery technology to a specified list of Battelle's pharmaceutical clients.
- 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

Table of Contents

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 NHF website, 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.

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-HT1B and 5-HT1D receptors. Triptans presumably exert their antimigrainous effect through binding to vascular 5-HT1 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 2012.

U.S. Triptan Market
(12 months ended December 2012)

| Triptan Form | Sales (millions) | $ Share | | Doses (millions) | Dose Share | |
|---|---|---|---|---|---|---|
| Oral Tablet | $3,410 | 78.0 | % | 126.6 | 85.9 | % |
| Oral Melt | 473 | 10.8 | | 13.7 | 9.3 | |
| Nasal | 120 | 2.7 | | 2.9 | 2.0 | |
| Injectable | 371 | 8.5 | | 4.1 | 2.8 | |
| Total | $4,374 | 100 | % | 147.3 | 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 $2.6 billion (59% dollar share of the triptan market). Of that amount, the injectable forms of sumatriptan accounted for $371 million. By comparison, ergotamine agents, another class of drugs used for the acute treatment of migraine, including injectable DHE and Migranal, accounted for $87 million in sales in the United States during the same 12-month

Table of Contents

period. (Source® PHAST Institution/Prescription January 2012 - December 2012). Sumatriptan is the only triptan available to patients in the injectable form and, with the exception of Sumavel DosePro, all other forms of injectable sumatriptan make use of needle-based injections for their administration.

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

Migraine Market Dynamics

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

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

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

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

The following table compares the time to maximum drug concentration in blood, or Tmax, and pain relief of oral forms, including melts and tablets, and nasal forms of marketed triptans to sumatriptan injection. The data are derived from Prescribing Information for the different formulations of these marketed triptans and not for head-to-head direct comparison studies:

Triptan Prescribing Information Data

Table of Contents

| 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 | % |

(1) Other than Sumavel DosePro (sumatriptan injection), we have estimated one-hour pain relief data for all forms/products based on Kaplan-Meier plots included in each product's Prescribing Information of the probability over time of obtaining headache response following treatment.

(2) Range reflects headache relief data obtained in placebo controlled clinical studies, which include different doses of the same triptan.

(3) Represents pain relief at four hours.

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

Table of Contents

Some of these limitations are more pronounced depending on the type of migraine episode the patient is suffering. For example, when waking with a migraine already in progress, speed to onset of pain relief is important. In migraines with nausea and/or vomiting, a patient may not be able to ingest an oral treatment.

Despite its speed of onset and completeness of pain relief advantages over oral and nasal triptans, needle-based sumatriptan injection has been limited to less than 10% of the U.S. triptan market on a dollar basis and less than 5% on a total dose basis (Source® PHAST Institution/Prescription, January 2012 — December 2012). 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, GlaxoSmithKline's, or 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 370,000 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, 2012 (Source Healthcare Analytics, Source® PHAST Prescription, January 2012 — December 2012). 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. in 2007 on our behalf.

Our Solution: Sumavel DosePro

Sumavel DosePro is a pre-filled, single-use disposable, needle-free drug delivery system that subcutaneously delivers 6 mg of sumatriptan in 0.5 mL of sterile liquid. Sumavel DosePro was designed to be portable, intuitive and easy-to-use. To use, the patient simply snaps off a plastic tip, flips back a lever and presses the end of the delivery system to the skin of the abdomen or thigh. Under the force of a small amount of compressed nitrogen gas, the liquid form of sumatriptan is expelled out of the device as a thin jet of medication, which pierces the skin and selectively deposits into the subcutaneous tissue. This process occurs in less than 1/10th of a second.

Due to its unique attributes, Sumavel DosePro has the potential to expand the dosage share for injectable sumatriptan beyond the traditional needle-based forms because it reduces the barriers inherent in needle-based delivery systems to being prescribed by physicians and accepted by patients. Sumavel DosePro may provide patients with the following benefits when compared to alternative triptan formulations:

- Rapid, more complete, migraine pain relief. Sumavel DosePro can provide onset of migraine pain relief in as little as ten minutes for some patients, according to its Prescribing Information. The Prescribing Information for the product indicates that an average of 81% (vs. an average of 34% for placebo) of patients show pain relief at two hours following administration of Sumavel DosePro, and that 49% of patients were pain free within 1 hour (vs. 9% for placebo) and 64% were pain free within two hours (vs. 15% for placebo) following administration.
- Help for sufferers of morning migraines, fast onset migraine and migraines with vomiting. According to two studies published in the October 2006 issue of Clinical Therapeutics, 48% and 57% of patients with waking migraines were pain free at two hours (vs. 18% and 19% for placebo) following administration of sumatriptan injection. Subcutaneous sumatriptan is also as efficacious when administered early during a migraine attack as when the attack is full-blown. In addition, the pharmacokinetics of subcutaneously delivered sumatriptan is not affected by gastric stasis, nausea and/or vomiting.
- Help for triptan tablet non-responders. Clinical research published in the January 2007 issue of Journal of Headache and Pain suggests injectable sumatriptan provides relief in up to 90% of migraine patients who have not responded to

oral tablet triptans in at least two of their last three migraines. In this study, 43 patients who had failed to respond to oral triptans in at least two of their last three migraines were given sumatriptan injection for their next migraine. Of these patients, 91% reported pain relief at two hours, 56% reported being pain free at two hours and 32% reported sustained pain freedom through 24 hours following treatment of their first headache.

- Simplicity, through a new, convenient and easy-to-use option. Sumavel DosePro is based on our unique delivery system which was designed to be portable, intuitive and easy-to-use, and can be disposed following use without the need of a

Table of Contents

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

We continue to develop and execute a sophisticated and comprehensive commercialization strategy for Sumavel DosePro supported by a range of marketing programs. The 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 that should be added to the patient's treatment toolbox;
- 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, as well as providing a co-pay discount program to all qualifying patients.

In support of these strategic objectives, we are executing a variety of marketing programs to educate customers, which include a premier patient toolbox for new customers, direct-to-physician promotional materials, speaker 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

Table of Contents

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 Arzneimittel GmbH, or Desitin, a private German pharmaceutical company focused on the development, manufacturing and distribution of products for the treatment of CNS disorders, 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.

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 submitted an NDA supplement to the FDA to demonstrate the manufacturability and stability of the new dosage strength in January 2013. We anticipate commercializing the 4mg dosage strength in late 2013 to early 2014, 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 submitted a Prior Approval Supplement to the FDA regarding

Table of Contents

the implementation of this minor change, and in October 2012, the FDA issued a complete response letter, or CRL, requesting more information. We plan to meet with the FDA to discuss the CRL and any additional steps required to implement this improvement. The CRL has no impact on the currently marketed Sumavel DosePro product.

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.

Zohydro ER for the Treatment of Moderate to Severe Chronic Pain

Our lead product candidate, Zohydro ER (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 ER in 2011, and we submitted an NDA for Zohydro ER to the FDA in May 2012. In July 2012, the FDA accepted our NDA as being sufficiently complete for a full review and assigned a PDUFA target action date of March 1, 2013. In December 2012, an advisory committee convened by the FDA voted 2-11 (with 1 abstention) against the approval of Zohydro ER. The advisory committee provides the FDA with independent expert advice and recommendations; however, the final decision regarding approval is made by the FDA. In February 2013, the FDA informed us of a delay in providing an action letter for our NDA for Zohydro ER and indicated that the delay would likely be brief and may last only several weeks after the PDUFA target action date of March 1, 2013. We believe Zohydro ER 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 ER 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 ER. 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 ER, if approved, 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 ER is approved by the FDA, it will be subject to a Risk Evaluation and Mitigation Strategy, or REMS, program, with the goal to reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of the drug while maintaining patient access to pain medication. The REMS program is required to comply with FDA mandates and will be consistent with the REMS program for other extended release opioids. This program recognizes the abuse potential of opioids and lays out specific prescriber education materials and requires a medication guide for patients to facilitate appropriate prescribing, dispensing and use of extended release opioids. Zohydro ER, if approved, 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 ER will not qualify for automatic refills. We believe these restrictions will help facilitate more responsible prescribing of Zohydro ER 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. 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

Table of Contents

medicine or pain specialist. Physicians generally assess the patient and, if appropriate, start treatment with a trial of opioid therapy to determine the optimal opioid regimen. At this point, physicians commonly prescribe opioids, including products from the codeine and morphine classes. The general objective of the physician is to safely achieve adequate control of pain.

Physicians generally prefer to start patients on less potent opioids where possible. A trial of opioid therapy usually begins with short-acting doses taken on an as-needed basis. This allows the clinician and patient to assess the total opioid requirement. Patients taking substantial doses of short-acting opioids multiple times per day may find substitution of an extended-release agent, taken one to two times per day, extremely helpful to provide more constant pain relief. In theory, the more constant opioid blood levels of extended-release products may provide better pain relief and better sleep quality. Dosing intervals 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 2012, our target market, which we define as prescription non-injectable codeine-based and extended-release morphine-based pain products, generated sales of approximately $14.0 billion in the United States on approximately 216 million prescriptions. Of the $14.0 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 131 million prescriptions. (Source® PHAST Prescription January 2012 - December 2012).

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 (ten 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 announced that it would require manufacturers to update labels of all prescription combination acetaminophen products to warn of the potential risk for severe liver injury. Along with this announcement, the FDA issued letters to sponsors of prescription acetaminophen drugs proposing various modifications to the drug labeling, including adding a boxed warning for hepatoxicity. Within 30 days of the date of the letters, the holders of approved applications for prescription acetaminophen drugs were required to submit a supplemental NDA to the FDA proposing labeling changes that reflect the new safety information about acetaminophen and liver toxicity, or a statement detailing the reasons why such change would not be warranted. There are currently no approved products formulated with hydrocodone alone, and we believe Zohydro ER has the potential to fill this treatment gap.

Table of Contents

In January 2013, the FDA organized a meeting of the Drug Safety and Risk Management Advisory Committee to discuss the public health benefits and risks, including the potential for abuse of drugs containing hydrocodone either combined with other analgesics or as an antitussive, and the impact of rescheduling these hydrocodone products from Schedule III to Schedule II. Nineteen of the 29 Advisory Committee members voted in favor of recommending that products containing hydrocodone be reclassified from a Schedule III to a Schedule II controlled substance. The Advisory Committee's recommendation is for the FDA's consideration and is not binding on the FDA. Zohydro ER is currently designed as a Schedule II product.

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 ER

We believe that Zohydro ER, if approved, may provide patients and physicians with the following benefits when compared to existing opioid pain medications:

- Single-entity hydrocodone. Zohydro ER, if 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.
- Twelve hour exposure provides true around-the-clock relief when administered twice daily. Zohydro ER, via its unique extended-release profile, is designed to provide consistent relief of moderate to severe chronic pain over a 12-hour period per dose. Clinical studies have shown a pharmacokinetic profile that supports the expected extended relief profile of Zohydro ER. In addition, there are five other marketed products using SODAS technology that are

dosed every 24 hours, which we believe helps validate the controlled release technology underlying the formulation of Zohydro ER.

- Easier adherence/greater patient convenience. Because of its 12-hour dosing regimen, Zohydro ER 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 ER provides another option for physicians investigating new alternatives to offer patients who require medication rotation due to tolerance, side effects or poor pain control.

Table of Contents

Zohydro ER 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 was a randomized, 12-week, double-blind, placebo-controlled trial to evaluate the safety and efficacy of Zohydro ER for the treatment of moderate to severe chronic lower back pain in opioid-experienced adult subjects. Our trial utilized 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 ER and titrated to an effective dose of Zohydro ER 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 was the mean change in average daily pain intensity scores between Zohydro ER 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 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 ER 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 ER 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 ER 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 ER 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 ER 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 (≤2%) 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 ER 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 ER for up to 12 months of treatment. The study further demonstrated that Zohydro ER 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 was submitted as part of our NDA to the FDA in May 2012.

We have also initiated 2-year carcinogenicity studies in two animal species. We obtained FDA agreement on the protocols for both studies and have agreed with the FDA that these studies are an ongoing commitment and are not required for submission or approval of the NDA for Zohydro ER. In July 2012, the FDA accepted our NDA as being sufficiently complete for a full review and assigned a PDUFA target action date of March 1, 2013. In December 2012, an advisory committee convened by the FDA voted 2-11 (with 1 abstention) against the approval of Zohydro ER. The advisory committee provides the FDA with independent expert advice and recommendations; however, the FDA is not bound by the advisory committee's recommendations and the final decision regarding approval is made by the FDA. In February 2013, the FDA informed us that we were unlikely to receive an action letter for our NDA for Zohydro ER by the PDUFA target action date of March 1, 2013. The FDA has not provided us with information as to the reason for the delay, but has indicated that the delay would likely be brief and may last only several weeks. We have not been informed of any deficiencies in the NDA for Zohydro ER during the review process to date.

Prior Clinical Development of Zohydro ER

Our licensor for Zohydro ER, Alkermes, conducted pre-clinical and clinical studies of Zohydro ER under an IND initiated in 2002.

Phase 1 and Phase 2 Clinical Development. In single and multiple dose pharmacokinetic evaluations, Zohydro ER demonstrated detectable plasma concentrations of hydrocodone within 15 minutes of administration. Zohydro ER 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 ER has been tested under both fed and fasted conditions and the amount of drug

Table of Contents

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 ER displays a consistent, extended-release profile, dose-proportional pharmacokinetics and an acceptable safety profile.

Zohydro ER 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 ER 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 ER (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 ER 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 ER 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 ER.

The second Phase 2 study was a four week, multiple-dose, safety, tolerability and pharmacokinetic dose-escalation study of Zohydro ER in opioid-experienced adults with chronic, moderate to severe osteoarthritis pain. The primary objective was to assess the safety, tolerability and pharmacokinetics of Zohydro ER at steady state over a range of escalating daily doses. Thirty-seven patients in two dosing cohorts received escalating doses of Zohydro ER 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 ER into pivotal Phase 3 clinical studies.

Relday for the Treatment of Schizophrenia

Relday is a proprietary, long-acting injectable formulation of risperidone using Durect's SABER™ controlled-release formulation technology. If successfully developed and approved, we believe Relday may be the first subcutaneous antipsychotic product that allows for once-monthly dosing. We believe Durect's SABER controlled-release technology will allow Relday to be delivered subcutaneously 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. In May 2012, we filed an IND application with the FDA. In July 2012, we initiated our first IND clinical trial for Relday. This Phase 1 clinical trial was a single-center, open-label, safety and pharmacokinetic trial of 30 patients with chronic, stable schizophrenia or schizoaffective disorder. We announced positive single-dose pharmacokinetic results from the Phase 1 clinical trial on January 3, 2013. Adverse events in the Phase 1 trial in patients diagnosed with schizophrenia were generally mild to moderate and consistent with other risperidone products. Based on the favorable safety and pharmacokinetic profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, we extended the study to include an additional cohort of 10 patients at a 100 mg dose of the same formulation. The addition of this 100 mg dose to the study will enable evaluation of dose proportionality across the full dose range that would be anticipated to be used in clinical practice. Positive results from this study extension would better position us to begin a multi-dose clinical trial, which would provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies. We expect to complete

the extension of the Phase 1 clinical trial during the second quarter of 2013.

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 National Institute of Mental Health, or NIMH, estimated in 1993 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,

Table of Contents

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 estimated in 2005 that the average age of onset for bipolar disorder is 25 years, and the 12-month prevalence of bipolar disorder is 2.6% of the U.S. adult population. In many cases, the recurring episodes of mania and depression are so severe that the patient cannot maintain normal relationships or function normally at home, work or school, and suicide attempts occur in 25-50% of bipolar disorder patients.

First line therapy for most schizophrenia patients today are drugs generally known as atypical or second generation antipsychotics. These antipsychotics have been named atypical for their ability to treat a broader range of negative symptoms with improved side effect profiles versus the first-generation or typical antipsychotics, which were mostly introduced in the 1950s with drugs such as chlorpromazine and haloperidol. The first atypical antipsychotics to be approved by FDA in the United States were Clozaril (clozapine) in 1989, followed by Risperdal (risperidone) in 1993 and Zyprexa (olanzapine) in 1996. Similarly, over the last decade, atypical antipsychotics have become increasingly utilized in the treatment of bipolar disorder, either as monotherapy or as part of a polytherapy regimen, most often being prescribed in conjunction with a mood stabilizer such as lithium or valproic acid, and sometimes in conjunction with both a mood stabilizer and additional medications.

Patient compliance with medication has been a long-standing problem in the treatment of both schizophrenia and bipolar disorder. Results from the Clinical Antipsychotic Trials in Intervention Effectiveness conducted between 2001 and 2004, and published in The New England Journal of Medicine in 2005, indicated that over 70% of schizophrenia patients became non-compliant with their medication within 18 months of commencing therapy. Similarly a 2004 study of the VA National Psychosis Registry published in the journal Bipolar Disorder in October 2006 found that, of the 45% of bipolar patients who were being prescribed an antipsychotic, just over half of individuals appeared to be fully adherent with their antipsychotic medications, while the remaining individuals were either partially adherent or non-adherent with their antipsychotic medications.

In an attempt to improve patient compliance, physicians increasingly administer antipsychotic drugs through long-acting depot injections. Long-acting depot injections release medication slowly over weeks rather than over hours or days for conventional injections or oral medications, thereby dramatically reducing the number of times a patient needs to take their medication. Currently available long-acting injectable products include Risperdal Consta and Invega Sustenna, both marketed by Johnson & Johnson, and Zyprexa Relprevv, marketed by Eli Lilly & Co. These drugs provide two to four weeks of therapy per dose.

Overall, the global atypical antipsychotic market was estimated to be in excess of $17.1 billion in 2011, based upon published sales reports of certain pharmaceutical companies. In 2012, atypical antipsychotics comprised approximately 91% of all antipsychotic prescriptions in the United States, according to data from Source Healthcare Analytics (Source® PHAST Prescription, January 2012 — December 2012). The existing long-acting injectable risperidone product, Risperdal Consta, achieved global net sales of $1.4 billion in 2012, according to industry reports, and has a wholesale acquisition cost of approximately $286 per bi-weekly dose, or more than $500 per month, for the 25 mg dosage strength (Source: Gold Standard). Finally, in the United States, prescribers of long-acting antipsychotics are highly concentrated with approximately 16,600 total prescribers of long-acting injectable products, including approximately 9,600 psychiatrists in 2012 (Source® PHAST Prescription, January 2012 — December 2012).

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 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

Table of Contents

Durect's SABER technology, Relday has been designed to be administered subcutaneously with injection volumes of 0.5 mL to 1.0 mL.

- No reconstitution: Relday is formulated as a pre-filled, 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 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 2012 (Source® PHAST Prescription, January 2012 — December 2012).
- Potential Needle-free delivery: 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. The development of Relday will first focus on its delivery by conventional needle and syringe in order to allow the administration of different volumes of the same formulation of Relday by a healthcare professional. We anticipate that the introduction of our DosePro needle-free technology for administration of Relday can occur later in development or as part of life cycle management after further work involving formulation development, technology enhancements, and applicable regulatory approvals.

We 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. We acquired the DosePro technology and related intellectual property from Aradigm in August 2006. 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. in 2007, 76% of patients indicated that they preferred the Sumavel DosePro 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. in 2006 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

Table of Contents

version will sound like the click of a pen upon drug delivery. We submitted a Prior Approval Supplement to the FDA regarding the implementation of this minor change, and the FDA issued a CRL requesting more information. We plan to meet with the FDA to discuss the CRL and any additional steps required to implement this improvement. The CRL has no impact on the currently marketed Sumavel DosePro product.

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 and pharmacodynamic equivalence study using granulocyte colony-stimulating factor. 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.

We are building our internal product pipeline by investigating proven drugs that can be paired with DosePro to enhance their benefits and commercial attractiveness. 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 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. In March 2012, we entered into a co-marketing and option agreement with Battelle Memorial Institute, or Battelle, pursuant to which we granted to Battelle the exclusive right to co-market our DosePro drug delivery technology to a specified list of Battelle's pharmaceutical clients.

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. As of December 31, 2012, our sales and marketing organization is comprised of 103 professionals, which includes approximately 85 field sales personnel. Our field sales force 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 personnel have an average of approximately 14 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 10 years of sales management experience. Each of our sales representatives and regional

business directors undergoes a formal training program focused on disease background, our product, competitive products and territory management, as well as compliance with applicable laws. Our training program also includes significant ongoing and field-based learning to provide a comprehensive understanding and perspective as to our markets and disease states and the needs of both physicians and patients.

In addition to our field sales team, we also have an experienced team of field-based managed markets and trade directors. This team works closely with our regional business directors to engage with third-party payors to ensure and expand reimbursement coverage and patient access for our product and implement pharmacy based educational programs. To date, we have entered into a number of contracts with private health insurers, managed care organizations, government entities and other third-party payors that provide coverage for our products.

Table of Contents

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 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 terminated on March 31, 2012, at which time we assumed full responsibility for the commercialization of Sumavel DosePro. We have expanded the focus of our existing sales force to include targeting a portion of the high-prescribing primary care physicians that were previously part of the Astellas Segment. In June 2012, we entered into a co-promotion agreement with Mallinckrodt, pursuant to which we granted to Mallinckrodt a co-exclusive right (with us) to promote Sumavel DosePro to a mutually agreed prescriber audience in the United States. Mallinckrodt began promoting Sumavel DosePro in August 2012 and has committed to a minimum number of sales representatives for the initial term of the co-promotion agreement.

In March 2008, we entered into a licensing and distribution agreement with Desitin. 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.

For the launch of Zohydro ER, 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 100 and 200 representatives, to support broader reach to pain specialists for both Zohydro ER and Sumavel DosePro, and neurologists for 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 ER to reach a broader physician audience. We are seeking and evaluating 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 & Co., and Pfizer, Inc. in the United States.

Table of Contents

We also face competition from generic sumatriptan injectable, now marketed in the United States as an authorized generic of Imitrex STATdose by Par Pharmaceutical Companies and Sandoz Inc. (a Novartis AG company). In addition, 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, Merck and Allergan, Inc. and smaller companies such as OptiNose AS, Inc. In addition, Allergan, is now marketing BOTOX botulinum toxin for the treatment of chronic migraine, and Nupathe, Inc. received FDA approval for its migraine patch, Zecuity, in January 2013.

Zohydro ER

If approved for the treatment of moderate to severe chronic pain, Zohydro ER will compete against other marketed branded and generic pain therapeutics and may compete with additional product candidates currently under development or developed in the future. Current competitors in the opioid pain therapeutics space include, but are not limited to, Abbott Laboratories, 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 ER 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. In March 2013, the FDA approved Abilify Maintena, a once-monthly depot formulation of apripiprazole from Otsuka Pharmaceutical Co, Ltd. and H. Lundbeck A/S. Currently approved and marketed oral atypical antipsychotics include Risperdal (risperidone) and Invega (paliperidone) marketed by Johnson & Johnson, generic risperidone, Zyprexa (olanzapine) marketed by Eli Lilly and Company, Seroquel (quetiapine) marketed by AstraZeneca plc, Abilify (aripiprazole) marketed by BMS/Otsuka Pharmaceutical Co., Ltd., Geodon (ziprasidone) marketed by Pfizer, Fanapt (iloperidone) marketed by Novartis AG, Saphris (asenapine) marketed by Merck, 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, NuPathe 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 AG. 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

Table of Contents

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. Two wholesale pharmaceutical distributors, Cardinal Health, Inc. and McKesson Corporation, individually comprised 36.1% and 35.5%, respectively, of our total gross sales of Sumavel DosePro for the year ended December 31, 2012.

We use a third-party logistics provider, Cardinal Health 105, Inc. (a/k/a Specialty Pharmaceutical Services), for key services related to logistics, warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management and call center management. In addition, we utilize third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services.

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 2013. 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 2014 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 ER 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. Further, an affiliate of Alkermes, Alkermes Pharma Ireland Limited, or APIL, will be the exclusive manufacturer and supplier (subject to certain exceptions) for Zohydro ER, if approved for commercialization, under the terms of our commercial manufacturing and supply agreement described 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 £311,000, or approximately $502,000 (based on the exchange rate as of December 31, 2012), over the remaining term of the

agreement, aggregating to £3,111,000, or approximately $5,025,000, 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

Table of Contents

service fees increasing if annual production exceeds a specified volume. The agreement has an initial five-year term, which expires October 31, 2013.

In February 2013, we entered into an additional manufacturing services agreement, or the amended services agreement, with Patheon which will replace the Company's original manufacturing services agreement upon its expiration on October 31, 2013. The amended services agreement has similar terms to the original agreement and will expire on April 30, 2015. The parties may mutually agree in writing to renew the term for additional terms prior to the expiration of the then-current term.

Under both the original manufacturing services agreement and the amended services agreement, either party may terminate the agreement (1) upon specified written notice to the other party, (2) upon written notice if the other party has failed to remedy a material breach of any of its representations, warranties or other obligations under the agreement within a specified period following receipt of written notice of such breach, and (3) immediately upon written notice to the other party in the event that the other party is declared insolvent or bankrupt by a court of competent jurisdiction, a voluntary petition of bankruptcy is filed in any court of competent jurisdiction by such other party or the agreement is assigned by such other party for the benefit of creditors. Patheon may also terminate the agreement upon specified written notice if we assign the agreement to certain specified parties.

Nypro Limited

Nypro Limited, located in Bray, Ireland, manufactures the actuator assemblies and injection molded components for our DosePro device pursuant to purchase orders. We do not currently have a long-term commercial supply agreement with Nypro.

Nipro Glass, Germany AG (formerly MGlas AG)

In May 2009, we entered into a commercial manufacturing and supply agreement with Nipro Glass, Germany AG, or Nipro Glass, located in Munnerstadt, Germany. Under the terms of the agreement, Nipro Glass 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 had an initial three-year term, which expired in May 2012. Although the commercial manufacturing and supply agreement with Nipro Glass expired in May 2012, we have continued to exclusively purchase glass capsule from Nipro Glass under the expired agreement terms. We are currently negotiating an extension of the commercial manufacturing and supply agreement with Nipro Glass to continue the exclusive supply of the glass capsule.

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.

Alkermes Pharma Ireland Limited

In November 2012, we entered into a commercial manufacturing and supply agreement for Zohydro ER finished commercial product with APIL. Under the agreement, APIL will be the exclusive manufacturer and supplier to us (subject to certain exceptions) of Zohydro ER. We must purchase all of our requirements of Zohydro ER, subject to certain exceptions, from APIL.

Under the agreement, we will provide APIL with an 18 month forecast on a monthly basis and with a three-year forecast on an annual basis for commercial supply requirements of Zohydro ER. In each of the four months following the submission of the 18-month forecast, we are obligated to order the quantity of Zohydro ER specified in the forecast. APIL will use commercially reasonable efforts to supply the orders of Zohydro ER subject to the availability of the DEA quota for hydrocodone. APIL is not obligated to supply us with quantities of Zohydro ER in excess of forecasted amounts, but has agreed

Table of Contents

to use commercially reasonable efforts to do so. Further, we are obligated to purchase at least 75% of forecasted quarterly quantities of Zohydro ER from APIL, and are required to make compensatory payments if we do not purchase 100% of our requirements from APIL, subject to certain exceptions.

If a failure to supply occurs under the agreement, other than a force majeure event, APIL must use commercially reasonable efforts to assist us in transferring production of Zohydro ER to either us or a third-party manufacturer, provided that such third party is not a technological competitor of APIL. In a failure to supply circumstance, we would be able to utilize (or sublicense to a third party who is not a technological competitor of APIL) the manufacturing license rights granted to us in the license agreement with Alkermes, until such time as APIL can resume supply of Zohydro ER.

Either party may terminate the agreement 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. Unless otherwise terminated due to a material breach, the agreement will continue until the expiry or termination of the license agreement with Alkermes described below.

Collaborations, Commercial and License Agreements

Mallinckrodt LLC Co-Promotion Agreement

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

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

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

We may terminate the agreement with 60 days' written notice if Mallinckrodt does not achieve an agreed-upon minimum sales effort.

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

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 agreement, whereby the agreement terminated on March 31, 2012. Under the terms of the agreement, we were responsible for the manufacture, supply and distribution of

Table of Contents

commercial product for sale in the United States. In addition, we supplied product samples to Astellas, 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 fell outside the Astellas Segment. In addition, our representatives 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 amended 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 professionals within the Astellas Segment pursuant to a promotion transition plan. We then assumed full responsibility for the commercialization of Sumavel DosePro following termination of the agreement in March 2012.

Under the agreement, Astellas paid us upfront and milestone payments in an aggregate amount of $20.0 million. Astellas is not obligated to pay us any additional milestone payments. In consideration for Astellas' performance of its commercial efforts, we were required to pay Astellas a service fee on a quarterly basis that represents a fixed percentage of between 45% and 55% of Sumavel DosePro net sales to the Astellas Segment. Astellas was not compensated for Sumavel DosePro sales to neurologists, any other prescribers not included in the Astellas Segment or for non-retail sales. In addition, following completion of the co-promotion term in March 2012, we are 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 during the 12 months ending March 31, 2012.

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 are responsible for the clinical development and commercialization of Relday. Durect is 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.

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.

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,

Table of Contents

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 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 ER 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 ER 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 negotiation of a supply agreement with Alkermes, or an affiliate of Alkermes, would have the sole and exclusive right to manufacture and supply finished commercial product of Zohydro ER to us under agreed upon financial terms. As discussed above, we entered into a commercial manufacturing and supply agreement with an affiliate of Alkermes in November 2012.

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 additional milestone payments to Alkermes in the amount of $0.8 million in August 2011 in connection with the completion of the treatment phase of our pivotal efficacy Phase 3 clinical trial, Study 801, and $1.0 million upon submission of the first NDA to the FDA in May 2012. We may be obligated to pay Alkermes up to $2.8 million in total future milestone payments with respect to Zohydro ER depending upon the achievement of various development and regulatory events. These future milestone payments include a payment of $0.8 million upon successful completion of an FDA pre-approval inspection of the manufacturing facility and a payment of $2.0 million upon the first NDA approval of Zohydro ER. 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

Table of Contents

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 ER is prohibited by regulatory authorities, or if, despite commercially reasonable efforts, we are unable to obtain regulatory approval for Zohydro ER. We may also terminate the agreement, with or without cause, at any time upon six months' written notice prior to NDA approval for Zohydro ER and at any time upon 12 months' prior written notice after NDA approval for Zohydro ER.

Aradigm Corporation Asset Purchase Agreement

In August 2006, we entered into an asset purchase agreement with Aradigm. Under the terms of the agreement, Aradigm assigned and transferred to us all of its right, title and interest to tangible assets and intellectual property related to the DosePro (formerly known as Intraject) needle-free drug delivery system. Aradigm also granted to us a non-exclusive, fully paid, worldwide, perpetual, irrevocable, transferable, sublicensable license under all other intellectual property of Aradigm that was owned, controlled or employed by Aradigm prior to the closing of the asset purchase and that is necessary or useful to the development, manufacture or commercialization of the DosePro delivery system. Aradigm also retained a worldwide, royalty-free, non-exclusive license, with a right to sublicense, under all transferred intellectual property rights solely for purposes of the pulmonary field, and we granted Aradigm a license under other intellectual property rights solely for use in the pulmonary field.

At the time of the closing of the asset purchase, we paid to Aradigm a sum of $4.0 million as consideration. Under the agreement, we also paid a subsequent milestone payment to Aradigm of $4.0 million upon the U.S. commercialization of Sumavel DosePro in February 2010. We are also required to pay a 3% royalty on global net sales of Sumavel DosePro, by us or one of our licensees, if any, until the 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 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, 2013, we have 20 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 12 issued U.S. patents, 4 pending U.S. patent applications, 40 issued foreign patents and 4 pending foreign patent applications relating to various aspects of Sumavel DosePro and our DosePro technology.

Our issued U.S. Patent No. 5,891,086 covers a particular actuator mechanism forming a part of the needleless injector device, and is expected to expire in 2014. We have a corresponding patent in Canada, and two each in Germany, Spain, France, United Kingdom, Italy and Japan, which are all expected to expire in 2013. Our issued U.S. Patent No. 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. 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. Patents Nos. 7,776,007 and 8,287,489 each cover devices with a cap and latch mechanism, and are expected to expire in 2026 and 2024, respectively. We have a corresponding patent in Japan. Our issued U.S. Patent Nos. 7,901,385 and

Table of Contents

8,267,903 encompass various embodiments of the casing for enclosing the injection devices, and are expected to expire in 2026 and 2023. We have corresponding patents in Australia, Canada, Germany, Spain, France, United Kingdom, Italy, and Japan. Our issued U.S. Patent Nos. 8,118,771, 8,241,243 and 8,241,244 correspond to methods of reducing breakage of glass capsules used in the device, and are expected to expire in 2023, 2025 and 2022, respectively. We have corresponding patents in Canada, Germany, France, United Kingdom and Japan. We have two U.S. Patents, Nos. 7,231,945 and 7,320,346, related to methods of proof testing glass drug containers, such as those used in the manufacture of Sumavel DosePro, which both expire in 2023. U.S. Patents 5,891,086; 5,957,886; 6,135,979; 7,776.007; 7,901,385; 8,267,903; 8,118,771; 8,241,243; 8,241,244; and 8,287,489 are listed in the FDA Orange Book for Sumavel DosePro.

We also have three U.S. Patents Nos., 7,150,297, 6,554,818 and 6,280,410, and one each in Canada and Japan, and two each in Germany, France and the United Kingdom corresponding to methods of filling needle-free injector capsules and the filled capsules, such as those used in the manufacture of Sumavel DosePro. These patents, and applications if they issue, are expected to expire in 2022, 2017 and 2017, respectively.

We also have three U.S. Patents Nos. 6,174,304, 6,681,810 and 6,251,091, and one in Japan corresponding to needle-free injector drug capsules as well as methods and adaptors for filling capsules with liquid drug, such as those used in the manufacture of Sumavel DosePro. These patents are expected to expire in 2022, 2025 and 2016, respectively.

Our remaining issued patents, pending U.S. patent applications 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 ten U.S. patents listed in the FDA Orange Book for Sumavel DosePro expire on various dates between 2014 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 nine patents.

Zohydro ER

Zohydro ER 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 ER 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, 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.

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;

Table of Contents

- 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 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.

Table of Contents

- 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 PDUFA, the FDA agrees to specific performance goals for NDA review time through a two-tiered classification system, Standard Review and Priority Review. Standard Review NDAs have a goal of being completed within a ten-month timeframe. A Priority Review designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. The goal for completing a Priority Review is six months. It is likely that our product candidates will be granted a Standard Review. The review process may be extended by the FDA for three additional months to consider certain information or obtain clarification regarding information already provided in the submission, or for other reasons. In February 2013, the FDA informed us that we were unlikely to receive an action letter for our NDA for Zohydro ER by the PDUFA target action date of March 1, 2013. The FDA has not provided us with information as to the reason for the delay, but has indicated that the delay would likely be brief and may last only several weeks. We have not been informed of any deficiencies in the NDA for Zohydro ER during the review process to date.

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. In December 2012, the FDA convened an advisory committee that voted 2-11 (with 1 abstention) against the approval of Zohydro ER. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully when making decisions. The final decision regarding NDA approval is made by the FDA. 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. During 2012, the FDA inspected two clinical sites where Zohydro ER studies were conducted and did not issue any inspection observations.

After the FDA evaluates the NDA and, in some cases, the related manufacturing facilities, it may issue an approval letter or a 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.

Table of Contents

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 authority to prevent or limit further marketing of a product based on the results of these post-marketing programs. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label, and, even if the FDA approves a product, it may limit the approved indications for use for the product or impose other conditions, including labeling or distribution restrictions or other risk-management mechanisms. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require us to develop additional data or conduct additional pre-clinical studies and clinical trials.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug/device listing, recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. There also are extensive U.S. Drug Enforcement Agency, or DEA, regulations applicable to marketed controlled substances.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and generally require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

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 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

Table of Contents

whether the drug is a new molecular entity. If the FDA determines a REMS is necessary, the drug sponsor must agree to the REMS plan at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the drug's risks, limitations on who may prescribe or dispense the drug, or other measures that the FDA deems necessary to assure the safe use of the drug. In addition, the REMS must include a timetable to assess the strategy at 18 months, three years, and seven years after the strategy's approval. The FDA may also impose a REMS requirement on a drug already on the market if the FDA determines, based on new safety information, that a REMS is necessary to ensure that the drug's benefits outweigh its risks.

In February 2009, the FDA informed drug manufacturers that it will require a REMS for sustained release opioid drug products. Subsequently, the FDA initiated efforts to develop a new standardized REMS for these opioid medications to ensure their safe use. An extended-release formulation of hydrocodone would also be required to have a REMS. The FDA's authority to take this action is based on risk management and post market safety provisions within the Food and Drug Administration Amendments Act, or 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 submitted a REMS at the time of the NDA submission for Zohydro ER, which is consistent with current FDA and industry-wide guidelines for extended-release opioid products, and have also provided the FDA-approved opioid analgesic REMS as a supplement to our NDA submission in response to the FDA's request.
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 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.

Table of Contents

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 ER, 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 ER, our proprietary oral, extended-release version of hydrocodone, if approved, is expected to be listed by the DEA as a Schedule II controlled substance under the CSA. Consequently, its manufacture, shipment, storage, sale and use will be subject to a high degree of regulation. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized.

The DEA typically inspects a facility to review its security measures prior to issuing a registration. Security requirements vary by controlled substance schedule, with the most stringent requirements applying to Schedule I and Schedule II substances. Required security measures include background checks on employees and physical control of inventory through measures such as cages, surveillance cameras and inventory reconciliations. Records must be maintained for the handling of all controlled substances, and periodic reports made to the DEA, for example distribution reports for Schedule I and II controlled substances, Schedule III substances that are narcotics, and other designated substances. Reports must also be made for thefts or losses of any controlled substance, and to obtain authorization to destroy any controlled substance. In addition, special authorization and notification requirements apply to imports and exports.

In addition, a DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. Distributions of any Schedule I or II controlled substance must also be accompanied by special order forms, with copies provided to the DEA. Because Zohydro ER, 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 ER. 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

Table of Contents

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.

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

Table of Contents

provides that the government may assert that a claim including items or services resulting from a violation of 42 U.S.C. § 1320a-7b constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes fines against any person who is determined to have presented or caused to be presented claims to a federal health care program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Moreover, the lack of uniform court interpretation of the Anti-Kickback Statute makes compliance with the law difficult.

Recognizing that the Anti-Kickback Statute is broad and may technically prohibit many innocuous or beneficial arrangements within the healthcare industry, the U.S. Department of Health and Human Services' Office of Inspector General, or OIG, issued regulations in July of 1991, and periodically since that time, which the OIG refers to as "safe harbors." These safe harbor regulations set forth certain provisions which, if met in form and substance, will assure pharmaceutical companies, healthcare providers and other parties that they will not be prosecuted under the federal Anti-Kickback Statute. Additional safe harbor provisions providing similar protections have been published intermittently since 1991. Although full compliance with these provisions ensures against prosecution under the federal Anti-Kickback Statute, the failure of a transaction or arrangement to fit within a specific safe harbor does not necessarily mean that the transaction or arrangement is illegal or that prosecution under the federal Anti-Kickback Statute will be pursued. However, conduct and business arrangements that do not fully satisfy each applicable safe harbor may result in increased scrutiny by government enforcement authorities, such as the OIG or federal prosecutors. Additionally, there are certain statutory exceptions to the federal Anti-Kickback Statute, one or more of which could be used to protect a business arrangement, although we understand that OIG is of the view that an arrangement that does not meet the requirements of a safe harbor cannot satisfy the corresponding statutory exception, if any, under the federal Anti-Kickback Statute.

Additionally, many states have adopted laws similar to the federal Anti-Kickback Statute. Some of these state prohibitions apply to referral of patients for healthcare items or services reimbursed by any third-party payor, not only the Medicare and Medicaid programs in at least some cases, and do not contain safe harbors or statutory exceptions. Government officials have focused their enforcement efforts on marketing of healthcare services and products, among other activities, and have brought cases against numerous pharmaceutical and medical device companies, and certain sales and marketing personnel for allegedly offering unlawful inducements to potential or existing customers in an attempt to procure their business or reward past purchases or recommendations.

Another development affecting the healthcare industry is the increased use of the federal civil False Claims Act and, in particular, actions brought pursuant to the False Claims Act's "whistleblower" or "qui tam" provisions. The civil False Claims Act imposes liability on any person or entity who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The qui tam provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically. In addition, various states have enacted false claim laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third-party payor and not merely a federal healthcare program. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties of $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.

Table of Contents

The PPACA also imposes new reporting and disclosure requirements on drug manufacturers for any "transfer of value" made or distributed to prescribers and other healthcare providers, effective March 30, 2013. Such information will be made publicly available in a searchable format beginning September 30, 2013. In addition, drug manufacturers will also be required to report and disclose any investment interests held by physicians and their immediate family members during the preceding calendar year. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (and up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests not reported in an annual submission.

In addition, under California law, pharmaceutical companies must adopt a comprehensive compliance program that is in accordance with both the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers, or OIG Guidance, and the Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals, or the PhRMA Code. The PhRMA Code seeks to promote transparency in relationships between health care professionals and the pharmaceutical industry and to ensure that pharmaceutical marketing activities comport with the highest ethical standards. The PhRMA Code contains strict limitations on certain interactions between health care professionals and the pharmaceutical industry relating to gifts, meals, entertainment and speaker programs, among others. Also, certain states, such as Massachusetts, Vermont and Minnesota, have imposed restrictions on the types of interactions that pharmaceutical and medical device companies or their agents (e.g., sales representatives) may have with health care professionals, including bans or strict limitations on the provision of meals, entertainment, hospitality, travel and lodging expenses, and other financial support, including funding for continuing medical education activities.

Healthcare Privacy and Security Laws

We may be subject to, or our marketing activities may be limited by, HIPAA, and its implementing regulations, which established uniform standards for certain "covered entities" (healthcare providers, health plans and healthcare clearinghouses) governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of protected health information. The American Recovery and Reinvestment Act of 2009, commonly referred to as the economic stimulus package, included sweeping expansion of HIPAA's privacy and security standards called the Health Information Technology for Economic and Clinical Health Act, or HITECH, which became effective on February 17, 2010. Among other things, the new law makes HIPAA's privacy and 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. Further, the law imposes a significant annual, nondeductible fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with health care practitioners. A number of states have challenged the constitutionality of certain provisions of the PPACA, and many of these challenges are still pending final adjudication in several jurisdictions. Congress has also proposed a number of legislative initiatives, including

possible repeal of the PPACA. At this time, it remains unclear whether there will be any changes made to the PPACA, whether to certain provisions or its entirety. We will not know the full effects of PPACA until applicable federal and state agencies issue regulations or guidance under the new law and these provisions are implemented. Although it is too early to determine the full effect of PPACA, the new law appears likely to continue the pressure on pharmaceutical pricing, and may also increase our regulatory burdens and operating costs.

Moreover, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the President signed into law the Budget Control Act of 2011, which, among other things, creates the Joint Select Committee on

Table of Contents

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.

Employees

As of December 31, 2012, we employed 149 full-time employees. Of the full-time employees, 103 were engaged in sales and marketing, 8 were engaged in manufacturing operations, 19 were engaged in product development, quality assurance and clinical and regulatory activities and 19 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 ER. 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 $21.4 million, $33.0 million and $28.6 million in research and development in the years 2012, 2011 and 2010, respectively.

About Zogenix

Table of Contents

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 12400 High Bluff Drive, Suite 650, 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.

## 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 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 and are at an early stage of commercialization. Our business and prospects must be considered in light of the risks and uncertainties frequently encountered by pharmaceutical companies in the early stages of commercialization.

We have generated substantial net losses and negative cash flow from operations since our inception in 2006. For example, for the years ended 2012, 2011 and 2010, we incurred net losses of $47.4 million, $83.9 million and $73.6 million, respectively, our net cash used in operating activities was $52.2 million, $80.5 million and $72.0 million, respectively, and, at December 31, 2012, our accumulated deficit was $329.4 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next several years primarily as a result of the expenses incurred in connection with our efforts in seeking marketing approval for Zohydro ER, the clinical development for Relday, any additional required testing for Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro ER. Our ability to generate revenues from Sumavel DosePro or any of our product candidates will depend on a number of factors, including, in the case of Sumavel DosePro, the factors described in risk factors below 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.

Table of Contents

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

Our operations have consumed substantial amounts of cash since inception. To date, our operations have been primarily financed through the proceeds from the issuance of our common and preferred stock, including the proceeds from our initial public offering completed in November 2010, our follow-on public offerings completed in September 2011 and July 2012, and borrowings under our loan and financing agreements with Healthcare Royalty Partners, or Healthcare Royalty, Oxford Finance LLC, as successor in interest to Oxford Finance Corporation, or Oxford, and Silicon Valley Bank, or SVB. Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of December 31, 2012, and our projected product revenues from Sumavel DosePro, will be sufficient to fund our operations into the fourth quarter of 2013. We will need to obtain additional funds to finance our operations beyond that point, or possibly earlier, in order to:

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

Further, if we receive FDA approval of Zohydro ER, we may need to obtain additional capital to finance the commercial launch of Zohydro ER, possibly prior to the fourth quarter of 2013.

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

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

In its report on our consolidated financial statements for the year ended December 31, 2012, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern. A “going concern” opinion means, in general, that our independent registered public accounting firm has substantial doubt about our ability to continue our operations without continuing infusions of capital from external sources and this opinion could impair our ability to finance our operations through the sale of debt or equity securities or commercial bank loans.

Until we can generate a sufficient amount of product revenue and cash flow from operations and achieve profitability, we expect to finance future cash needs through public or private equity offerings, 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

Table of Contents

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, 2012, 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.

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

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

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

We cannot be certain that our continued marketing of Sumavel DosePro will result in increased demand for, and sales of, the product. For example, while we have generally experienced annual growth in total prescriptions from the launch of Sumavel DosePro in January 2010 through December 31, 2012, we have at certain times experienced a reduction in total and new prescriptions month over month. If we and Mallinckrodt fail to successfully maintain and increase sales of Sumavel DosePro, we may be unable to generate sufficient revenues to grow or sustain our business and we may never become profitable, and our business, financial condition and results of operations will be materially adversely affected.

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

Prior to the launch of Sumavel DosePro in January 2010, we built a commercial sales and marketing organization including sales, marketing, communications, managed markets, trade and distribution functions, which is now focused exclusively on marketing and selling Sumavel DosePro primarily to physicians, nurses and other healthcare

professionals in the United States. Our field sales force was comprised of approximately 85 field sales personnel as of December 31, 2012, and has historically promoted Sumavel DosePro primarily to neurologists and other prescribers of migraine medications, including headache clinics and headache specialists in the United States.

To complement our sales force, we entered into an exclusive co-promotion agreement with Astellas in July 2009 under which Sumavel DosePro was promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and

Table of Contents

urologists, or collectively the Astellas Segment, in the United States by approximately 400 Astellas sales representatives. This agreement terminated on March 31, 2012, and beginning in the second quarter of 2012 our sales force assumed full responsibility for the continued promotion of Sumavel DosePro. We have expanded the focus of our existing sales force to include targeting a portion of the high-prescribing primary care physicians that were previously part of the Astellas Segment. We also entered into a new co-exclusive (with us) co-promotion agreement with Mallinckrodt in June 2012, or the Mallinckrodt co-promotion agreement, under which in August 2012 Mallinckrodt began promoting Sumavel DosePro to a mutually agreed prescriber audience in the United States. Mallinckrodt has committed to a minimum number of sales representatives for the initial term of the co-promotion agreement. Although we believe we have adequately sized our sales force in order to reach our historically targeted audience, our existing sales force, along with the collaboration of Mallinckrodt's sales force, may be unable to effectively target these additional primary care physicians.

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

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

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

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

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

expand our own sales and marketing capabilities or utilize our existing sales force effectively to cover this segment and any such expansion could, in any event, substantially increase our expenses and capital requirements that we might not be able to fund.

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

Table of Contents

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

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

- our ability to provide acceptable evidence of safety and efficacy;
- acceptance by physicians and patients of the product as a safe and effective treatment;
- the relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- limitations or warnings contained in a product's FDA-approved labeling;
- the clinical indications for which the product is approved;
- in the case of product candidates that are controlled substances, the U.S. Drug Enforcement Agency, or DEA, scheduling classification;
- availability and perceived advantages of alternative treatments;
- any negative publicity related to our or our competitors' products;
- the effectiveness of our or any current or future collaborators' sales, marketing and distribution strategies;
- pricing and cost effectiveness;
- our ability to obtain sufficient third-party payor coverage or reimbursement; and
- the willingness of patients to pay out of pocket in the absence of third-party payor coverage.

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

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

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

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

Despite the implementation of security measures, our internal computer systems and those of our current and any future partners, contractors and consultants are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. For example, we have in the past experienced failures in our information systems and computer servers, which may have been the result of a cyber-attack. These failures resulted in an interruption of our normal business operations and required substantial

expenditure of financial and administrative resources to remedy. We cannot be sure that similar failures will not occur in the future. System failures, accidents or security breaches can cause interruptions in our operations, and can result in a material disruption of our commercialization activities, drug development programs and our business operations. The loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval 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

Table of Contents

security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the commercialization of Sumavel DosePro and development of Zohydro ER, Relday or any of our other product candidates could be delayed.

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

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

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

The majority of our sales of Sumavel DosePro are to wholesale pharmaceutical distributors who, in turn, sell the products to pharmacies, hospitals and other customers. Two wholesale pharmaceutical distributors, Cardinal Health, Inc. and McKesson Corporation, individually comprised 36.1% and 35.5%, respectively, of our total gross sales of Sumavel DosePro for the year ended December 31, 2012, which may result in substantial fluctuations in our results of operations from period to period. The loss of any of these wholesale pharmaceutical distributors' accounts or a material reduction in their purchases could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

Table of Contents

Pharmaceutical International. In addition, Allergan, Inc., is now marketing BOTOX botulinum toxin for the treatment of chronic migraine. We also face competition from generic sumatriptan oral tablets and sumatriptan injection, now marketed in the United States as an authorized generic of the Imitrex STATdose System, or Imitrex STATdose, by Par Pharmaceutical Companies, Inc. and Sandoz Inc. (a Novartis AG company). In addition, in June 2010, the FDA approved Alsuma (sumatriptan injection), a needle-based autoinjector which was developed and is manufactured and marketed by Pfizer and its subsidiary, Meridian Medical Technologies. Finally, generic injectable sumatriptan in the form of vials and prefilled syringes is available from a number of pharmaceutical companies, and most recently, the FDA granted approval for a needle-based generic sumatriptan auto-injector from Sun Pharmaceutical Industries Limited in June 2011. Although these products may not be directly substituted for Sumavel DosePro, generic versions of sumatriptan injection and alternative autoinjector forms of sumatriptan injection may reduce the future adoption of Sumavel DosePro by third-party payors and consumers, as financial pressure to use generic products may encourage the use of a generic product over Sumavel DosePro. Sumavel DosePro is currently more expensive on a per dose basis than most of the competing branded and all of the generic triptan products for migraine, which may also limit the coverage and reimbursement by third-party payors, which could adversely affect adoption by physicians and patients.

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

In addition to already marketed therapeutics, we also face competition from product candidates that are or could be under development by many of the above-mentioned entities and others. For example, there are several products for the treatment of migraine under development by large pharmaceutical companies such as GSK, Merck & Co., and Allergan, Inc. and smaller companies such as OptiNose AS, Inc. In addition, Nupathe, Inc. received FDA approval for its migraine patch, Zecuity, in January 2013. If approved, Zohydro ER may also compete with a significant number of opioid product candidates under development, including abuse and tamper resistant formulations of currently available opioids, novel opioids and alternative delivery forms of various opioids under development at other pharmaceutical companies, including single-entity extended-release hydrocodone product candidates being developed by Egalet A/S, Pfizer, Purdue Pharma L.P. and Teva Pharmaceutical Industries Limited. Zohydro ER may also face competition from non-opioid product candidates including new chemical entities, as well as alternative delivery forms of non-steroidal anti-inflammatory drugs. These new opioid and non-opioid product candidates are being developed by companies such as Acura Pharmaceuticals, Inc., Altea Therapeutics Corporation, Collegium Pharmaceutical, Inc., Eli Lilly and Company, Elite Pharmaceuticals, Inc., Hospira Inc., Inspirion Delivery Technologies, LLC, Intellipharmaceuticals International, Inc., Nektar Therapeutics, Pfizer and QRxPharma Ltd.

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

antipsychotic product candidates.

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

Table of Contents

any products that we are able to market from those of our competitors, successfully develop or introduce new products that are less costly or offer better results than those of our competitors, or offer purchasers of our products payment and other commercial terms as favorable as those offered by our competitors.

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

- capital resources;
- research and development resources and experience, including personnel and technology;
- drug development, clinical trial and regulatory resources and experience;
- sales and marketing resources and experience;
- manufacturing and distribution resources and experience;
- name recognition; and
- resources, experience and expertise in prosecution and enforcement of intellectual property rights.

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

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

While we own most of the specialized equipment used to manufacture critical components of Sumavel DosePro, we do not own or operate manufacturing facilities and currently lack the in-house capability to manufacture Sumavel DosePro, Zohydro ER, Relday or any other product candidates. Our DosePro device and Sumavel DosePro are manufactured by contract manufacturers, component fabricators and secondary service providers. Aseptic fill, finish, assembly and packaging of Sumavel DosePro are performed at Patheon UK Limited, Swindon, United Kingdom, or Patheon, a specialist in the aseptic fill/finish of injectables and other sterile pharmaceutical products. In May 2012, Patheon announced plans to wind down or transfer its commercial production capacity for a number of products at this facility over a period of 24 to 36 months.We are presently identifying alternative suppliers for these services and expect to identify an alternative supplier in sufficient time so that we can transfer the manufacturing processes that are presently handled by Patheon to a new supplier in advance of the expected closure date of the Swindon, United Kingdom facility. In addition, Nypro Limited, located in Bray, Ireland, manufactures the actuator assemblies and injection molded components for our DosePro device and Nipro Glass, Germany AG (formerly MGlas AG), located in Münnerstadt, Germany, manufactures the specialized glass capsule (cartridge) that houses the sumatriptan active pharmaceutical ingredient, or API, in our DosePro device. Each of these manufacturers and each other company that supplies, fabricates or manufactures any component used in our DosePro device is currently the only qualified source of their respective components. We currently rely on Dr. Reddy's Laboratories as the only supplier of sumatriptan API for use in Sumavel DosePro. We also outsource all manufacturing and packaging of the clinical trial materials for Zohydro ER and Relday to third parties. Although we plan to qualify additional manufacturers and suppliers of some of the components used in Sumavel DosePro, there can be no assurance that we will be able to do so and the current manufacturers and suppliers of these components will likely be single source suppliers to us for a significant period of time. Similarly, an affiliate of Alkermes is the exclusive manufacturer of Zohydro ER and Durect is the exclusive manufacturer of the risperidone formulation using Durect's SABER™ controlled-release technology for all Relday

clinical trials through Phase 2 and has the option to supply the same formulation for Phase 3 clinical trials and, if approved, commercial production. We have restrictions on establishing a second source of supply under our agreement with an affiliate of Alkermes, and we may never be able to establish additional sources of supply for Zohydro ER or Relday's risperidone formulation.

Manufacturers and suppliers are subject to regulatory requirements covering, among other things, manufacturing, testing, quality control and record keeping relating to our product and product candidates, and are subject to ongoing inspections by regulatory agencies. Failure by any of our manufacturers or suppliers to comply with applicable regulations may result in long delays and interruptions to our manufacturing supply, and increase our costs, while we seek to secure another supplier who

Table of Contents

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

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

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

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

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

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

Table of Contents

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

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

Under the policies agreed to by the FDA under The Prescription Drug User Fee Act, or PDUFA, as renewed by the Food and Drug Administration Safety and Innovation Act, or FDASIA, the FDA is subject to a two-tiered system of review times for new drugs - Standard Review and Priority Review. For certain drugs subject to standard review, such as Zohydro ER, the FDA has a goal to complete its review of the NDA and respond to the applicant within ten months from the date of receipt of an NDA. The FDA assigned a target action date of March 1, 2013 for the Zohydro ER NDA. The review process and the PDUFA target action date may be extended by three months if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the three months prior to the PDUFA target action date. The FDA's review goals are subject to change, and the duration of the FDA's review may depend on the number and type of other NDAs that are submitted with the FDA around the same time period. In February 2013, the FDA informed us that we were unlikely to receive an action letter for our NDA for Zohydro ER by the PDUFA target action date of March 1, 2013. The FDA has not provided us with information as to the reason for the delay, but has indicated that the delay would likely be brief and may last only several weeks past the PDUFA target action date. We have not been informed of any deficiencies in the NDA for Zohydro ER during the review process to date.

The FDA may also refer applications for novel products or products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. In connection with the acceptance of our NDA for Zohydro ER, the FDA convened an advisory committee on December 7, 2012, which voted 2-11 (with 1 abstention) against the approval of Zohydro ER. The FDA is not bound by the recommendation of the advisory committee and the final decision regarding approval is made by the FDA. However, due to the advisory committee's recommendation against the approval of our NDA, we may not be able to succeed in securing approval for Zohydro ER. Even if we obtain regulatory approval for Zohydro ER, the matters discussed at the advisory committee meetings, and in particular any concerns regarding safety and abuse potential, could limit our ability to successfully commercialize the product candidate.

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

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

- the FDA may not deem a product candidate safe and effective;
- the FDA may not find the data from pre-clinical studies and clinical trials sufficient to support approval;

Table of Contents

- the FDA may require additional pre-clinical studies or clinical trials;
- the FDA may not approve of our third-party manufacturers' processes and facilities; or
- the FDA may change its approval policies or adopt new regulations.

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

Relday and any of our other product candidates may fail to achieve their specified endpoints in clinical trials. We initiated a Phase 1 safety and pharmacokinetic clinical trial for Relday in July 2012 and announced positive single-dose pharmacokinetic results from this trial in January 2013. Based on the favorable safety and pharmacokinetic profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, we extended the study to include an additional cohort of 10 patients at a 100 mg dose of the same formulation. We expect to complete the extension of the Phase 1 clinical trial during the second quarter of 2013. The timing and outcome of this study and the subsequent development of Relday will be subject to most of the risks described above.

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

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

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

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

In light of widely publicized events concerning the safety risk of certain drug products, particularly opioid drug products, regulatory authorities, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the

withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products after approval. In addition, the FFDCA, as amended by the Food and Drug Administration Amendments Act of 2007, grants significant expanded authority to the FDA, much of which is aimed at improving the safety of drug products before and after approval. In particular, the FFDCA authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information and require a REMS for certain drugs, including certain currently approved drugs. It also significantly expands the federal

Table of Contents

government's clinical trial registry and results databank, which we expect will result in significantly increased government oversight of clinical trials. Under the FFDCA, companies that violate these and other provisions of the law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties.

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

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

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

Clinical trials are very expensive, time consuming and difficult to design and implement. Delays in the commencement or completion of any additional testing for Zohydro ER, if required, or clinical testing for Relday, or pre-clinical or clinical testing for any of our other product candidates could significantly affect our product development costs and business plan. We initiated clinical testing for Relday in patients with schizophrenia in July 2012 and announced positive single-dose pharmacokinetic results from the Phase 1 clinical trial in January 2013. Based on the favorable safety and pharmacokinetic profile demonstrated in the Phase 1 trial, we extended the study to include an additional dose of the same formulation and expect to complete the extension during the second quarter of 2013. We do not know whether the extension of this trial will be completed on schedule, or whether any of our other pre-clinical or clinical trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

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

- identifying, recruiting and training suitable clinical investigators;
- identifying, recruiting and enrolling subjects to participate in clinical trials for a variety of reasons, including competition from other clinical trial programs for the treatment of pain, migraine or similar indications;
- retaining patients who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy, personal issues, or for any other reason they choose, or who are lost to further follow-up;
- uncertainty regarding proper dosing; and
- scheduling conflicts with participating clinicians and clinical institutions.

In addition, if a significant number of patients fail to stay enrolled in any of our current or future clinical trials of Relday or any of our other product candidates and such failure is not adequately accounted for in our trial design and enrollment

Table of Contents

assumptions, our clinical development program could be delayed. Clinical trials may also be delayed or repeated as a result of ambiguous or negative interim results or unforeseen complications in testing. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or other regulatory authorities due to a number of factors, including:

- failure to design appropriate clinical trial protocols;
- failure by us, our employees, our CROs or their employees to conduct the clinical trial in accordance with all applicable FDA, DEA or other regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- discovery of serious or unexpected toxicities or side effects experienced by study participants or other unforeseen safety issues;
- lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties;
- lack of effectiveness of any product candidate during clinical trials;
- slower than expected rates of subject recruitment and enrollment rates in clinical trials;
- failure of our CROs or other third-party contractors to comply with all contractual requirements or to perform their services in a timely or acceptable manner;
- inability or unwillingness of medical investigators to follow our clinical protocols; and
- unfavorable results from on-going clinical trials and pre-clinical studies.

Additionally, changes in applicable regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. All of the above risks will be applicable to Zohydro ER to the extent we are required by the FDA to conduct any additional clinical trials. If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for Zohydro ER, Relday and our other product candidates may be harmed, which may have a material adverse effect on our business, results of operations, financial condition and prospects.

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

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

Certain of our competitors may file a 505(b)(2) application for extended-release hydrocodone prior to the approval of our own NDA for Zohydro ER. The first approved 505(b)(2) applicant for a particular condition of use, or change to a marketed product, such as a new extended-release formulation for a previously approved product, may be granted three-year Hatch-Waxman exclusivity if one or more clinical studies, other than bioavailability or bioequivalence studies, was essential to the approval of the application and was conducted/sponsored by the applicant. Three-year Hatch-Waxman exclusivity delays the FDA's approval of other 505(b)(2) applicants for the same condition of use or change to the drug product that was granted exclusivity, regardless of the date of submission of each NDA. We believe that several competitors are developing extended-release hydrocodone products, and if the FDA approves a competitor's 505(b)(2) application for its extended-release hydrocodone product before our application, and granted

the competitor three-year exclusivity, the FDA would be precluded from making effective our NDA for Zohydro ER until after that three-year exclusivity period has expired, and such delay would dramatically reduce our expected market potential for Zohydro ER. Additionally, even if our 505(b)(2) application for extended-release hydrocodone is approved first, we may still be subject to competition by other hydrocodone products, including approved products or other 505(b)(2) applications for different conditions of use that would not be restricted by the three-year exclusivity.

Table of Contents

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

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

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

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

We conducted our Phase 3 trials for Zohydro ER under agreements with third-party CROs. We are also conducting our Phase 1 clinical trial for Relday under an agreement with a third-party CRO, and we anticipate that we may enter into agreements with third-party CROs in the future regarding Zohydro ER, if further clinical trials are required, 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 and implementation of a REMS for Zohydro ER could cause significant delays in the approval process for Zohydro ER and will add additional layers of regulatory requirements, including the requirement for a Medication Guide and educational requirements for prescribers and patients, which could significantly impact our

ability to commercialize Zohydro ER and dramatically reduce its market potential.

The Food and Drug Administration Amendments Act, or FDAAA, added Section 505-1 to the FFDCA. Section 505-1 permits FDA to require a REMS for a drug product to ensure the safe use of the drug. A REMS is a strategic safety program that the FDA requires to ensure that the benefits of a drug outweigh its risks. In determining whether a REMS is necessary, the

Table of Contents

FDA will consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment and the seriousness of known or potential adverse events. If the FDA determines a REMS is necessary, the drug sponsor must agree to the REMS plan at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the drug's risks, limitations on who may prescribe or dispense the drug, requirements that patients enroll in a registry or undergo certain health evaluations or other measures that the FDA deems necessary to assure the safe use of the drug. In addition, the REMS must include a timetable to assess the strategy minimally at 18 months, three years and seven years after the strategy's approval.

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

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

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

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

Table of Contents

approval for or commercialize Sumavel DosePro in countries for which it has exclusive rights, other than in Germany, where Desitin is required to develop, seek approval for and commercialize Sumavel DosePro. Any failure by Desitin to successfully commercialize Sumavel DosePro or to successfully obtain applicable foreign regulatory approval for Sumavel DosePro would limit our opportunity to receive revenue from the territories licensed to Desitin. Furthermore, negative developments occurring in those territories controlled by Desitin could have a negative impact on physician and patient impressions of our product in the United States and elsewhere.

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

Major pharmaceutical companies usually employ groups of sales representatives numbering in the thousands to call on the large number of primary care physicians. In connection with the launch of Sumavel DosePro in January 2010 we built a sales and marketing organization to promote Sumavel DosePro in the United States, including a focused sales force, which as of December 31, 2012 was comprised of approximately 85 field sales personnel, primarily targeting neurologists and other prescribers of migraine medications, including headache clinics and headache specialists. In July 2009, we entered into an exclusive agreement with Astellas under which Sumavel DosePro was also being marketed by Astellas in the United States and promoted primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists by approximately 400 Astellas sales representatives. Our Astellas agreement terminated on March 31, 2012. In June 2012, in order to maintain and expand the market opportunity for Sumavel DosePro into the broader primary care physician audiences, we entered into a new co-exclusive (with us) co-promotion agreement with Mallinckrodt under which in August 2012 Mallinckrodt began promoting Sumavel DosePro to its customer base of prescribers.

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

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

As part of our growth strategy we intend to seek to expand our product pipeline by exploring acquisition or in-licensing opportunities of proven drugs that can be paired with our DosePro needle-free drug delivery system. However, the current version of our DosePro drug delivery system cannot be used with drug formulation volumes greater than 0.5 mL. Many marketed and development-stage injectable products, including most biologics, have

formulation volumes greater than 0.5 mL and would require reformulation, if possible, to accommodate the approved doses in smaller volumes that are compatible with DosePro. Any reformulation may increase the risk of failure during development, extend the development timelines, increase development costs and add complexity to the regulatory approval process and in some cases reformulation may not be possible. If we are not able to identify additional drug compounds that can be delivered via the current version of our DosePro technology, or if we are unable to successfully develop higher dose versions of this technology, our ability to develop additional product candidates and grow our business would be adversely affected. We and Battelle Memorial Institute, or Battelle, our technology co-marketing partner, are also seeking opportunities to out-license the DosePro technology to partners seeking to enhance, differentiate, or extend the life-cycle of their injectable products. However, there can be no assurance that our or

Table of Contents

Battelle's efforts to secure such a partnership will be successful. If we are unable to secure partnerships with companies that have compounds that can be delivered via the current version of our DosePro technology, or if we are unable to successfully develop higher dose versions of this technology, we will not be able to generate revenues from out-licensing our DosePro technology.

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

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

Furthermore, we intend to in-license, acquire, develop and/or market additional products and product candidates in the areas of pain and central nervous system, or CNS, disorders. Because our internal research and development capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify and select promising pharmaceutical product candidates and products, negotiate licensing or acquisition agreements with their current owners and finance these arrangements.

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

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

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

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

We increased our full-time employees from 48 as of October 31, 2009 to 149 as of December 31, 2012. In addition, we have expanded our sales force in the United States from approximately 80 field sales personnel to approximately 85 field sales personnel as of December 31, 2012, and we intend to increase our sales force if Zohydro ER is approved

by the FDA. Any such increases in our sales force could substantially increase our expenses. We may need to continue to expand our managerial, operational and other resources in order to grow, manage and fund our existing business. Our management and personnel, systems and facilities currently in place may not be adequate to support this recent and any future growth, and we may be

Table of Contents

unable to fund the costs and expenses required to increase our necessary headcount and infrastructure. Our need to effectively manage our operations, any future growth and various projects requires that we:

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

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

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

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

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

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;

Table of Contents

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

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

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

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

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

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

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

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

The commercial use of our product and clinical use of our product and product candidates expose us to the risk of product liability claims. This risk exists even if a product is approved for commercial sale by the FDA and manufactured in facilities licensed and regulated by the FDA, such as the case with Sumavel DosePro, or an applicable foreign regulatory authority. Our product and product candidates are designed to affect important bodily functions and processes. Any side effects, manufacturing defects, misuse or abuse associated with Sumavel DosePro or our product candidates could result in injury to a patient or even death. For example, because our DosePro technology is designed to be self-administered by patients, it is possible that a patient could fail to follow instructions

and as a result apply a dose in a manner that results in injury. In addition, Zohydro ER is an opioid pain reliever that contains hydrocodone, which is a regulated “controlled substance” under the Controlled Substances Act of 1970, or CSA, and could result in harm to patients relating to its potential for abuse. In addition, a liability claim may be brought against us even if our product or product candidates merely appear to have caused an injury.

Table of Contents

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

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

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

Table of Contents

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, 2012, $17.1 million (based on exchange rates as of December 31, 2012) 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.

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.

Table of Contents

We launched our only approved product, Sumavel DosePro, in January 2010. Without a long history of sales, we may not accurately predict future sales, and we may never be able to significantly increase these sales, especially in light of the termination of our partnership with Astellas in March 2012 to co-promote Sumavel DosePro and our reliance on our new co-promotion partner, Mallinckrodt. We have financed our operations almost exclusively through the proceeds from the issuance of our common and preferred stock, including the proceeds from our initial public offering completed in November 2010, our follow-on public offerings completed in September 2011 and July 2012, and debt, and have incurred losses and negative cash flow from operations in each year since our inception. Our net loss was $47.4 million in 2012, $83.9 million in 2011 and $73.6 million in 2010, and our cash used in operating activities was $52.2 million in 2012, $80.5 million in 2011 and $72.0 million in 2010. As of December 31, 2012, we had an accumulated deficit of $329.4 million. These losses and negative cash flow from operations have had a material adverse effect on our stockholders' equity and working capital. Further, despite the revenues from Sumavel DosePro, we expect our losses to continue for at least the next several years primarily as a result of the expenses incurred in connection with our efforts in seeking marketing approval for Zohydro ER, the potential additional clinical development of Relday, any additional required testing for Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro ER. As a result, we may remain dependent upon external sources of financing to finance our business and the development and commercialization of our approved product and product candidates. To the extent we need to raise additional capital in the future, we cannot ensure that debt or equity financing will be available to us in amounts, at times or on terms that will be acceptable to us, or at all. Any shortfall in our cash resources could require that we delay or abandon certain development and commercialization activities and could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

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

As of December 31, 2012, we had $30.0 million of outstanding indebtedness under a financing agreement with Healthcare Royalty Partners, or the Healthcare Royalty financing agreement. Our outstanding debt and related debt service obligations could have important adverse consequences to us, including:

- heightening our vulnerability to downturns in our business or our industry or the general economy and restricting us from making improvements or acquisitions, or exploring business opportunities;
- requiring a significant amount of interest payments and fixed payments 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.

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

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

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

Table of Contents

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

There can be no assurance that we will not breach the terms of, or that an event of default or termination event will not occur under, our Healthcare Royalty financing agreement and, if a breach or event of default or termination event occurs, there can be no assurance that we will be able to obtain necessary waivers or amendments from Healthcare Royalty or refinance the related indebtedness or other amounts due and payable on terms we find acceptable, or at all. As a result, any failure to pay our debt service obligations when due, any breach or default of our obligations under our Healthcare Royalty financing agreement, or any other event that allows Healthcare Royalty to demand immediate repayment of borrowings or termination payments, could have a material adverse effect on our business, results of operations, financial condition and prospects. Furthermore, the arrangement under the Healthcare Royalty financing agreement may make us significantly less attractive to potential acquirers, and in the event that we exercised our change of control pay-off option in order to carry out a change of control, the payment of such funds out of our available cash or acquisition proceeds would reduce acquisition proceeds for our stockholders.

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

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

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

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

The Healthcare Royalty financing agreement contains provisions which allows Healthcare Royalty to accelerate the debt and seize and sell the collateral if, among other things, we fail to pay interest payments and fixed payments when due or breach our obligations under the agreement or if a material adverse change in our business or any other event of default occurs. Any future debt financing we enter into may involve more onerous covenants that restrict our operations, may be secured by some or all of our assets, and will likely allow the lenders to accelerate the debt and seize and sell any collateral following a default. Our obligations under our outstanding Healthcare Royalty financing agreement or any future debt financing will need to be

Table of Contents

repaid, which creates additional financial risk for our company, particularly if our business or prevailing financial market conditions are not conducive to paying-off or refinancing our outstanding debt obligations.

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

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the IRC, substantial changes in our ownership may limit the amount of net operating loss and research and development income tax credit carryforwards (collectively, tax attributes) that could be utilized annually in the future to offset taxable income, if any. Specifically, this limitation may arise in the event of a cumulative change in ownership of our company of more than 50% within a three-year period as determined under the IRC, which we refer to as an ownership change. Any such annual limitation may significantly reduce the utilization of these tax attributes before they expire. Prior to our initial public offering in November 2010, we performed an IRC Section 382 and 383 analysis and determined that we had one ownership change, which occurred in August 2006 upon the issuance of convertible preferred stock. We performed an additional IRC Section 382 and 383 analysis upon the issuance of common stock in our follow-on public offering in September 2011, and together with the issuance of common stock in our initial public offering and certain other transactions involving our common stock, resulted in an additional ownership change. As a result of these ownership changes, our ability to use our then existing tax attributes to offset future taxable income, if any, was limited. We are currently in the process of completing a Section 382 and 383 study to determine the impact that ownership changes during the year ended December 31, 2012 have had on our carryforwards and expect to complete the analysis within the next three months. As a result of this analysis, we may have an adjustment in the net operating losses that are recorded at December 31, 2012. 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, or the restriction in a REMS program. We will also be subject to ongoing FDA obligations and continued regulatory review with respect to the manufacturing, processing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and with GCPs and good laboratory practices, which are regulations and guidelines enforced by the FDA for all of our products in clinical and pre-clinical development, and for any clinical trials that we conduct post-approval. To the extent that a product is approved for sale in other countries, we may be subject to similar restrictions and requirements imposed by laws and government regulators in those countries.

In the case of Zohydro ER and any other product candidates or products containing controlled substances, we and our contract manufacturers will also be subject to ongoing DEA regulatory obligations, including, among other things, annual registration renewal, security, recordkeeping, theft and loss reporting, periodic inspection and annual quota

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

Table of Contents

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. For example, the FDASIA requires the FDA to issue new guidance on permissible forms of internet and social media promotion of regulated medical products, and the FDA may soon specify new restrictions on this type of promotion. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. If we are not able to achieve and maintain regulatory compliance, we may not be permitted to market our drugs, which would adversely affect our ability to generate revenue and achieve or maintain profitability.

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

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

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

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

weakness (5%), and neck pain/stiffness (5%).

The incidence of adverse events was 33.7% and 28.8% in the open label titration and double blind treatment periods of our Phase 3 efficacy trial for Zohydro ER, respectively. Overall, the most commonly reported adverse events (>2%) in this trial

Table of Contents

were constipation, nausea, somnolence, vomiting, diarrhea, insomnia, fatigue, headache, dizziness and dry mouth. These are typical adverse events associated with chronic opioid therapy.

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

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

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

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

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

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

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

Individual states also have controlled substances laws. Though state controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule drugs, as well. While some states automatically schedule a drug when the DEA does so, in other states there has to be rulemaking or a legislative action.

State scheduling may delay commercial sale of any controlled substance drug product for which we obtain federal regulatory approval and adverse scheduling could have a material adverse effect on the commercial attractiveness of such product. We or our partners must also obtain separate state registrations in order to be able to obtain, handle, and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions from the states in addition to those from the DEA or otherwise arising under federal law.

Table of Contents

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

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

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

The DEA limits the availability and production of all Schedule II substances through a quota system which includes a national aggregate quota and individual quotas. Because hydrocodone is subject to the DEA's production and procurement quota scheme, the DEA establishes annually an aggregate quota for how much hydrocodone may be produced in total in the United States based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. This limited aggregate amount of hydrocodone that the DEA allows to be produced in the United States each year is allocated among individual companies, who must submit applications annually to the DEA for individual production and procurement quotas. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments. Alkermes, which has licensed us the right to sell Zohydro ER in the United States, if approved, was allocated a sufficient quantity of hydrocodone to meet our planned clinical and pre-clinical needs during 2012. However, in future years, we will need significantly greater amounts of hydrocodone to implement our commercialization plans if the FDA approves Zohydro ER.

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

We may 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.

Table of Contents

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, Norway, Switzerland and Turkey, in order to seek to accelerate the development and regulatory approvals in those territories. We may also seek to establish commercial partnerships for Sumavel DosePro in other foreign countries. In order to market Sumavel DosePro or any other products outside of the United States, we, Desitin, or any potential partner must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our products. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed in these "Risk Factors" and elsewhere in this 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. 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;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

Table of Contents

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in April 2010 and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and others, including reporting any "transfer of value" made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year beginning in 2012, and manufacturers will be required to begin data collection on August 1, 2013 and report such data to the Centers for Medicare & Medicaid Services by March 31, 2014;
- 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.

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

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

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

In certain foreign markets, the pricing of prescription drugs is subject to government control and reimbursement and may, in some cases, be unavailable. In the United States, the commercial success of Sumavel DosePro and our product candidates, if and when commercialized, will depend, in part, upon the availability of coverage and reimbursement from third-party payors at the federal, state and private levels. Third-party payors include governmental programs such as Medicare or Medicaid, private insurance plans and managed care plans. These third-party payors may deny

coverage or reimbursement for a product or therapy in whole or in part if they determine that the product or therapy was not medically appropriate or necessary. Also, third-party payors have attempted to control costs by limiting coverage through the use of formularies and other cost-containment mechanisms and the amount of reimbursement for particular procedures or drug treatments.

Additionally, given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform, the cost of prescription drugs and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to market our products and generate revenues. In addition, legislation has been

Table of Contents

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 Statute, which constrains our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, and which may apply to entities like us which provide coding and billing advice to customers;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, and its implementing regulations, 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; 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

Table of Contents

operations. Any penalties, damages, fines, curtailment or restructuring of our operations could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

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

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

Risks Related to Intellectual Property

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

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

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

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

In addition, as part of the agreement where we acquired patents related to DosePro from Aradigm, Aradigm retained, and we granted to Aradigm, a non-exclusive, worldwide, royalty free license to the acquired patents solely for

purposes of the delivery of one or more aerosolized APIs directly into the bronchia or lungs. The agreement with Aradigm also includes a covenant not to compete with us regarding technologies or products for the delivery of one or more APIs via needle free injection. That covenant expired on August 26, 2010, giving Aradigm or its licensees the right to develop and sell other needle-free injection technologies and products.

The patent positions of pharmaceutical, biopharmaceutical and medical device companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in patents in these fields has emerged to date in the United States. There have been recent changes regarding how patent laws are interpreted, and both the PTO and Congress have recently proposed radical changes to the patent system. We cannot accurately predict future changes in the interpretation of patent laws or changes to patent laws which might be enacted into law. Those changes may materially affect our patents, our ability to obtain patents and/or the patents and applications of our collaborators and licensors. The patent situation in these fields outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in the patents we own or to which we have a license or third-party patents.

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;

Table of Contents

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

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

If any of our owned or in-licensed patents are found to be invalid or unenforceable, or if we are otherwise unable to adequately protect our rights, it could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Likewise, our patents covering certain technology used in our DosePro device are expected to expire on various dates from 2014 through 2026 and the patents licensed to us by Alkermes are expected to expire in 2019. As of December 31, 2012, our patent portfolio included twelve issued U.S. patents, four pending U.S. patent applications, 40 issued foreign patents and four pending foreign patent applications relating to various aspects of Sumavel DosePro and our DosePro technology. Ten of our U.S. patents relating to our DosePro technology, U.S. Patent Nos. 5,891,086, 5,957,886, 6,135,979, 7,776,007, 7,901,385, 8,267,903, 8,118,771, 8,241,243, 8,241,244 and 8,287,489 are expected to expire in 2014, 2016, 2017, 2026, 2026, 2023, 2023, 2025, 2022 and 2024, respectively. U.S. Patent No. 5,891,086 covers a particular actuator mechanism forming a part of the needleless injector device; U.S. Patent No. 5,957,886 claims a needleless injector system using a viscous damping medium; U.S. Patent No. 6,135,979 covers the needleless injector with particular safety mechanisms; U.S. Patent Nos. 7,776,007 and 8,287,489 cover devices with a cap and latch mechanism; U.S. Patent Nos. 7,901,385 and 8,267,903 encompass various embodiments of the casing for enclosing the injection devices; and U.S. Patent Nos. 8,118,771,

8,241,243 and 8,241,244 cover a method of reducing breakage of glass capsules used in the Sumavel DosePro device. Upon the expiration of these patents, we will lose the right to exclude others from practicing these inventions. Additionally, since these ten 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.

Table of Contents

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

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

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

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

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

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

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

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

Table of Contents

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

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

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

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

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

continue our operations or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

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

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

Table of Contents

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

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

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

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

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

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

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

The market prices for securities of biotechnology and pharmaceutical companies have historically been highly volatile, and the market has 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, 2012, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price of $1.11 to a high sale price of $3.16. 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:

Table of Contents

- announcements concerning our and Mallinckrodt's commercial progress in promoting and selling Sumavel DosePro, including sales and revenue trends;
- announcements concerning our NDA for Zohydro ER;
- FDA or international regulatory actions, including results and announcements from FDA advisory committee meetings convened with respect to hydrocodone and whether and when we receive regulatory approval for Zohydro ER or any of our other product candidates;
- the development status of Relday or any of our other product candidates, including the results from our clinical trials;
- other regulatory developments, including the FDA's potential grant of regulatory exclusivity to a competitor who receives FDA approval before us for an extended-release hydrocodone product, which could significantly delay our ability to receive approval for Zohydro ER;
- announcements of the introduction of new products by us or our competitors;
- announcements concerning product development results or intellectual property rights of others;
- announcements relating to litigation, intellectual property or our business, and the public's response to press releases or other public announcements by us or third parties;
- variations in the level of expenses related to Zohydro ER, Relday or any of our other product candidates or clinical development programs, including relating to the timing of invoices from, and other billing practices of, our CROs and clinical trial sites;
- market conditions or trends in the pharmaceutical sector or the economy as a whole;
- changes in operating performance and stock market valuations of other pharmaceutical companies and price and volume fluctuations in the overall stock market;
- litigation or public concern about the safety of Sumavel DosePro or our product candidates;
- actual and anticipated fluctuations in our quarterly operating results;
- the financial projections we may provide to the public, any changes in these projections or our failure to meet these projections;
- deviations from securities analysts' estimates or the impact of other analyst comments;
- ratings downgrades by any securities analysts who follow our common stock;
- additions or departures of key personnel;
- third-party payor coverage and reimbursement policies;
- developments concerning current or future strategic collaborations, and the timing of payments we may make or receive under these arrangements;
- developments affecting our contract manufacturers, component fabricators and service providers;
- the development and sustainability of an active trading market for our common stock;
- future sales of our common stock by our officers, directors and significant stockholders;
- other events or factors, including those resulting from war, incidents of terrorism, natural disasters, security breaches, system failures or responses to these events;
- changes in accounting principles; and
- discussion of us or our stock price by the financial and scientific press and in online investor communities.

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.

Table of Contents

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

Our quarterly operating results may fluctuate significantly.

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

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

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

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

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

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

Our executive officers and directors and their affiliates together control, as of March 1, 2013, approximately 29% 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

Table of Contents

stockholders will collectively be able to significantly influence and may be able to control all matters requiring approval of our stockholders, including the election of directors and approval of significant corporate transactions such as mergers, consolidations or the sale of all or substantially all of our assets. The concentration of ownership may delay, prevent or deter a change in control of our company even when such a change may be in the best interests of some stockholders, impede a merger, consolidation, takeover or other business combination involving us, or could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might adversely affect the prevailing market price of our common stock.

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

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

Persons who were our stockholders prior to the sale of shares in our initial public offering in November 2010 continue to hold a substantial number of shares of our common stock that they are able to sell in the public market, subject in some cases to certain legal restrictions. Significant portions of these shares are held by a small number of stockholders. If these stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. The perception in the market that these sales may occur could also cause the trading price of our common stock to decline. As of December 31, 2012, we had 100,808,601 shares of common stock outstanding. Of these shares, approximately 71,702,414 are freely tradeable, without restriction, in the public market.

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

We have registered under the Securities Act 15,784,200 shares of our common stock issuable upon the exercise of the warrants we issued in July 2012, which warrants will be exercisable beginning on July 27, 2013 at an exercise price of $2.50 per share (subject to restrictions on exercise set forth in such warrants), which means that upon exercise of warrants, such shares will be freely tradeable without restriction under the Securities Act, except for shares held by our affiliates. Further, certain holders of shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act, which, if registered, would also become freely tradeable without restriction under the Securities Act, except for shares held by our affiliates. In addition, our directors and executive officers may establish programmed selling plans under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for the purpose of effecting sales of our common stock. Any sales of securities by these stockholders, warrantholders or executive officers and directors, or the perception that those sales may occur, could have a material adverse effect on the trading price of our common stock.

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

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

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

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

Table of Contents

- 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 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 is required to deliver an attestation report on the effectiveness of our internal control over financial reporting commencing with the year ended December 31, 2012. We

Table of Contents

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 13,124 square feet of office space in San Diego under a lease that we entered in April 2012 which expires in November 2014. Prior to April 2012, we occupied 12,929 square feet of office space in San Diego under a lease that expired in April 2012.

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 San Diego and Emeryville is adequate to meet our needs in those locations, and that, if necessary, additional space can be leased to accommodate any future growth.

The manufacturing equipment used to produce our DosePro technology is currently located at our contract manufacturers' and component suppliers' facilities in Europe where we occupy an aggregate of more than 20,000 square feet of space that is used to manufacture Sumavel DosePro.

Item 3. Legal Proceedings

We are not currently a party to any legal proceedings.

Item 4. Mine Safety Disclosures

Not Applicable.

Table of Contents

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, 2012 | | |
| Fourth Quarter | 3.16 | 1.11 |
| Third Quarter | 2.86 | 1.99 |
| Second Quarter | 2.58 | 1.55 |
| First Quarter | 2.94 | 1.76 |
| 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 |

Holders of Common Stock

As of March 1, 2013, there were approximately 42 holders of record of our common stock.

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.

Table of Contents

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.

Equity Compensation Plan Information

The following table summarizes securities available under our equity compensation plans as of December 31, 2012 (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 | $3.45 | 1,292 | 0 | 1,292 | 0 |
| 2010 Equity Incentive Plan | $2.52 | 8,609 | 0 | 8,609 | 702 |
| Total Equity Incentive Plans | | 9,901 | 0 | 9,901 | 702 |
| 2010 Employee Stock Purchase Plan | | 0 | 0 | 0 | 464 |
| Total Equity compensation plans approved by security holders | | 9,901 | 0 | 9,901 | 1,166 |
| Equity compensation plans not approved by security holders: | | | | | |
| None. | | | | | |

Recent Sales of Unregistered Securities

None.

Issuer Repurchases of Equity Securities

None.

Table of Contents

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, 2012, 2011, 2010, 2009 and 2008 have been derived from our audited financial statements, of which the consolidated statement of operations and comprehensive loss data for the three fiscal years ending December 31, 2012, 2011 and 2010 and consolidated balance sheet data as of December 31, 2012 and 2011 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.

| | Year Ended December 31, | | | | |
|---|---|---|---|---|---|
| | 2012 | 2011 | 2010 | 2009 | 2008 |
| | (In Thousands, Except Per Share Amounts) | | | | |
| Statement of Operations and Comprehensive Loss Data | | | | | |
| Revenue: | | | | | |
| Net product revenue | $35,864 | $30,411 | $19,069 | $— | $— |
| Contract revenue | 8,462 | 7,165 | 4,373 | — | — |
| Total revenue | 44,326 | 37,576 | 23,442 | — | — |
| Operating expenses: | | | | | |
| Cost of sales | 19,496 | 19,293 | 12,846 | — | — |
| Royalty expense | 1,353 | 1,205 | 843 | — | — |
| Research and development | 21,414 | 33,043 | 28,643 | 21,438 | 33,910 |
| Selling, general and administrative | 49,494 | 60,459 | 51,270 | 14,102 | 11,820 |
| Total operating expenses | 91,757 | 114,000 | 93,602 | 35,540 | 45,730 |
| Loss from operations | (47,431) | (76,424) | (70,160) | (35,540) | (45,730) |
| Other income (expense): | | | | | |
| Interest income | 53 | 37 | 5 | 10 | 696 |
| Interest expense | (10,313) | (7,644) | (10,013) | (9,188) | (1,718) |
| Change in fair value of warrant liability | 11,811 | 445 | 6,725 | (755) | 1,119 |
| Change in fair value of embedded derivatives | (147) | (240) | — | — | — |
| Other income (expense) | (1,354) | (86) | (111) | (416) | 63 |
| Total other income (expense) | 50 | (7,488) | (3,394) | (10,349) | 160 |
| Loss before income taxes | (47,381) | (83,912) | (73,554) | (45,889) | (45,570) |
| Provision for income taxes | (5) | 9 | (10) | — | — |
| Net loss | $(47,386) | $(83,903) | $(73,564) | $(45,889) | $(45,570) |
| Net loss per share, basic and diluted (1) | $(0.59) | $(1.96) | $(17.63) | $(40.97) | $(52.68) |
| Weighted-average shares outstanding, basic and diluted (1) | 80,558 | 42,712 | 4,173 | 1,120 | 865 |
| Comprehensive loss | (47,386) | (83,903) | (73,564) | (45,889) | (45,570) |

(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.

Table of Contents

| | As of December 31, | | | | |
|---|---|---|---|---|---|
| | 2012 | 2011 | 2010 | 2009 | 2008 |
| | (In Thousands) | | | | |
| Balance Sheet Data: | | | | | |
| Cash and cash equivalents and investment securities, available for sale | $41,228 | $56,525 | $49,172 | $44,911 | $14,255 |
| Working capital | 29,071 | 37,057 | 38,626 | 42,102 | 3,032 |
| Total assets | 80,686 | 100,640 | 94,268 | 74,568 | 27,625 |
| Long-term debt, less current portion | 28,481 | 42,070 | 19,934 | 8,778 | 15,336 |
| Convertible preferred stock warrant liability | — | — | — | 5,041 | 467 |
| Convertible preferred stock | — | — | — | 149,312 | 76,955 |
| Accumulated deficit | (329,391) | (282,005) | (198,102) | (124,538) | (78,649) |
| Total stockholders' equity (deficit) | 14,473 | 9,312 | 28,734 | (122,300) | (77,534) |

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, 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. We commercialize Sumavel DosePro through our internal sales and marketing organization and in collaboration with Mallinckrodt LLC, our co-promotion partner.

Our lead product candidate, Zohydro ER (hydrocodone bitartrate, formerly ZX002) is a 12-hour extended-release formulation of hydrocodone without acetaminophen for the treatment of moderate to severe chronic pain requiring around-the-clock opioid therapy. We completed Phase 3 development of Zohydro ER in 2011, and we submitted the New Drug Application, or NDA, for Zohydro ER to the FDA in May 2012. In July 2012, the FDA accepted our NDA as being sufficiently complete for a full review and assigned a Prescription Drug User Fee Act (PDUFA) target date of March 1, 2013. In December 2012, an advisory committee convened by the FDA voted 2-11 (with 1 abstention) against the approval of Zohydro ER. The advisory committee provides the FDA with independent expert advice and recommendations; however, the final decision regarding approval is made by the FDA. In February 2013, the FDA informed us that we were unlikely to receive an action letter for our NDA for Zohydro ER by the PDUFA target action date of March 1, 2013. The FDA has not provided us with information as to the reason for the delay, but has indicated that the delay would likely be brief and may last only several weeks. We have not been informed of any deficiencies in the NDA for Zohydro ER during the review process to date.

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

We are also developing Relday™, a proprietary, long-acting injectable formulation of risperidone using Durect Corporation's SABER™ controlled-release formulation technology through a development and license agreement with Durect, or the Durect License Agreement. Risperidone is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. If successfully developed and approved, we believe Relday may be the first once-monthly, subcutaneous antipsychotic product. In May 2012 we filed an investigational new drug, or IND, application with the FDA. In

Table of Contents

July 2012, we initiated our first IND clinical trial for Relday. This Phase 1 clinical trial was a single-center, open-label, safety and pharmacokinetic trial of 30 patients with chronic, stable schizophrenia or schizoaffective disorder. We announced positive single-dose pharmacokinetic results from the Phase 1 clinical trial on January 3, 2013. Based on the favorable safety and pharmacokinetic profile demonstrated with the 25 mg and 50 mg once-monthly doses tested in the Phase 1 trial, we extended the study to include an additional cohort of 10 patients at a 100 mg dose of the same formulation. The addition of this 100 mg dose to the study will enable evaluation of dose proportionality across the full dose range that would be anticipated to be used in clinical practice. We expect to complete the extension of the Phase 1 clinical trial during the second quarter of 2013. The development of Relday will first focus on its delivery by conventional needle and syringe in order to allow the administration of different volumes of the same formulation of Relday by a healthcare professional. We anticipate that the introduction of our DosePro needle-free technology for administration of Relday can occur later in development or as part of life cycle management after further work involving formulation development, technology enhancements, and applicable regulatory approvals.

We have experienced net losses and negative cash flow from operating activities since inception, and as of December 31, 2012, had an accumulated deficit of $329.4 million. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next several years primarily as a result of the expenses incurred in connection with our efforts in seeking marketing approval for Zohydro ER, any additional required clinical testing for Zohydro ER, the clinical development for Relday and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro ER. As of December 31, 2012, we had cash and cash equivalents of $41.2 million.

On July 27, 2012, we completed a public offering of common stock and warrants for net proceeds of approximately $65.4 million (including over-allotment purchase), after deducting underwriting discounts and commissions of $4.2 million and offering expenses of $0.5 million. We sold a total of 32,500,000 shares of our common stock and warrants to purchase 14,625,000 shares of common stock (excluding over-allotment purchase) in the offering, at a purchase price to the public of $1.99 per share of common stock and $0.01 per share underlying each warrant. The underwriters were granted a 30-day option to cover over-allotments, to purchase up to an additional 4,875,000 shares of common stock and warrants to purchase 2,193,750 shares of common stock, of which the underwriters exercised their option with respect to 2,558,300 shares of common stock and warrants for 1,159,200 shares of common stock. The warrants will be exercisable beginning on July 27, 2013 at an exercise price of $2.50 per share and will expire on July 27, 2017, which is five years from the date of issuance.

Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of December 31, 2012, and our projected product revenues from Sumavel DosePro, will be sufficient to fund our operations into the fourth quarter of 2013. We will need to obtain additional capital to finance our operations beyond that point, or possibly earlier. Further, if we receive FDA approval of Zohydro ER, we may need to obtain additional capital to finance the commercial launch of Zohydro ER, possibly prior to the fourth quarter of 2013. We intend to raise additional capital, if necessary, 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, 2012, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern.

Mallinckrodt Co-Promotion Agreement

In June 2012, we entered into a co-promotion agreement with Mallinckrodt. Under the terms of the co-promotion agreement Mallinckrodt has committed to a minimum number of sales representatives for the initial term of the agreement, which runs through June 30, 2014, and can be extended by mutual agreement of the parties in additional six month increments. We remain responsible for the manufacture, supply and distribution of commercial product for

sale in the United States. In addition, we will supply product samples to Mallinckrodt at an agreed upon transfer price and Mallinckrodt will reimburse us for all other promotional materials used.

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

Table of Contents

For the year ended December 31, 2012, we incurred service fee expenses of $0.2 million under the co-promotion agreement.

Astellas Co-Promotion Agreement

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

In December 2011, we entered into an amendment to the Astellas co-promotion agreement, whereby the agreement terminated on March 31, 2012. As a result of the agreement termination, and pursuant to a promotion transition plan, beginning in the second quarter of 2012, our field sales force then consisting of approximately 95 representatives assumed full responsibility from approximately 400 Astellas sales representatives for the continued marketing of Sumavel DosePro. This promotion transition expanded our focus to include a portion of the high-prescribing primary care physicians previously covered by Astellas under the Astellas co-promotion agreement.

At the inception of the Astellas co-promotion agreement and in exchange for the right to promote Sumavel DosePro, Astellas made a non-refundable up-front payment of $2.0 million to us and made aggregate additional payments of $18.0 million to us upon the achievement of a series of milestones. These proceeds are reflected as $8.5 million of deferred revenues on our consolidated balance sheet at December 31, 2011. Beginning with the launch of Sumavel DosePro in January 2010, we began recognizing these proceeds as contract revenues on a ratable basis over 42 months (the original term of the agreement). Upon amendment of the Astellas co-promotion agreement on December 20, 2011, the remaining deferred proceeds were recognized as contract revenues on a ratable basis over 3.4 months (the remaining term of the amended agreement). This acceleration in the recognition of the contract proceeds resulted in the recognition of $8.5 million of contract revenue during the three months ended March 31, 2012.

Under the terms of the amended Astellas co-promotion agreement, we are required to make two annual tail payments to Astellas, estimated as a total of $5.3 million, calculated as decreasing fixed percentages (ranging from a mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion. The present value of such tail payments was recorded as a long-term liability on the amendment date and is payable in July 2013 and July 2014. The fair value of the tail payments will be accreted through interest expense on a monthly basis through the date of payment. As of December 31, 2012, the short-term and long-term tail payment liability was $1.8 million and $1.0 million, respectively (including the service fee reduction discussed below), and there was $0.6 million of related interest expense recognized during the year ended December 31, 2012.

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

In August 2012, we and Astellas completed a final reconciliation under the terms of the co-promotion agreement and agreed to adjust the service fees paid to Astellas over the term of the co-promotion agreement, resulting in a service fee receivable of $1.5 million, which will offset the two annual tail payments, and a reduction to the annual tail payment liability of $0.7 million. The present value of the service fee receivable and tail payment reduction of $1.9 million was recorded as a reduction in selling, general and administrative expenses during the twelve months ended December 31, 2012, and an offset to the tail payment liability. The fair value of the service fee receivable and tail payment reduction will be accreted through interest income through the dates of the two tail payments in July 2013 and July 2014.

For the years ended December 31, 2012, 2011 and 2010, we recognized shared marketing expense of $0.3 million, $1.7 million and $3.9 million, respectively. For the years ended December 31, 2012, 2011 and 2010, excluding tail payments recorded as service fee expenses, we recorded $1.8 million, $6.7 million and $3.7 million in service fee expenses, respectively.

Durect License Agreement

Table of Contents

In July 2011, we paid a non-refundable upfront fee to Durect of $2.25 million under the development and license agreement with Durect, or 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. In connection with the license agreement, we incurred $2.1 million and $2.7 million (excluding the upfront fee of $2.25 million paid in July 2011) of research and development expenses for the years ended December 31, 2012 and 2011, respectively.

Critical Accounting Policies and Estimates

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

While our significant accounting policies are more fully described in Note 2 to our consolidated financial statements appearing elsewhere in this 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, Net

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. We recognize product sales at the time title transfers to our customer, and we reduce product sales for estimated future product returns and sales allowances in the same period the related revenue is recognized. Product sales allowances include wholesaler and retail pharmacy distribution fees, prompt pay discounts, chargebacks, rebates and patient discount programs, and 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.

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.

Product Returns. Our estimated product return allowances for Sumavel DosePro require a high degree of judgment and are subject to change based on our experience and certain quantitative and qualitative factors. Sumavel DosePro's shelf life is

Table of Contents

determined by the shorter expiry date of its two subassemblies, which is currently approximately 30 months from the date of manufacture. Our return policy allows for the customer to return unused product six months before and up to one year after its expiration date for a credit at the then-current wholesaler acquisition cost, or WAC, reduced by a nominal fee for processing the return.

We have monitored actual return history on an individual product lot basis since product launch. Actual product return experience in 2012 and 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 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. Because of the shelf life of Sumavel DosePro and the duration of time under which our customers may return product to us through our return policy, there may be a significant period of time between when the product is shipped and when we issue credits on returned product. Accordingly, we may have to adjust these estimates, which could have an effect on product sales and earnings in the period of adjustments. A 1% increase or decrease in our returns reserve as a percentage of product shipped in the years ended December 31, 2012 and 2011 would have a financial statement impact of approximately $0.5 million and $0.6 million for the years ended December 31, 2012 and 2011, respectively.

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 approximately three to four weeks of product on hand. As of December 31, 2012, wholesale distributors reported approximately four weeks of our product on hand.

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

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

Chargebacks. We provide discounts primarily 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 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.

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

Table of Contents

utilization to us; and discounts determined under federal guidelines, which affect our rebate programs with U.S. federal government agencies, may differ from those estimated. On a quarterly basis, we analyze our estimates against actual rebate, chargeback and incentive program activity and adjust our estimates as necessary. Given our limited history with the commercialization of Sumavel DosePro, we may experience variability in our provisions for these sales allowances as we continue to initiate new sales initiatives and/or managed care programs in connection with the commercialization of our product. An adjustment to our estimated liabilities for rebates, chargebacks and other incentive programs of 1% of product sales, based on operating results for the year ended December 31, 2012, would have resulted in an increase or decrease to net product sales for that period of approximately $0.5 million. The sensitivity of our estimates can vary by program and type of customer. Additionally, there is a time lag between the date we determine the estimated liability and when we actually pay the liability. Due to this time lag, we may record adjustments to our estimated liabilities over several reporting periods, which can result in a net increase to net revenues or a net decrease to net revenues in those periods. Material differences may result in the amount of revenue we recognize from product sales if the actual amount of rebates, chargebacks and incentives differ materially from the amounts estimated by management. To date, there have been no material differences between the amount recorded in a period and actual charges incurred.

Contract Revenue

Contract revenue consists of the amortization of license fees and milestone payments received under our co-promotion agreements, which have multiple deliverables. 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. The selling price for each deliverable is determined using: (i) vendor-specific objective evidence of selling price, or VSOE, if it exists, (ii) third-party evidence of selling price, or TPE, if VSOE does not exist, and (iii) our 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, we 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.

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

We classify common 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 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 and comprehensive loss.

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 and comprehensive loss. We measure the fair value of the embedded derivatives using various discounted cash flow valuation models.

Fair Value Measurements

GAAP requires us to estimate the fair value of certain assets and liabilities as of the date of their acquisition or incurrence, on an ongoing basis, or both. Determining the fair value of an asset or liability requires the use of accounting estimates and assumptions which are judgmental in nature and could have a significant impact on the determination of the amount of the fair value ascribed to the asset or liability.

Table of Contents

Clinical Trial Expenses

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

Stock-Based Compensation

Stock-based compensation expense is measured at the grant date, based on the estimated fair value of the award, and is recognized as expense over the employee's requisite service period, or vesting period, on a straight-line basis. Equity awards issued to non-employees are recorded at their fair value on the grant date and are periodically re-measured as the underlying awards vest unless the instruments are fully vested, immediately exercisable and nonforfeitable on the date of grant.

Results of Operations

Comparison of Years Ended December 31, 2012, 2011 and 2010

Revenue. We recognize net product sales upon the shipment of product to wholesale pharmaceutical distributors and retail pharmacies. 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 distribution fees, 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 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 and year ended December 31, 2012 consisting of Sumavel DosePro shipped to wholesale distributors and retail pharmacies, net of product-related discounts, allowances and product returns, as applicable.

Revenue for the years ended December 31, 2012, 2011 and 2010 was $44.3 million, $37.6 million and $23.4 million, respectively. Net product revenue for the years ended December 31, 2012, 2011 and 2010 was $35.9 million, $30.4 million and $19.1 million, respectively.

The aggregate $5.5 million, or 18%, increase in net product revenue during 2012 compared to 2011 was primarily due to an increase in unit volume of 16%, offset by a decrease in our average selling price of approximately 1%. This decrease in our average selling price per unit was driven by charges related to estimated product returns and a 13% increase in sales allowances as a percentage of gross U.S. product revenue through increased third-party payor contracting/rebates and patient incentives.

The aggregate $11.3 million, or 59%, increase in net product revenue during 2011 compared to 2010 was 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. While prescription volume increased in 2011 over 2010, the increase was 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. Further, 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, 2012, 2011 and 2010 was $8.5 million, $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 Astellas co-promotion agreement we entered into in July 2009 and which we began recognizing upon the commencement of sales of Sumavel DosePro in January 2010. 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 the Astellas co-promotion agreement whereby the agreement terminated on March 31, 2012, rather than the initial termination date of June 30, 2013. Based upon this revised termination date, all deferred contract revenue was recognized on an accelerated basis during the year ended December 31, 2012. This acceleration resulted in the recognition of an additional $0.9 million of contract revenue during the year ended December 31, 2011.

Table of Contents

Cost of Sales. Cost of sales consists primarily of materials, third-party manufacturing costs, freight and indirect personnel and other overhead costs associated with sales of Sumavel DosePro based on units sold to wholesale pharmaceutical distributors and retail pharmacies, as well as reserves for excess, dated or obsolete commercial inventories and production manufacturing variances. It represents the cost of Sumavel DosePro units recognized as net product revenues in the period and the impact of underutilized production capacity and other manufacturing variances. Cost of sales for the years ended December 31, 2012, 2011 and 2010 was $19.5 million, $19.3 million and $12.8 million, respectively. Product gross margin for the year ended December 31, 2012 was 45.6% compared to 36.6% for the year ended December 31, 2011 and 32.6% for the year ended December 31, 2010. The improvement in product gross margin of 9.1% in 2012 compared to 2011 was primarily a result of a decrease in excess capacity charges of our contract manufacturing organizations. The improvement in product gross margin of 4.0% in 2011 compared to 2010 was primarily a result of increased product sales, offset by an increase in excess capacity charges. 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 in 2010 compared to 2011. 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.

Royalty Expense. Royalty expense consists of royalties payable to Aradigm based on net sales of Sumavel DosePro by us or one of our licensees and the amortization of the $4.0 million milestone payment paid by us to Aradigm upon the first commercial sale of Sumavel DosePro in the United States (which occurred in January 2010). We are not required to make any further milestone payments to Aradigm. We are required to pay to Aradigm a 3% royalty on global net sales of Sumavel DosePro, by us or one of our licensees, if any, until the expiration of the last valid claim of the transferred patents covering the manufacture, use, or sale of the product. During the years ended December 31, 2012, 2011 and 2010, we recorded $1.4 million, $1.2 million and $0.8 million, respectively, in royalty expense. The increases in royalty expense are primarily due to the increases in sales.

Research and Development Expenses. Research and development expenses consist of expenses incurred in developing, testing and seeking marketing approval of our product candidates, including: license and milestone payments; payments made to third-party CROs and investigational sites, which conduct our trials on our behalf, and consultants; expenses associated with regulatory submissions, pre-clinical development and clinical trials; payments to third-party manufacturers, which produce our active pharmaceutical ingredient and finished product; personnel related expenses, such as salaries, benefits, travel and other related expenses, including stock-based compensation; and facility, maintenance, depreciation and other related expenses. We expense all research and development costs as incurred.

We utilize CROs, contract laboratories and independent contractors for the conduct of pre-clinical studies and clinical trials. We track third-party costs by type of study being conducted. We recognize the expenses associated with the services provided by CROs based on the percentage of each study completed at the end of each reporting period. We coordinate clinical trials through a number of contracted investigational sites and recognize the associated expense based on a number of factors, including actual and estimated subject enrollment and visits, direct pass-through costs and other clinical site fees.

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| | (In Thousands) | | |
| Research and development expenses: | | | |
| Zohydro ER | $11,544 | $20,461 | $20,174 |
| Relday | 3,358 | 5,066 | 761 |
| Sumavel DosePro | 757 | 1,129 | 1,672 |
| Other (1) | 5,755 | 6,387 | 6,036 |

| | | | |
|---|---|---|---|
| Total | $21,414 | $33,043 | $28,643 |

(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.

Table of Contents

Research and development costs decreased by $11.6 million for the year ended December 31, 2012 compared to the year ended December 31, 2011 primarily due to a decrease in development expenses for Zohydro ER and Relday. The decrease in Zohydro ER development expenses is the result of Phase 3 clinical trials that were initiated in March 2010 and were completed in December 2011 and a milestone payment made to Alkermes in 2011 upon completion of the Phase 3 clinical trials for Zohydro ER. These cost decreases were partially offset by increased expenses related to fees paid in connection with our Zohydro ER NDA submission to the FDA in May 2012 and costs related to preparation for and participation in the December 2012 FDA advisory committee meeting for Zohydro ER. The decrease in Relday development expenses was primarily due to an upfront fee paid to Durect in July 2011 upon execution of the Relday license agreement.

Research and development costs increased by $4.4 million for the year ended December 31, 2011 compared to the year ended December 31, 2010 primarily due to an increase in development expenses for Relday, which was primarily related to an upfront fee paid Durect in July 2011 upon execution of the Relday license agreement and an increase in costs for pre-clinical studies and formulation and stability testing for Relday in 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.

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

Selling, General and Administrative Expenses. Selling expenses, which include sales and marketing costs, consists primarily of salaries and benefits of sales and marketing management and sales representatives, shared marketing and advertising costs and service fees under our Astellas co-promotion agreement prior to its termination in March 2012, service fees under our Mallinckrodt co-promotion agreement, sample product costs, and consulting fees. General and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, accounting, business development and internal support functions. In addition, general and administrative expenses include facility costs and professional fees for legal, consulting and accounting services.

Selling, general and administrative expenses decreased to $49.5 million for the year ended December 31, 2012 compared to $60.5 million for the year ended December 31, 2011. Selling expenses were $35.9 million for the year ended December 31, 2012 compared to $47.7 million for the year ended December 31, 2011. General and administrative expenses were $13.6 million for the year ended December 31, 2012 compared to $12.8 million for the year ended December 31, 2011. The decrease of $11.0 million in selling, general and administrative expenses was due to a decrease of $11.8 million of sales and marketing expenses, offset by an increase of $0.8 million of general and administrative expenses.

- The decrease in sales and marketing expenses is primarily the result of a $10.8 million decrease in service fees to Astellas due to the termination of the co-promotion agreement on March 31, 2012 and resulting reduction of service fees paid over the life of the agreement, and a decrease in other advertising and promotional activities. These selling and marketing expense decreases are partially offset by an increase in sales and marketing personnel costs primarily due to an increase in non-cash stock compensation expense and sales incentive compensation.
- The increase in general and administrative expenses is primarily a result of an increase in non-cash stock-based compensation charges, salary expense and recruiting expenses, partially offset by a decrease in professional service related costs, such as legal and accounting and advisory services.

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 was due to an increase of $5.4 million of sales and marketing expenses and an increase of $3.8 million of general and administrative expenses.

The increase in sales and marketing expenses is primarily a result of increased service fees to Astellas resulting from higher product revenues and accrued tail payments recorded in connection with the termination of the Astellas co-promotion agreement in December 2011. Sales and marketing expenses also increased due to an increase in sales force costs resulting from an increase in the average number of sales representatives, as well as an increase in advertising and promotional efforts. These selling and marketing expense increases are partially offset by a decrease in sampling efforts.

Table of Contents

- The increase in general and administrative expenses is primarily a result of an 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, as well as an increase in non-cash stock-based compensation charges.

We do not expect a significant change in general and administrative expense in 2013 as compared to 2012 levels; however, our selling expenses may increase significantly in 2013 if Zohydro ER is approved.

Interest Income. During the years ended December 31, 2012, 2011 and 2010, interest income was $53,000, 37,000 and $5,000, respectively. The increase in interest in 2012 compared to 2011 and in 2011 compared to 2010, was primarily due to the increase in average cash and cash equivalent balances during the respective periods.

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

- our $30.0 million financing agreement, or the Healthcare Royalty financing agreement, with Healthcare Royalty Partners (formerly Cowen Healthcare Royalty Partners II, LP), or Healthcare Royalty;
- our $10.0 million revolving credit facility with Oxford Finance Corporation, or Oxford, and Silicon Valley Bank, or SVB;
- our $25.0 million loan and security agreement with Oxford and SVB, or the amended Oxford/SVB loan agreement;
- $4.5 million borrowed under our loan and security agreement with General Electric Capital Corporation, or GE Capital; and
- imputed interest from the two annual tail payments to Astellas.

Interest expense increased to $10.3 million for the year ended December 31, 2012 compared to $7.6 million for the year ended December 31, 2011. The increase of $2.7 million was primarily due to:

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

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 was primarily was due to:

- a decrease in interest expense 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 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 in interest expense related to the early settlement of our outstanding principal balance on our $18.0 million amended loan and security agreement with Oxford and CIT; offset by
- an increase in interest payments related to the $30.0 million borrowed from Healthcare Royalty and an an increase in accrued non-cash interest expense based on our estimate of future interest payments on this facility; and
- an increase in interest expense due to higher debt balances associated with the amended Oxford/SVB loan agreement.

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

Change in Fair Value of Warrant Liabilities. The change in fair value of warrant liabilities relates to a fair value adjustment recorded on the warrants to purchase common stock issued in connection with our July 2012 public offering and issued in connection with our Healthcare Royalty financing agreement. See Note 7 to the Consolidated Financial Statements.

Change in Fair Value of Embedded Derivatives. The change in fair value of embedded derivatives relates to a fair value adjustment recorded on the embedded derivatives associated with the Healthcare Royalty financing agreement. See Note 3 to the Consolidated Financial Statements.

90

Table of Contents

Other Expense. Other expense for the year ended December 31, 2012 consists of expense incurred in July 2012 from the issuance of warrants in our public offering, slightly offset by foreign currency transaction gains. Other expense for the year ended December 31, 2011 and 2010 consists primarily of foreign currency transaction gains and losses.

Provision for Income Tax (Expense) Benefits. Provision for income tax (expense) benefit is primarily 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, 2012, we had available federal and state net operating loss carryforwards of approximately $158.3 million and $164.1 million, respectively. If not utilized, the net operating loss carryforwards will begin expiring in 2026 for federal tax purposes and 2015 for state tax purposes. As of December 31, 2012, we had federal and state research and development tax credit carryforwards of approximately $0.3 million and $2.0 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 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, 2011 we had two ownership changes. The first ownership change occurred in August 2006 upon the issuance of our 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 in our follow-on offering. 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. We are currently in the process of completing a Section 382 and 383 study to determine the impact that ownership changes during the year ended December 31, 2012 have had on our carryforwards and expect to complete the analysis within the next three months. As a result of this analysis, we may have an adjustment in the net operating losses that are recorded at December 31, 2012.

Pursuant to IRC Section 382 and 383, the use of 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 and comprehensive loss.

Liquidity and Capital Resources

We have experienced net losses and negative cash flow from operations since inception, and as of December 31, 2012, had an accumulated deficit of $329.4 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 efforts in seeking marketing approval for Zohydro ER, the clinical development for Relday, any additional required testing for Zohydro ER, and the cost of the sales and marketing expense associated with Sumavel DosePro, and, if approved, Zohydro ER. As of December 31, 2012, we had cash and cash equivalents of $41.2 million.

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

Although it is difficult to predict future liquidity requirements, we believe that our cash and cash equivalents as of December 31, 2012, and our projected product revenues from Sumavel DosePro, will be sufficient to fund our

operations into the fourth quarter of 2013. We will need to obtain additional capital to finance our operations beyond that point, or possibly earlier. Further, if we receive FDA approval of Zohydro ER, we may need to obtain additional capital to finance the commercial launch of Zohydro ER, possibly prior to the fourth quarter of 2013. We intend to raise additional capital, if necessary, through public or private equity offerings, debt financings, receivables financings or through collaborations or partnerships with other

Table of Contents

companies. If we are unsuccessful in raising additional required funds, we may be required to significantly delay, reduce the scope of or eliminate one or more of our development programs or our commercialization efforts, or cease operating as a going concern. We also may be required to relinquish, license or otherwise dispose of rights to product candidates or products that we would otherwise seek to develop or commercialize ourselves on terms that are less favorable than might otherwise be available.

In its report on our consolidated financial statements for the year ended December 31, 2012, our independent registered public accounting firm included an explanatory paragraph expressing substantial doubt regarding our ability to continue as a going concern. A “going concern” opinion means, in general, that our independent registered public accounting firm has substantial doubt about our ability to continue our operations without continuing infusions of capital from external sources and this opinion could impair our ability to finance our operations through the sale of debt or equity securities or commercial bank loans. Our ability to continue as a going concern depends, in large part, on our ability to generate positive cash flow from operations and obtain additional financing, neither of which is certain. If we are unable to achieve these goals, our business would be jeopardized and we may not be able to continue operations and have to liquidate our assets and may receive less than the value at which those assets were carried on our financial statements, and it is likely that investors will lose all or part of their investment.

Since inception, our operations have been financed primarily through equity and debt financings, the issuance of convertible notes and payments received from Astellas under our Astellas co-promotion agreement. Through December 31, 2012, we received aggregate net cash proceeds of approximately $341.2 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 Healthcare Royalty financing agreement pursuant to which we sold 388,601 shares of our common stock, resulting in $1.4 million of net proceeds;
- in September 2011 and October 2011, we issued and sold a total of 30,711,566 shares of common stock in a follow-on public offering, including shares issued upon the exercise of the underwriters’ option to purchase shares, for aggregate net proceeds of $57.9 million; and
- in July 2012, we issued and sold a total of 35,058,300 shares of common stock and warrants to purchase 15,784,200 shares of common stock in a public offering, including the underwriters' over-allotment purchase, for aggregate net proceeds of $65.4 million.

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

In connection with the repayment and termination of the amended Oxford/SVB loan agreement, we repaid $19.5 million of outstanding principal and interest under the agreement. In addition to the repayment of all principal and interest outstanding, we were also required to make a final payment of $1.2 million and a prepayment premium of $0.4 million, or 2% of the then outstanding principal. We also paid a $0.1 million prepayment premium to terminate the revolving credit facility. As a result of the termination of the amended Oxford/SVB loan agreement, the lenders no

longer have a security interest in our intellectual property and personal property (including, among other things, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash).

On July 18, 2011, we closed the Healthcare Royalty financing agreement. Under the terms of the Healthcare Royalty Financing agreement, we borrowed $30.0 million and we are obligated to repay such borrowed amount together with a specified return to Healthcare Royalty, through the payment of tiered royalties ranging from .5% to 5% of our direct product sales, co-promotion revenues and out-license revenues, or collectively, Revenue Interest, that we may record or receive as a result of worldwide commercialization of our products including Sumavel DosePro, Zohydro ER, if approved, and other future

Table of Contents

products. Pursuant to the terms of the Healthcare Royalty financing agreement, our royalty rate increased to 5.75% in April 2012 in connection with the early termination of the Astellas co-promotion agreement.

We are also obligated to make three fixed payments of $10.0 million on (or before at our option) each of January 31, 2015, January 31, 2016 and January 31, 2017.

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

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

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

Cash and Cash Equivalents. Cash and cash equivalents totaled $41.2 million and $56.5 million at December 31, 2012 and December 31, 2011, respectively.

The following table summarizes our cash flows from (used in) operating, investing and financing activities for the years ended December 31, 2012, 2011 and 2010:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| | (In Thousands) | | |
| Statement of Cash Flows Data: | | | |
| Total cash provided by (used in): | | | |
| Operating activities | $(52,202) | $(80,471) | $(71,952) |
| Investing activities | (293) | (617) | (3,442) |
| Financing activities | 37,198 | 88,441 | 79,655 |
| Net (decrease) increase in cash and cash equivalents | $(15,297) | $7,353 | $4,261 |

Operating Activities. Net cash used in operating activities was $52.2 million, $80.5 million and $72.0 million for the years ended December 31, 2012, 2011 and 2010, respectively. Net cash used for the year ended December 31, 2012 and 2011 primarily reflects the use of $49.3 million and $75.9 million, respectively, for operations (excluding non-cash items), which includes personnel-related costs, research and development costs (primarily for Zohydro ER and Relday), sales and marketing expenses for Sumavel DosePro, and other professional services. Net cash used for the year ended December 31, 2012 and 2011 also includes $6.8 million and $6.1 million, respectively, used for other working capital purposes, offset by $3.9 million and $1.5 million, respectively, in the reduction of commercial inventory of Sumavel DosePro. 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.

Investing Activities. Net cash used in investing activities was $0.3 million, $0.6 million, and $3.4 million for the years ended December 31, 2012, 2011 and 2010, 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 $4.0 million to $5.0 million in 2013. These planned capital expenditures primarily relate to further investments in our manufacturing operations for Sumavel DosePro and toward

enhancing our existing manufacturing technology and equipment.

Financing Activities. Net cash provided by financing activities was $37.2 million, $88.4 million and $79.7 million for the years ended December 31, 2012, 2011 and 2010, respectively. Net cash provided by financing activities for the year ended

Table of Contents

December 31, 2012 includes net proceeds from the issuance of common stock and warrants to purchase common stock during our July 2012 public offering, and net proceeds provided by our revolving credit facility with Oxford/SVB, offset by payments on our borrowed debt. Net cash provided by financing activities for the year ended December 31, 2011 includes net proceeds received from the issuance of common stock in our follow-on public offering, net proceeds received in connection with our Healthcare Royalty financing agreement, net proceeds received from our $10.0 million revolving credit facility and proceeds from the issuance of common stock purchased through our Employee Stock Purchase Plan, offset by payments on borrowings of debt. Net cash provided by financing activities for the year ended December 31, 2010 includes net proceeds received in connection with our initial public offering, net proceeds received in connection with the amended Oxford loan agreement and proceeds received in connection with our issuance of convertible promissory notes in 2010, offset by principal repayments made on our outstanding debt facilities.

Our sources of liquidity include our cash balances and cash receipts from the sale of Sumavel DosePro. Through December 31, 2012, we received aggregate net cash proceeds of approximately $341.2 million from the sale of shares of our preferred and common stock. As of December 31, 2012, we had $41.2 million in cash and cash equivalents. Other potential sources of near-term liquidity include (i) entering into a commercialization agreement for Zohydro ER, if approved, or a licensing arrangement for Relday, (ii) equity, debt or other financing or (iii) leveraging our sales force capacity to promote a new product.

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

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

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

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

Contractual Obligations and Commitments

The following table describes our long-term contractual obligations and commitments as of December 31, 2012:

94

Table of Contents

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| | Total | Less than 1 Year | 1-3 Years | 4-5 Years | More than 5 Years |
| | (In Thousands) | | | | |
| Debt obligations (1) | $30,000 | $— | $10,000 | $20,000 | $— |
| Debt interest (2) | 24,930 | 2,526 | 9,748 | 10,325 | 2,331 |
| Operating lease obligations (3) | 3,688 | 1,572 | 2,116 | — | — |
| Co-Promotion tail payments (4) | 3,250 | 2,032 | 1,218 | — | — |
| Purchase obligations (5) | 9,225 | 8,899 | 326 | — | — |
| Total | $71,093 | $15,029 | $23,408 | $30,325 | $2,331 |

(1) Represents annual payments under the Healthcare Royalty financing agreement, which occur on January 1 of 2015, 2016 and 2017.

(2) Includes the interest on scheduled debt payments under the Healthcare Royalty financing agreement, estimated using the effective interest method and revenue projections.

(3) Includes the minimum rental payments for our San Diego, California office pursuant to a lease entered into in April 2012, which expires in November 2014. Also includes the minimum rental payments for our Emeryville, California office pursuant to a lease entered into in July 2007, which expires, 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 the two annual tail payments due to Astellas for the termination of our Astellas co-promotion agreement in March 2012, which are to be paid in July 2013 and July 2014.

(5) Primarily represents non-cancellable purchase orders for the production of key components of Sumavel DosePro, a minimum manufacturing fee payable to Patheon UK Limited through the remaining term of our manufacturing services agreement, and a minimum annual spend in external expenses for the development of Relday. These purchase obligations are based on the exchange rate at December 31, 2012.

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 development and license agreement with Alkermes we may be required to pay up to $2.8 million in total future milestone payments with respect to Zohydro ER, depending upon the achievement of various development and regulatory events. These future milestone payments include a payment of $0.8 million upon successful completion of FDA pre-approval inspection of the manufacturing facility and a payment of $2.0 million upon the first NDA approval of Zohydro ER. In addition, if Zohydro ER 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 Relday license 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 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 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.

Under our Healthcare Royalty financing agreement we are obligated to pay to Healthcare Royalty Revenue Interest on product sales between 5.0% and 0.5%, depending upon the level of product sales made. Upon termination of our

Astellas co-promotion agreement on March 31, 2012, the Revenue Interest rate increased to 5.75%.

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

Table of Contents

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 did not 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 did not have a material effect on our results of operations.

Off-Balance Sheet Arrangements

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

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

Our cash and cash equivalents as of December 31, 2012 consisted of cash and money market funds. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. The primary objective of our investment activities is to preserve principal. Instruments that meet this objective include commercial paper, money market funds and government and non-government debt securities. Some of the investment securities available-for-sale that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the value of the investment securities available-for-sale to fluctuate. To minimize this risk, we intend to continue to maintain our portfolio of cash and money market funds. Due to the short-term nature of our investments and our ability to hold them to maturity, we believe that there is no material exposure to interest rate risk.

Foreign Exchange Risk

All of the revenues we have generated to date have been paid in U.S. dollars and we expect that our revenues will continue to be generated primarily in U.S. dollars for at least the next several years. Payments to our material suppliers and contract 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, 2012, approximately $17.1 million (based on exchange rates as of December 31, 2012) 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, 2012 would have resulted in approximately $0.7 million or $1.0 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-31.

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

96

Table of Contents

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

As required by Securities and Exchange Commission Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as of the end of the period covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2012 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, 2012, the end of our most recent fiscal year. Pursuant to Section 404(c) of the Sarbanes-Oxley Act, our independent registered public accounting firm has issued an attestation report on the effectiveness of our internal control over financial reporting for the year ended December 31, 2012, which is included below.

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Zogenix, Inc.

We have audited Zogenix, Inc.'s internal control over financial reporting as of December 31, 2012, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the

Treadway Commission (the COSO criteria). Zogenix, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit. We conducted our audit 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 effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding

Table of Contents

of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting 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 the assets of the company; (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 receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; 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.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Zogenix, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2012, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Zogenix, Inc. as of December 31, 2012 and 2011, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2012 of Zogenix, Inc. and our report dated March 15, 2013 expressed an unqualified opinion thereon that included an explanatory paragraph regarding Zogenix, Inc.'s ability to continue as a going concern.

/s/ ERNST & YOUNG LLP

San Diego, California
March 15, 2013

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.

Table of Contents

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 2013 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, 2012, 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.

Table of Contents

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, 2012, 2011 and 2010. All other schedules are omitted as the required information is inapplicable, or the information is presented in the consolidated financial statements or related notes.

3. Exhibits.

A list of exhibits to this Annual Report on Form 10-K is set forth on the Exhibit Index immediately preceding such exhibits and is incorporated herein by reference.

(b) See Exhibit Index.

(b) See Item 15(a)(2) above.

Table of Contents

Zogenix, Inc.
Index to Consolidated Financial Statements

Table of Contents

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, 2012 and 2011, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2012. 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as 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, 2012 and 2011, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2012, 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.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. 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, 2012 financial statements do not include any adjustments that might result from the outcome of this uncertainty.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Zogenix, Inc.'s internal control over financial reporting as of December 31, 2012, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 15, 2013 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

San Diego, California

March 15, 2013

Table of Contents

Zogenix, Inc.
Consolidated Balance Sheets
(In Thousands, except Par Value)

| | December 31, 2012 | 2011 |
|---|---|---|
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | $41,228 | $56,525 |
| Trade accounts receivable, net | 5,643 | 4,913 |
| Inventory, net | 12,886 | 16,776 |
| Prepaid expenses and other current assets | 1,968 | 2,210 |
| Total current assets | 61,725 | 80,424 |
| Property and equipment, net | 13,561 | 14,590 |
| Other assets | 5,400 | 5,626 |
| Total assets | $80,686 | $100,640 |
| Liabilities and stockholders' equity | | |
| Current liabilities: | | |
| Accounts payable | $4,592 | $5,168 |
| Accrued expenses | 14,343 | 10,748 |
| Common stock warrant liabilities | 9,493 | 345 |
| Accrued compensation | 4,226 | 3,805 |
| Revolving credit facility | — | 5,081 |
| Long-term debt, current portion | — | 9,758 |
| Deferred revenue, current portion | — | 8,462 |
| Total current liabilities | 32,654 | 43,367 |
| Long-term debt, less current portion | 28,481 | 42,070 |
| Other long-term liabilities | 5,078 | 5,891 |
| Commitments and contingencies | | |
| Stockholders' equity: | | |
| Common stock, $0.001 par value; 200,000 shares authorized at December 31, 2012 and 100,000 shares authorized at December 31, 2011; 100,809 and 65,369 shares issued and outstanding at December 31, 2012 and 2011, respectively. | 101 | 65 |
| Additional paid-in capital | 343,763 | 291,252 |
| Accumulated deficit | (329,391) | (282,005) |
| Total stockholders' equity | 14,473 | 9,312 |
| Total liabilities and stockholders' equity | $80,686 | $100,640 |

See accompanying notes.

Table of Contents

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| Revenue: | | | |
| Net product revenue | $35,864 | $30,411 | $19,069 |
| Contract revenue | 8,462 | 7,165 | 4,373 |
| Total revenue | 44,326 | 37,576 | 23,442 |
| Operating expenses: | | | |
| Cost of sales | 19,496 | 19,293 | 12,846 |
| Royalty expense | 1,353 | 1,205 | 843 |
| Research and development | 21,414 | 33,043 | 28,643 |
| Selling, general and administrative | 49,494 | 60,459 | 51,270 |
| Total operating expenses | 91,757 | 114,000 | 93,602 |
| Loss from operations | (47,431) | (76,424) | (70,160) |
| Other income (expense): | | | |
| Interest income | 53 | 37 | 5 |
| Interest expense | (10,313) | (7,644) | (10,013) |
| Change in fair value of warrant liabilities | 11,811 | 445 | 6,725 |
| Change in fair value of embedded derivatives | (147) | (240) | — |
| Other expense | (1,354) | (86) | (111) |
| Total other income (expense) | 50 | (7,488) | (3,394) |
| Loss before income taxes | (47,381) | (83,912) | (73,554) |
| Provision for income tax benefit (expense) | (5) | 9 | (10) |
| Net loss | $(47,386) | $(83,903) | $(73,564) |
| Net loss per share, basic and diluted | $(0.59) | $(1.96) | $(17.63) |
| Weighted average shares outstanding, basic and diluted | 80,558 | 42,712 | 4,173 |
| Comprehensive loss | (47,386) | (83,903) | (73,564) |

See accompanying notes.

Table of Contents

Zogenix, Inc.
Consolidated Statements of Stockholders' Equity (Deficit)
(In Thousands, except Per Share Amounts)

| | Common Stock | | Additional Paid-in Capital | Accumulated Deficit | Total Stockholders' Equity (Deficit) |
|---|---|---|---|---|---|
| | Shares | Amount | | | |
| Balance at December 31, 2009 | 1,444 | $1 | $2,237 | $(124,538) | $ (122,300) |
| Net loss | — | — | — | (73,564) | (73,564) |
| Issuance of common stock from initial public offering, net of issuance costs of $6,013 | 14,436 | 14 | 51,719 | — | 51,733 |
| Conversion of convertible preferred stock to common stock at initial public offering | 14,240 | 14 | 149,298 | — | 149,312 |
| Issuance of common stock from conversion of convertible notes, net of issuance costs of $18 | 3,874 | 5 | 15,472 | — | 15,477 |
| Beneficial conversion feature from issuance of convertible notes | — | — | 4,696 | — | 4,696 |
| Conversion of warrants from warrants for preferred stock to warrants for common stock | — | — | 743 | — | 743 |
| Issuance of common stock in conjunction with exercise of stock options | — | — | 71 | — | 71 |
| Vesting of early exercised stock options | 23 | — | 59 | — | 59 |
| Stock-based compensation | — | — | 2,507 | — | 2,507 |
| Balance at December 31, 2010 | 34,017 | 34 | 226,802 | (198,102) | 28,734 |
| Net loss | — | — | — | (83,903) | (83,903) |
| Issuance of common stock from secondary offering, net of issuance costs of $3,564 | 30,712 | 31 | 57,828 | — | 57,859 |
| Issuance of common stock from financing agreement at $3.86 per share, net of issuance costs of $96 | 389 | — | 1,404 | — | 1,404 |
| Issuance of common stock in conjunction with exercise of stock options | 67 | — | 92 | — | 92 |
| Issuance of common stock from ESPP purchase | 172 | — | 263 | — | 263 |
| Issuance of common stock warrants | — | — | 39 | — | 39 |
| Release of restricted stock units | 12 | — | — | — | — |
| Vesting of early exercised stock options | — | — | 15 | — | 15 |
| Stock-based compensation | — | — | 4,809 | — | 4,809 |
| Balance at December 31, 2011 | 65,369 | 65 | 291,252 | (282,005) | 9,312 |
| Net loss | — | — | — | (47,386) | (47,386) |
| Issuance of common stock from July 2012 offering, net of issuance costs of $3,328 | 35,058 | 35 | 45,774 | — | 45,809 |
| Issuance of common stock in conjunction with exercise of stock options | 18 | — | 33 | — | 33 |
| Issuance of common stock from ESPP purchase | 364 | 1 | 547 | — | 548 |
| Stock-based compensation | — | — | 6,157 | — | 6,157 |

| | | | | | |
|---|---|---|---|---|---|
| Balance at December 31, 2012 | 100,809 | $101 | $343,763 | $(329,391) | $ 14,473 |

See accompanying notes.

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| Operating activities: | | | |
| Net loss | $(47,386) | $(83,903) | $(73,564) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Stock-based compensation | 6,157 | 4,809 | 2,507 |
| Depreciation and amortization | 1,599 | 1,584 | 1,428 |
| Amortization of debt issuance costs and non-cash interest | 2,017 | 1,793 | 1,582 |
| Change in fair value of warrant liabilities | (11,811) | (445) | (6,725) |
| Change in fair value of embedded derivatives | 147 | 240 | — |
| Beneficial conversion feature from issuance of convertible notes | — | — | 4,696 |
| Loss on disposal and impairment of property and equipment | 9 | — | 2 |
| Changes in operating assets and liabilities: | | | |
| Trade accounts receivable | (730) | (439) | (4,474) |
| Inventory | 3,890 | 1,517 | (5,133) |
| Prepaid expenses and other current assets | 163 | 24 | 537 |
| Other assets | 11 | 338 | (3,976) |
| Accounts payable and accrued expenses | 2,283 | 4,955 | 10,866 |
| Deferred rent | (89) | (57) | (48) |
| Deferred revenue | (8,462) | (10,887) | 350 |
| Net cash used in operating activities | (52,202) | (80,471) | (71,952) |
| Investing activities: | | | |
| Purchases of property and equipment | (293) | (617) | (3,442) |
| Net cash used in investing activities | (293) | (617) | (3,442) |
| Financing activities: | | | |
| Proceeds from convertible notes, net of issuance costs | — | — | 14,957 |
| Proceeds from borrowings of debt and revolving credit facility, net of issuance costs | 9,900 | 39,124 | 31,072 |
| Payments on borrowings of debt | (25,000) | (825) | (18,178) |
| Payments on revolving credit facility | (15,051) | (9,477) | — |
| Proceeds from exercise of common stock options | 33 | 92 | 71 |
| Proceeds from issuance of common stock and common stock warrants, net of issuance costs | 67,316 | 59,527 | 51,733 |
| Net cash provided by financing activities | 37,198 | 88,441 | 79,655 |
| Net (decrease) increase in cash and cash equivalents | (15,297) | 7,353 | 4,261 |
| Cash and cash equivalents at beginning of period | 56,525 | 49,172 | 44,911 |
| Cash and cash equivalents at end of period | $41,228 | $56,525 | $49,172 |
| Supplemental disclosure of cash flow information: | | | |
| Cash paid for interest | $5,284 | $4,186 | $2,403 |
| Noncash investing and financing activities: | | | |
| Warrants issued in connection with public offering | $20,959 | $— | $— |
| Asset retirement obligation | $286 | $— | $— |
| Warrants issued in connection with debt | $— | $866 | $— |
| Embedded derivatives related to debt | $— | $605 | $— |

| | | | |
|---|---|---|---|
| Purchase of property and equipment in accounts payable | $— | $123 | $126 |
| Vesting of early exercised stock options | $— | $15 | $59 |
| Conversion of convertible preferred stock to common stock at initial public offering | $— | $— | $149,312 |
| Conversion of convertible notes and related interest to common stock, net of issuance costs | $— | $— | $15,477 |
| Reclassification of convertible preferred stock warrants to common stock warrants | $— | $— | $743 |
| Acquisition of leasehold paid by landlord | $— | $— | $305 |

See accompanying notes.

Table of Contents

Zogenix, Inc.
Notes to Consolidated Financial Statements

1. Organization and Basis of Presentation

Zogenix, Inc. (the Company) is a pharmaceutical company 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.

On July 27, 2012, the Company completed a public offering (the July 2012 Offering) of common stock and warrants for net proceeds of $65,352,000 (including over-allotment purchase), after deducting underwriting discounts and commissions of $4,205,000 and offering expenses of $545,000. The Company sold a total of 32,500,000 shares of its common stock and warrants to purchase 14,625,000 shares of common stock (excluding over-allotment purchase) in the July 2012 Offering, at a purchase price of $1.99 per share of common stock and $0.01 per share underlying each warrant. The underwriters were granted a 30-day option to cover over-allotments, if any, to purchase up to an additional 4,875,000 shares of common stock and warrants to purchase 2,193,750 shares of common stock. The underwriters exercised their option to purchase over-allotment warrants for 1,159,200 shares of common stock concurrent with the July 2012 Offering at a purchase price of $0.01 per warrant and then exercised their option with respect to 2,558,300 shares of common stock at a purchase price of $1.99 per share on a subsequent date. The warrants will be exercisable beginning on July 27, 2013 at an exercise price of $2.50 per share and will expire on July 27, 2017, which is five years from the date of issuance.

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

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)

Table of Contents

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, 2012 and 2011 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 $2,000 and $127,000 at December 31, 2012 and 2011, respectively. The need for bad debt allowance is evaluated each reporting period.

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 the long-term portion of the tail payments due to Astellas Pharmaceutical US, Inc. (Astellas)), 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 annual tail payments due to Astellas (see Note 3) for the termination of the Company's co-promotion agreement were measured at fair value using a present value technique, which incorporated the Company's own credit risk as measured by the most recent round of debt financing with Healthcare Royalty Partners (Healthcare Royalty) (formerly Cowen Healthcare Royalty Partners II, L.P.).

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

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

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

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

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

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

| | Fair Value Measurements at Reporting Date Using | | | |
|---|---|---|---|---|
| | Quoted Prices in Active Markets for Identical Assets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) | Total |
| At December 31, 2012 | | | | |
| Assets | | | | |
| Cash equivalents (1) | $37,605 | — | — | $37,605 |
| Liabilities | | | | |
| Common stock warrant liabilities (2) | $— | — | 9,493 | $9,493 |
| Embedded derivative liabilities (3) | $— | — | 992 | $992 |
| | | | | |
| At December 31, 2011 | | | | |
| Assets | | | | |
| Cash equivalents (1) | $49,752 | — | — | $49,752 |
| Liabilities | | | | |
| Common stock warrant liability (4) | $— | — | 345 | $345 |
| Embedded derivative liabilities (3) | $— | — | 845 | $845 |

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

(2) Common stock warrants are measured at fair value using the Black-Scholes option pricing valuation model and the assumptions identified in (4) below. The following additional assumptions were used in the Black-Scholes option pricing valuation model to measure the fair value of the warrants sold in the July 2012 Offering: (a) management's projections regarding the probability of the occurrence of an extraordinary event that would require cash settlement of the warrants; and for the valuation scenario in which an extraordinary event occurs, (b) an expected volatility rate equal to the lesser of 40% and the 180-day volatility rate obtained from the HVT function on Bloomberg as of the trading day immediately following the public announcement of an extraordinary transaction. Significant increases in the probability of an extraordinary event occurring would result in a significantly lower fair value measurement.

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

exercise of the embedded derivative instruments. The significant unobservable inputs used in measuring the fair value of the embedded derivatives are management's revenue projections. Significant decreases in these significant inputs would result in a higher fair value measurement.

(4) Common stock warrants are measured at fair value using the Black-Scholes option pricing valuation model. The assumptions used in the Black-Scholes option pricing valuation model were: (a) a risk-free interest rate based on the rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the remaining contractual term of the warrants; (b) an assumed dividend yield of zero based on the Company's expectation that it will not pay dividends in the foreseeable future; (c) an expected term based on the remaining contractual term of the warrants; and (d) given the Company's lack of relevant historical data due to the Company's limited historical experience, an expected volatility based upon the

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

Company's historical volatility, supplemented with historical volatility of comparable companies whose share prices have been publicly available for a sufficient period of time. The significant unobservable input used in measuring the fair value of the warrant liabilities is the expected volatility. Significant increases in the volatility would result in a higher fair value measurement.

The following table provides a reconciliation of liabilities measured at fair value using significant unobservable inputs (Level 3) for the years ended December 31, 2012 and 2011 (in thousands):

| | Common Stock Warrant Liabilities | Embedded Derivative Liabilities |
|---|---|---|
| Balance at December 31, 2010 | $— | $— |
| Issuance | 790 | 605 |
| Changes in fair value | (445) | 240 |
| Balance at December 31, 2011 | 345 | 845 |
| Issuance | 20,959 | — |
| Changes in fair value | (11,811) | 147 |
| Balance at December 31, 2012 | $9,493 | $992 |

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

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. Two wholesale pharmaceutical distributors individually comprised 36.1% and 35.5% of the Company’s total gross sales of Sumavel DosePro for the year ended December 31, 2012. Approximately 71.8% of the trade accounts receivable balance as of December 31, 2012 represents amounts due from these two 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 $2,000 and $127,000 at December 31, 2012 and December 31, 2011, respectively.

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.

Inventory

Inventory is stated at the lower of cost or market. Cost includes amounts related to materials, labor and overhead, and 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:

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

| | |
|---|---|
| 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, 2012.

Warrants for Common 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 as current liabilities on the consolidated balance sheet. The Company adjusts the carrying value of these warrants for common stock that can be settled in cash 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 liabilities in the consolidated statement of operations and comprehensive loss.

Embedded Derivatives

The Company records embedded derivatives in the consolidated balance sheet at fair value. The carrying value of the embedded derivatives are adjusted 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 and comprehensive loss.

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, Net

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. The Company recognizes product sales at the time title transfers to its customer, and reduces product sales for estimated future product returns and sales allowances in the same period the related revenue is recognized. Product sales allowances include wholesaler and retail pharmacy distribution fees, prompt pay discounts, chargebacks, rebates and patient discount programs, and 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 its 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.

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 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.

Product Returns. The Company's 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's shelf life is determined by the shorter expiry date of its two subassemblies, which is currently approximately 30 months from the date of manufacture. The Company's return policy allows for customers to return unused product that is within six months before and up to one year after its expiration date for a credit at the then-current wholesaler acquisition cost, or WAC, reduced by a nominal fee for processing the return.

The Company has monitored actual return history on an individual product lot basis since product launch. Actual product return experience in 2012 and 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 its initial launch stocking initiatives. The Company considered these factors as well as the dating of its 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. Because of the shelf life of Sumavel DosePro and the duration of time under which the Company's customers may return product through the Company's return policy, 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.

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.

Wholesaler and Retail Pharmacy Distribution Fees. The Company offers distribution fees to certain wholesale distributors and retail pharmacies based on contractually determined rates. The Company accrues the distribution fees on shipment to the respective wholesale distributors and retail pharmacies and recognizes the distribution fees 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 federal 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 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 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. 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.

Contract Revenue

Contract revenue consists of the amortization of license fees and milestone payments received under co-promotion agreements, which have multiple deliverables. 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. 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 was 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

The Company records certain transactions between collaborators in the consolidated statement of operations and comprehensive loss 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 and comprehensive loss 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 and comprehensive loss 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 and comprehensive loss 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.

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 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 is received.

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 $522,000, $1,180,000 and $1,123,000 in advertising costs for the years ended December 31, 2012, 2011 and 2010, respectively. At December 31, 2012 and 2011, the Company capitalized advertising costs of $159,000 and $26,000 in prepaid expenses 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

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

Gains or losses resulting from transactions denominated in foreign currencies are included in other expense in the consolidated statements of operations and comprehensive loss. The Company recorded losses from foreign currency transactions in other income (expense) of $68,000, $86,000 and $111,000 for the years ended December 31, 2012, 2011 and 2010, 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, 2012, 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 treasury-stock method and as-if converted method, as applicable. For purposes of this calculation, stock options, restricted stock units, warrants and common stock subject to repurchase 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, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| Numerator | | | |
| Net loss | $(47,386) | $(83,903) | $(73,564) |
| Denominator | | | |
| Weighted average common shares outstanding | 80,558 | 42,715 | 4,267 |
| Weighted average shares subject to repurchase | — | (3) | (94) |
| Weighted average shares outstanding, basic and diluted | 80,558 | 42,712 | 4,173 |
| Basic and diluted net loss per share | $(0.59) | $(1.96) | $(17.63) |

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, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| Common stock subject to repurchase | — | — | 15 |
| Common stock options and restricted stock units | 47 | 184 | 1,416 |
| | 47 | 184 | 1,431 |

Segment Reporting

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

Recent Accounting Pronouncements

In May 2011, the Financial Accounting Standards Board (FASB) issued accounting guidance related to fair value measurements and disclosures to achieve common fair value measurements and disclosures between GAAP and International Financial Reporting Standards. This guidance clarifies the application of certain existing fair value measurement guidance and expands the disclosures for fair value measurements that are estimated using significant unobservable (Level 3) inputs. This guidance became effective on a prospective basis for annual and interim reporting periods beginning on or after December 15, 2011. The Company adopted this guidance on January 1, 2012 and it did

not have a material impact on the Company's results of operations.

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

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 became effective for fiscal and interim periods beginning after December 15, 2011, with early adoption permitted. The Company adopted this guidance on January 1, 2012 and it did not have a material impact on the Company's results of operations.

3. Collaboration, License and Purchase Agreements

Alkermes Commercial Manufacturing and Supply Agreement

On November 2, 2012, the Company entered into a commercial manufacturing and supply agreement for Zohydro ER finished commercial product (the Supply Agreement) with Alkermes Pharma Ireland Limited (APIL). Under the Supply Agreement, APIL is the exclusive manufacturer and supplier to the Company (subject to certain exceptions) of Zohydro ER. The Company must purchase all of its requirements of Zohydro ER, subject to certain exceptions, from APIL.

Under the Supply Agreement, the Company will provide APIL with an eighteen-month forecast on a monthly basis and with a three-year forecast on an annual basis for commercial supply requirements of Zohydro ER. In each of the four months following the submission of the eighteen-month forecast, the Company is obligated to order the quantity of Zohydro ER specified in the forecast. APIL will use commercially reasonable efforts to supply the orders of Zohydro ER subject to the availability of the United States Drug Enforcement Administration quota for hydrocodone. APIL is not obligated to supply the Company with quantities of Zohydro ER in excess of forecasted amounts, but has agreed to use commercially reasonable efforts to do so. Further, the Company is obligated to purchase at least 75% of forecasted quarterly quantities of Zohydro ER from APIL, and is required to make compensatory payments if it does not purchase 100% of its requirements from APIL, subject to certain exceptions.

If a failure to supply occurs under the Supply Agreement, other than a force majeure event, APIL must use commercially reasonable efforts to assist the Company in transferring production of Zohydro ER to either the Company or a third-party manufacturer, provided that such third party is not a technological competitor of APIL. In a failure to supply circumstance, the Company would be able to utilize (or sublicense to a third party who is not a technological competitor of APIL) the manufacturing license rights granted to it under the license agreement with Alkermes, an affiliate of APIL, until such time as APIL can resume supply of Zohydro ER.

Either party may terminate the Supply Agreement 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. Unless otherwise terminated due to a material breach, the Supply Agreement will continue until the expiry or termination of the license agreement with Alkermes.

Mallinckrodt LLC Co-Promotion Agreement

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

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

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

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

For the year ended December 31, 2012, the Company incurred $161,000 in service fee expenses under the Co-Promotion Agreement.

Astellas Pharma US, Inc. Co-Promotion Agreement

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

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

In accordance with accounting guidance for revenue arrangements with multiple deliverables, the Company initially recorded the $20,000,000 in upfront and milestone payments received from Astellas as deferred revenue. Beginning with the launch of Sumavel DosePro in January 2010, the Company began amortizing the upfront and milestone payments as contract revenue in the consolidated statement of operations and comprehensive loss over the term of the Astellas Co-Promotion Agreement. Upon termination of the Astellas Co-Promotion Agreement, the Company concluded that the remaining deferred revenue balance should be recognized ratably through the amended term of the agreement, and consequently, the remaining $8,462,000 of these deferred contract revenues as of December 31, 2011 was recognized during the three months ended March 31, 2012. For the years ended December 31, 2012, 2011 and 2010 the Company recognized $8,462,000, $7,165,000 and $4,373,000, respectively, of contract revenue.

The Company is required to make two annual tail payments to Astellas, calculated as decreasing fixed percentages (ranging from mid-twenties down to a mid-teen percentage) of net sales in the Astellas Segment in the last 12 months of its active promotion. The value of such tail payments was estimated at a total of $5,291,000 based upon the agreement termination date of March 31, 2012, and recorded as a long-term liability on the amendment date of December 20, 2011. The fair value of the tail payments will be accreted through interest expense through the dates of

payment in July 2013 and July 2014. As of December 31, 2012 and 2011, the tail payment liability, after considering the August 2012 service fee reduction discussed below, was $2,795,000 and $4,016,000, respectively. The Company recognized $550,000 of related interest expense during the year ended December 31, 2012 and did not recognize any related interest expense during the years ended December 31, 2011 and 2010.

Further, under the terms of the amended Astellas Co-Promotion Agreement, Astellas contributed its agreed upon portion of marketing expenses through March 31, 2012, and continued to earn a service fee based on product sales to the Astellas Segment during that period. As of April 1, 2012, the Company was no longer required to pay service fees to Astellas for sales

of Sumavel DosePro. Additionally, beginning in the second quarter of 2012, the Company's sales force assumed full responsibility for the commercialization and the continued marketing of Sumavel DosePro, expanding their focus to include headache specialists, neurologists and primary care physicians in the United States. Amounts received from Astellas for shared marketing costs and sample product are reflected as a reduction of selling, general and administrative expenses, and amounts payable to Astellas for shared marketing expenses and service fees are reflected as selling, general and administrative expenses, inclusive of the estimated cost of the tail payments owed upon the termination of the agreement.

In August 2012, the Company and Astellas completed a final reconciliation under the terms of the Astellas Co-Promotion Agreement and agreed to adjust the service fees paid to Astellas over the term of the Astellas Co-Promotion Agreement, resulting in a service fee reduction of $1,500,000, which offsets the two annual tail payments, and a reduction to the annual tail payment liability of $742,000. The present value of the service fee receivable and tail payment reduction of $1,924,000 was recorded as a reduction in selling, general and administrative expenses during the year ended December 31, 2012, and an offset to the tail payment liability. The fair value of the service fee receivable and tail payment reduction will be accreted through interest income through the dates of the two tail payments in July 2013 and July 2014.

For the years ended December 31, 2012, 2011 and 2010, the Company recognized shared marketing expense of $253,000, $1,663,000 and $3,853,000, respectively, under the Astellas Co-Promotion Agreement. For the years ended December 31, 2012, 2011 and 2010, the Company incurred $1,756,000 (excluding the $1,924,000 service fee adjustment discussed above), $6,657,000 (excluding the $4,016,000 expense recognized when the tail payments were initially recorded) and $3,660,000 in service fee expenses, respectively.

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 and comprehensive loss during the year ended December 31, 2011. 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 a New Drug Application (NDA) for Relday has been filed in the United States, the Company is obligated to spend no less than $1,000,000 in external expenses on the development of Relday in any trailing twelve months 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 monitoring 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.

Desitin Arzneimittel GmbH Licensing and Distribution Agreement

In 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. The Company recognized $397,000, $0 and $422,000 in revenue for sales to Desitin for the years ended December 31, 2012, 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 2007, the Company entered into a License Agreement with Alkermes, which was amended in 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 ER 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 ER 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 negotiation of the Supply Agreement, Alkermes, or an affiliate of Alkermes, would have the sole and exclusive right to manufacture and supply finished commercial product of Zohydro ER 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 additional milestone payments in the amount of $750,000 to Alkermes in August 2011 in connection with the completion of the treatment phase of the Company's pivotal efficacy Phase 3 clinical trial, Study 801, and $1,000,000 upon submission of the first Zohydro ER NDA to the FDA in May 2012, which were recorded as research and development expense. The Company may be obligated to pay Alkermes up to $2,750,000 in total future milestone payments with respect to Zohydro ER depending upon the achievement of various development and regulatory events. These future milestone payments include a payment of $750,000 upon successful completion of an FDA pre-approval inspection of the Company's manufacturing facility and a payment of $2,000,000 upon the first NDA approval of Zohydro ER. In addition, if Zohydro ER 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.

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

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 ER is prohibited by regulatory authorities, or if, despite commercially reasonable efforts, the Company is unable to obtain regulatory approval for Zohydro ER. 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 ER and at any time upon 12 months' prior written notice after NDA approval for Zohydro ER.

Aradigm Corporation Asset Purchase Agreement

In 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 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 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, 2012, 2011 and 2010, the Company recorded $1,353,000, $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 record annual amortization expense of approximately $286,000 during the years ended December 2013 through 2017, and $1,714,000 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, | |
|---|---|---|
| | 2012 | 2011 |
| Raw materials | $4,867 | $5,785 |
| Work in process | 6,134 | 7,338 |
| Finished goods | 1,885 | 3,653 |

| | | |
|---|---|---|
| Property and Equipment, Net (in thousands) | $12,886 | $16,776 |

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

| | December 31, | |
|---|---|---|
| | 2012 | 2011 |
| Machinery, equipment and tooling | $12,325 | $11,902 |
| Construction in progress | 5,068 | 5,416 |
| Computer equipment and software | 961 | 1,122 |
| Leasehold improvements | 783 | 780 |
| Furniture and fixtures | 685 | 562 |
| Property and equipment, at cost | 19,822 | 19,782 |
| Less accumulated depreciation | (6,261) | (5,192) |
| | $13,561 | $14,590 |

Depreciation expense for the years ended December 31, 2012, 2011 and 2010 was $1,599,000, $1,584,000 and $1,428,000, respectively.

Other Assets (in thousands)

| | December 31, | |
|---|---|---|
| | 2012 | 2011 |
| Prepaid Aradigm royalty expense | $3,143 | $3,429 |
| Deposits | 840 | 565 |
| Debt acquisition costs | 1,217 | 1,432 |
| Restricted cash | 200 | 200 |
| | $5,400 | $5,626 |

Accrued Expenses (in thousands)

| | December 31, | |
|---|---|---|
| | 2012 | 2011 |
| Accrued discounts and allowances | $4,088 | $2,153 |
| Accrued product returns | 3,034 | 2,446 |
| Accrued interest expense, current portion | 2,526 | 1,924 |
| Astellas tail payment, current portion | 1,820 | — |
| Other accrued expenses | 2,875 | 4,225 |
| | $14,343 | $10,748 |

Other Long-Term Liabilities (in thousands)

| | December 31, | |
|---|---|---|
| | 2012 | 2011 |
| Interest expense payable, less current portion | $2,607 | $— |
| Astellas tail payment, less current portion | 975 | 4,016 |
| Embedded derivatives | 992 | 845 |
| Deferred Rent | 214 | 303 |
| Term loan final payment | — | 642 |
| Other long-term liabilities | 290 | 85 |
| | $5,078 | $5,891 |

5. Commitments

Operating Leases

The Company had an operating lease for office facilities in San Diego, California, which commenced in September 2008 and expired in April 2012. In April 2012, prior to the expiration of this lease, the Company entered into a new operating lease

Table of Contents

for office facilities located in San Diego, California, which commenced on April 23, 2012 and will expire on November 27, 2014. The Company received free rent for the second, third and fourth months of the lease term. The base rent will increase approximately 3% on an annual basis throughout the term. The lease also requires the Company to pay, following the first 12 lease months, additional rent consisting of a portion of common area and pass-through expenses in excess of base year amounts. 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, as extended, in September 2015. 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, 2012, 2011 and 2010 was $828,000, $826,000 and $839,000, respectively.

Future minimum lease payments as of December 31, 2012 are as follows (in thousands):

| | |
|---|---|
| 2013 | $1,572 |
| 2014 | 1,473 |
| 2015 | 643 |
| 2016 and thereafter | — |
| Total | $3,688 |

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. In February 2013, the Company entered into an additional manufacturing services agreement (the Amended Services Agreement), with Patheon which will replace the Company's original manufacturing services agreement upon its expiration on October 31, 2013. The Amended Services Agreement has similar terms to the original agreement and will expire on April 30, 2015. The parties may mutually agree in writing to renew the term for additional terms prior to the expiration of the then-current term.

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, 2012, the Company has non-cancellable purchase orders for 2013 totaling approximately $3,327,000 under these arrangements. In addition, the Company is required to pay Patheon a monthly manufacturing fee of £311,000 or approximately $502,000 (based on the exchange rate as of December 31, 2012). As of December 31, 2012, the Company was committed to pay Patheon a total manufacturing fee of £3,111,000, or approximately $5,025,000 (based on the exchange rate as of December 31, 2012), which is payable monthly over the remaining 10 months of the original Patheon manufacturing services agreement.

6. Debt

Maturities of long-term debt as of December 31, 2012, are as follows (in thousands):

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

| | |
|---|---|
| 2013 | $2,526 |
| 2014 | 4,226 |
| 2015 | 15,521 |
| 2016 | 15,104 |
| 2017 | 15,221 |
| 2018 | 2,332 |
| Total minimum payments | 54,930 |
| Less amount representing interest | (24,930) |
| Total long-term debt | 30,000 |
| Less current portion | — |
| Long-term portion | $30,000 |

Interest expense related to long-term debt for the years ended December 31, 2012, 2011 and 2010 was $6,708,000, $5,562,000 and $4,727,000, respectively.

Healthcare Royalty Financing Agreement

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

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

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

- 5% to 5.75% of the first $75,000,000 of Revenue Interest recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year (initially 5% and then 5.75% after the Astellas Co-Promotion Agreement terminated on March 31, 2012, with a reversion back to 5% if certain net sales of Sumavel DosePro are achieved or if Zohydro ER is commercialized in the four calendar quarters immediately following the effective date of termination);
- 2.5% of the next $75,000,000 of Revenue Interest recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year; and
- 0.5% of Revenue Interest over and above $150,000,000 recorded (in the case of net product sales) or received (in the case of co-promotion revenues and license fees) by the Company in a calendar year.

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

As security for the payment of the Company's obligations under the Financing Agreement, the Company also entered into a security agreement whereby the Company granted to Healthcare Royalty a security interest in all assets of the Company, including intellectual property and other rights of the Company to the extent necessary or used to

commercialize the Company products. Healthcare Royalty entered into an intercreditor agreement under which its security interest was junior to the security interest of the lenders under the Company's $25.0 million loan and security agreement with Oxford Finance LLC (Oxford) and Silicon Valley Bank (SVB). The intercreditor agreement terminated on July 30, 2012 when the Company terminated its $25.0

million loan and security agreement. Healthcare Royalty's security interest will be extinguished at the end of the term or once the aggregate payments made by the Company to Healthcare Royalty equal $75,000,000, whichever is sooner. The Company has agreed to specified positive and negative covenants in connection with the Financing Agreement. The Company has the option to terminate the Financing Agreement at the Company's election in connection with a change of control of the Company, upon the payment of a base amount of $52,500,000, or, if higher, an amount that generates a 19% internal rate of return on the Borrowed Amount as of the date of prepayment, in each case reduced by the Revenue Interest and principal payments received by Healthcare Royalty up to the date of prepayment. Healthcare Royalty has the option to terminate the Financing Agreement at its election in connection with a change of control of the Company (which includes the sale, transfer, assignment or licensing of the Company's rights in the United States to either Sumavel DosePro or Zohydro ER), or an event of default (which includes the occurrence of a bankruptcy event or other material adverse change in the Company's business), as defined in the Financing Agreement. Upon such a termination by Healthcare Royalty, the Company is obligated to make a payment of a base amount of $45,000,000, or, if higher, an amount that generates a 17% internal rate of return on the Borrowed Amount as of the date of prepayment, in each case reduced by the Revenue Interest and principal payments received by Healthcare Royalty up to the date of prepayment.

The rights of the Company and Healthcare Royalty to terminate the Financing Agreement early, 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, meet the definition of an embedded derivative. As a result, the Company carved out these embedded derivatives from the Financing Agreement and determined the fair value of each derivative using various discounted cash flow valuation models taking into account the probability of these events occurring and various scenarios surrounding the potential Revenue Interest payments that would be made if these events occurred (see Note 2). The aggregate fair value of the embedded derivatives as of December 31, 2012 and 2011 was $992,000 and $845,000, respectively, and is included in other long-term liabilities. As the Company agreed to early terminate the Astellas Co-Promotion Agreement in December 2011, the related embedded derivative was derecognized, resulting in a $417,000 adjustment to the fair value of embedded derivatives for the year ended December 31, 2011.

The Company received aggregate net proceeds of $29,485,000 from the Financing Agreement (including the purchase of common stock). The discounts, which are being amortized using the effective interest method over the term of the arrangement within interest expense, include the fair value of the common stock warrants issued to Healthcare Royalty of $790,000 upon the closing of the Financing Agreement, fees payable to Healthcare Royalty in connection with the execution of the arrangement of $476,000 and the fair value of embedded derivatives of $605,000 upon the closing of the Financing Agreement. The Company has recognized other income in relation to the change in the fair value of the Healthcare Royalty common stock warrant of $160,000 and $445,000 for the years ended December 31, 2012 and 2011, respectively, in the statement of operations and comprehensive loss. The Company has recognized other expense in relation to the change in the fair value of the embedded derivatives of $147,000 and $240,000 for the years ended December 31, 2012 and 2011, respectively, in the statements of operations and comprehensive loss.

Term Debt

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

The Amended Oxford/SVB Agreement consisted of a $25,000,000 term loan and a $10,000,000 revolving credit facility. The obligations under the Amended Oxford/SVB Agreement were collateralized by the Company's intellectual property (including among other things, copyrights, patents, patent applications, trademarks, service marks and trade secret rights) and personal property (including, among other things, accounts receivable, equipment, inventory, contract rights, rights to payment of money, license agreements, general intangibles and cash). The $25,000,000 term loan bore an interest rate of 12.06% per annum. Under the terms of the revolving credit facility, $10,000,000 was available to be borrowed within a specified

percentage of the Company's eligible accounts receivable and inventory balances (as defined in the Amended Oxford/SVB Agreement). Amounts outstanding under the revolving credit facility accrued interest payable monthly at a floating rate per annum equal to the greater of 3.29% above SVB's prime rate or 7.29%. In addition, the Company paid a monthly fee equal to 0.5% per annum of the average unused portion of the revolving credit facility. The outstanding principal balance of the term loan and the revolving credit facility as of December 31, 2011 was $25,000,000 and $5,151,000, respectively.

On July 30, 2012, the Company exercised its right to terminate the Amended Oxford/SVB Agreement prior to the loan maturity date of January 2, 2014 and repaid $19,492,000 of outstanding principal and interest under the agreement. In addition to the repayment of all principal and interest outstanding, the Company was also required to make a final payment of $1,200,000 and a prepayment premium of $400,000, or 2% of the then outstanding principal. The Company also paid a $100,000 prepayment premium to terminate the revolving credit facility. As a result of the termination of the Amended Oxford/SVB Agreement, the lenders no longer have a security interest in the Company's intellectual property and personal property.

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 (the 2010 Notes). Outstanding balances under the 2010 Notes 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 and 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.

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 was under a promissory note repayable in 48 monthly installments based upon a monthly 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 was repaid in full on June 30, 2011.

7. Preferred Stock and Stockholders’ Equity

Preferred Stock

Under the Company’s amended and restated certificate of incorporation, as of December 31, 2012 and 2011, the Company is authorized to issue 10,000,000 shares of preferred stock with a $0.001 par value. As of December 31, 2012 and 2011, there were no shares of preferred stock issued or outstanding.

As of December 1, 2010, there were 77,891,000 shares of Series A convertible preferred stock for $76,955,000 and 64,507,000 shares of Series B convertible preferred stock for $72,357,000 outstanding. All of these 142,398,000 shares of preferred stock were converted to 14,240,000 shares of common stock on a 10 for 1 basis upon completion of the Company's IPO in 2010.

Common Stock

Under the Company's amended and restated certificate of incorporation, as of December 31, 2012 and 2011, the Company was authorized to issue 200,000,000 and 100,000,000 shares of common stock, respectively, 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

Table of Contents

whenever funds are legally available, when declared by the board of directors, subject to the prior rights of holders of convertible preferred stock.

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

| | December 31, | |
|---|---|---|
| | 2012 | 2011 |
| Stock options | 9,901 | 3,517 |
| Warrants to purchase common stock | 16,292 | 508 |
| Shares authorized for future issuance under equity and purchase plans | 1,166 | 1,681 |
| | 27,359 | 5,706 |

Common Stock Warrants

In connection with the July 2012 Offering (see Note 1), the Company sold warrants to purchase 15,784,200 shares of common stock (including over-allotment purchase). The warrants will be exercisable beginning on July 27, 2013 at an exercise price of $2.50 per share and will expire on July 27, 2017, which is five years from the date of issuance. As the warrants contain a cash settlement feature upon the occurrence of certain events that may be outside of the Company's control, the warrants are recorded as a current liability and are marked to market at each reporting date (see Note 2). The fair value of the warrants was approximately $9,308,000 as of December 31, 2012.

In July 2011, upon the closing of and in connection with the Financing Agreement (see Note 6), the Company issued to Healthcare Royalty a warrant exercisable into 225,000 shares of common stock. The warrant is exercisable at $9.00 per share of common stock and has a term of 10 years. As the warrant contains covenants where compliance with such covenants may be outside of the Company’s control, the warrant was recorded as a current liability and is marked to market at each reporting date (see Note 2). The fair value of the warrant was approximately $185,000 and $345,000 as of December 31, 2012 and 2011, respectively.

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.

Convertible Preferred Stock Warrants

In connection with the execution of the amended Oxford Agreement in July 2010, the Company issued warrants to Oxford and SVB 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 and comprehensive loss. 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.

Options granted pursuant to the 2006 Plan generally vest over four years 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, 2012 and 2011 there were zero unvested shares of common stock issued to employees of the Company in connection with the early exercise of stock option grants.

During 2010, the Company adopted the 2010 Equity Incentive Award Plan (the 2010 Plan), which became effective immediately prior to the completion of the IPO. An initial 2,243,668 shares were 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, as well as an annual increase pursuant to an evergreen provision. 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.

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.

In June 2012, the Company amended and restated the 2010 Plan (the Restated 2010 Plan). Pursuant to the Restated 2010 Plan, the number of shares that are reserved for issuance under the 2010 Plan was increased to 9,300,000, plus any shares related to outstanding options granted under the 2006 Plan that are repurchased, forfeited, expire or are canceled on or after the effective date of the Restated 2010 Plan. Further, the 2010 Plan's evergreen provision was amended such that, commencing on January 1, 2013, and on each January 1 thereafter during the term of the Restated 2010 Plan, the aggregate number of shares available for issuance under the Restated 2010 Plan shall be increased by that number of shares of the Company's common stock equal to the lower of:

- 4% of the Company’s outstanding common stock on the applicable January 1; or
- an amount determined by the board of directors.

At December 31, 2012 and 2011, 701,976 and 1,103,579 shares of common stock were available for future issuance under the Restated 2010 Plan, respectively.

The 2006 Plan and Restated 2010 Plan 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, 2012 and 2011, a total of 463,973 and 577,852 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 was from June 1, 2011 through May 31, 2012 with two purchase periods of six months each. A total of 138,826, 225,053 and 172,148 shares were purchased under the Purchase Plan in November 2012, May 2012 and November 2011, respectively.

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

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

| | Shares | Weighted Average Exercise Price | Weighted Average Remaining Contractual Term (years) | Aggregate Intrinsic Value (in thousands) |
|---|---|---|---|---|
| Outstanding at December 31, 2011 | 3,517 | $4.01 | | |
| Granted | 6,698 | $1.94 | | |
| Exercised | (18) | $1.86 | | |
| Canceled/Forfeited | (296) | $3.24 | | |
| Outstanding at December 31, 2012 | 9,901 | $2.64 | 8.8 | $39 |
| Exercisable at December 31, 2012 (1) | 3,081 | $3.13 | 8 | $39 |
| Vested at December 31, 2012 | 9,423 | $2.66 | 8.75 | $39 |

(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 $1.33 at December 31, 2012, and the contractual exercise prices.

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| Stock Options and Restricted Stock Units | | | |
| Weighted-average grant date fair value | $1.35 | $2.88 | $11.52 |
| Aggregate intrinsic value of options exercised | $9,000 | $226,000 | $61,000 |
| Total fair value of shares vested | $3,564,000 | $2,340,000 | $660,000 |

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, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| Stock Options and Restricted Stock Units | | | |
| Risk free interest rate | 0.2% to 1.2% | 1.2% to 2.6% | 1.7% to 2.3% |
| Expected term | 5.0 to 6.1 years | 5.1 to 6.1 years | 5.0 to 6.1 years |
| Expected volatility | 80.1% to 86.8% | 72.3% to 89.7% | 90.8% to 96.0% |
| Expected dividend yield | —% | —% | —% |
| Employee Stock Purchase Plan | | | |
| Risk free interest rate | 0.1% | 0.1% | N/A |
| Expected term | 0.5 to 1.0 years | 0.5 to 1.0 years | N/A |
| Expected volatility | 81.5% to 85.7% | 75.2% to 77.1% | N/A |
| Expected dividend yield | —% | —% | 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 expected term of options was calculated using the simplified method as prescribed by accounting guidance for stock-based compensation. This decision was based on the lack of relevant historical data due to the Company’s limited historical experience. In addition, due to the Company’s limited historical data, the estimated volatility was calculated based upon the Company's historical volatility, supplemented with historical volatility of comparable companies whose share prices are publicly available for a sufficient period of time.

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

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| Cost of sales | $181 | $137 | $105 |
| Research and development | 921 | 768 | 393 |
| Selling, general and administrative | 5,055 | 3,904 | 2,009 |
| Total | $6,157 | $4,809 | $2,507 |

As of December 31, 2012, there was approximately $12,047,000 of total unrecognized compensation costs related to outstanding employee and board of director options, which is expected to be recognized over a weighted average period of 2.9 years.

At December 31, 2012, there were 157,000 unvested stock options outstanding to consultants, with approximately $138,000 of related unrecognized compensation expense based on a December 31, 2012 measurement date. These stock options outstanding to consultants are expected to vest over approximately 3.3 years. In accordance with accounting guidance for stock-based compensation, the Company re-measures the fair value of stock option grants to non-employees at each reporting date and recognizes the related income or expense during their vesting period. Expense recognized for stock options to consultants was immaterial for the years ended December 31, 2012, 2011 and 2010, respectively. Stock option expense for awards issued to consultants is included in the consolidated statement of operations and comprehensive loss within selling, general and administrative expense in the year ended December 31, 2012 and within research and development expense in the years ended December 31, 2011 and 2010.

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, | |
|---|---|---|
| | 2012 | 2011 |
| Beginning balance of unrecognized tax benefits | $678 | $562 |
| Gross increases based on tax positions related to current year | 36 | 116 |
| Gross increases based on tax positions related to prior year | — | — |
| Settlements with taxing authorities | — | — |
| Expiration of statute of limitations | — | — |
| Ending balance of unrecognized tax benefits | $714 | $678 |

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, 2012 and 2011 and has recognized no interest and/or penalties in the consolidated statements of operations and comprehensive loss through the year ended December 31, 2012.

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, 2012, the Company had available federal and state income tax net operating loss carryforwards of approximately $158,282,000 and $164,122,000, respectively. The federal tax loss carryforwards will begin expiring in 2026
unless previously utilized, and the state tax loss carryforwards will begin expiring in 2015 unless previously utilized. In addition, the Company has federal and California research and development income tax credit carryforwards of $311,000 and $1,970,000, 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.

In January 2013, the American Taxpayer Relief Act of 2012 (the "Act") was signed into law. The Act retroactively restored several expired business tax provisions, including the research and experimentation credit. The impact to the Company of the reinstated credits was not recognized in 2012 as a change in tax law is accounted for in the period of enactment. The additional credits that will be reported within the 2013 consolidated financial statements will have no impact on operations due to the existence of a full valuation allowance on all deferred tax assets.

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 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 Company is currently in the process of completing a Section 382 and 383 study to determine the impact that ownership changes during the year ended December 31, 2012 have had on its carryforwards and expects to complete the analysis within the next three months. As a result of this analysis, the Company may have an adjustment in the net operating losses that are recorded at December 31, 2012.

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

| | December 31, | | |
|---|---|---|---|
| | 2012 | 2011 | 2010 |
| Tax at statutory rate | $(16,109) | $(28,530) | $(25,008) |
| State taxes, net of federal benefit | (1,580) | (2,780) | (2,953) |
| Change in valuation allowance | 21,990 | (16,807) | 27,968 |
| Section 382 limitation | — | 45,728 | — |
| Permanent Interest Disallowed | (4,466) | (70) | 526 |
| Credits and other | 170 | 2,450 | (523) |
| | $5 | $(9) | $10 |

Significant components of the Company's deferred tax assets as of December 31, 2012 and 2011 are listed below. A valuation allowance of $80,347,000 and $58,359,000 for the years ended December 31, 2012 and 2011, 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):

Table of Contents
Zogenix, Inc.
Notes to Consolidated Financial Statements (continued)

| | December 31, 2012 | 2011 |
|---|---|---|
| Deferred tax assets: | | |
| Net operating losses | $61,739 | $38,357 |
| Capitalized research and development | 8,903 | 7,901 |
| Accrued expenses | 3,707 | 3,728 |
| Research and development credits | 1,237 | 1,078 |
| Accrued product returns | 1,087 | 916 |
| Inventory reserve and UNICAP | 688 | 983 |
| Depreciation and amortization | 645 | 824 |
| Deferred revenue | — | 3,169 |
| Other, net | 2,341 | 1,403 |
| Total deferred tax assets | 80,347 | 58,359 |
| Less valuation allowance | (80,347) | (58,359) |
| Net deferred tax assets | $— | $— |

The Company incurred $5,000 in income tax expense for the year ended December 31, 2012 and 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, 2012 and 2011 are as follows:

| | Fiscal 2012 Quarter Ended | | | |
|---|---|---|---|---|
| | March 31, | June 30, | September 30, | December 31, |
| | (in thousands, except per share amounts) | | | |
| Revenue | $18,347 | $8,030 | $8,453 | $9,496 |
| Cost of Sales | $5,062 | $4,167 | $4,249 | $6,018 |
| Gross Profit | $13,285 | $3,863 | $4,204 | $3,478 |
| Net loss | $(10,292) | $(17,169) | $(19,282) | $(643) |
| Net loss per share, basic and diluted | $(0.16) | $(0.26) | $(0.21) | $(0.01) |
| Weighted-average shares outstanding, basic and diluted | 65,369 | 65,449 | 90,370 | 100,714 |

| | 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 |

Table of Contents

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: | | | | |
| 2012 | $ 1,659 | $607 | $(1,069) | $1,197 |
| 2011 | $ 1,681 | $1,887 | $(1,909) | $1,659 |

Table of Contents

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 15, 2013 By: /s/ Roger L. Hawley
Chief Executive Officer

Date: March 15, 2013 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<br>Roger L. Hawley | Chief Executive Officer and Director (Principal Executive Officer) | March 15, 2013 |
| /S/ ANN D. RHOADS<br>Ann D. Rhoads | Executive Vice President, Chief Financial Officer, Treasurer and Secretary<br>(Principal Financial and Accounting Officer) | March 15, 2013 |
| /S/ CAM L. GARNER<br>Cam L. Garner | Chairman of the Board | March 15, 2013 |
| /S/ JAMES C. BLAIR, PH.D.<br>James C. Blair, Ph.D. | Director | March 15, 2013 |
| /S/ LOUIS C. BOCK<br>Louis C. Bock | Director | March 15, 2013 |
| /S/ STEPHEN J. FARR, PH.D.<br>Stephen J. Farr, Ph.D. | President, Chief Operating Officer and Director | March 15, 2013 |
| /S/ MARK WIGGINS<br>Mark Wiggins | Director | March 15, 2013 |
| /S/ ERLE T. MAST<br>Erle T. Mast | Director | March 15, 2013 |
| /S/ KURT C. WHEELER | Director | March 15, 2013 |

Kurt C. Wheeler

Table of Contents

EXHIBIT INDEX

| Exhibit Number | Description |
|---|---|
| 3.1(3) | Fifth Amended and Restated Certificate of Incorporation of the Registrant |
| 3.2(7) | Certificate of Amendment of Fifth Amended and Restated Certificate of Incorporation of the Registrant |
| 3.3(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 |

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| 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. |

Table of Contents

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| 10.14†(1) | License Agreement dated November 27, 2007 by and between the Registrant and Elan Pharma International Limited |
| 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#(1) | 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(8)†† | Amendment to Co-Promotion Agreement dated December 20, 2011 by and between the Registrant and Astellas Pharma US, Inc. |
| 10.28(9)† | Co-Marketing and Option Agreement dated March 29, 2012 by and between the Registrant and Battelle Memorial Institute |
| 10.29(9)† | Sublease dated April 12, 2012 by and between the Registrant and Relational Investors, LLC |
| 10.30(9) | Independent Director Compensation Policy as amended and restated effective April 16, 2012 |
| 10.31(10)† | Co-Promotion Agreement dated June 6, 2012 by and between the Registrant and Mallinckrodt, LLC |

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| 10.32 | Commercial Manufacturing and Supply Agreement dated November 2, 2012 by and between the Registrant and Alkermes Pharma Ireland Ltd. |
| 10.33 | Employment Agreement dated November 26, 2012 by and between the Registrant and Richard Scott Shively |
| 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) |

Table of Contents

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| 101 | The following financial statements from Zogenix, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2012, filed on March 15, 2013, formatted in XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations and Comprehensive Loss, (iii) Consolidated Statements of Cash Flows, and (iv) the Notes to Consolidated Financial Statements, tagged as blocks of text. |

(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.
(7) Filed with the Registrant's Quarterly Report on Form 10-Q on November 8, 2012.
(8) Filed with the Registrant's Quarterly Report on Form 10-K on March 12, 2012.
(9) Filed with the Registrant's Quarterly Report on Form 10-Q on May 15, 2012.
(10) Filed with the Registrant's Quarterly Report on Form 10-Q on August 9, 2012.

† 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

# Indicates management contract or compensatory plan.