ZOGENIX, INC.
Form 10-K
March 10, 2017
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

Form 10-K

(Mark One)
x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2016
or
¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: 001-34962
Zogenix, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware	20-5300780
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
5858 Horton Street, #455 Emeryville, California	94608
(Address of Principal Executive Offices)	(Zip Code)

510-550-8300
(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. x

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, 2016, the aggregate market value of the registrant’s common stock held by non-affiliates of the registrant was approximately $142.5 million, based on the closing price of the registrant’s common stock on the Nasdaq Global Market of $8.05 per share.

As of March 6, 2017, there were 24,813,169 shares of the registrant’s common stock outstanding.

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 2016 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, 2016.

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Signatures

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PART I

Forward-Looking Statements and Market Data

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

- the progress and timing of clinical trials for ZX008 and Relday;
- the safety and efficacy of our product candidates;
- the timing of submissions to, and decisions made by, the U.S. Food and Drug Administration, or FDA, and other regulatory agencies, including foreign regulatory agencies, with regards to the demonstration of the safety and efficacy of our product candidates to the satisfaction of the FDA and such other regulatory agencies;
- the goals of our development activities and estimates of the potential markets for our product candidates, and our ability to compete within those markets;
- adverse side effects or inadequate therapeutic efficacy of Zohydro ER and Zohydro ER ADT pipeline product that could result in product liability claims;
- estimates of the capacity of manufacturing and other facilities to support our product candidates;
- our and our licensors ability to obtain, maintain and successfully enforce adequate patent and other intellectual property protection of our 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 any of our product candidates that may be approved for sale, the extent of such coverage and reimbursement and the willingness of third-party payors to pay for our products versus less expensive therapies;
- the impact of healthcare reform laws; 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 ZX008, Relday and other product candidates, including data regarding the estimated size of those markets, their projected growth rates, the incidence of certain medical conditions, statements that certain drugs, classes of drugs or dosages are the most widely prescribed in the United States or other markets, the perceptions and preferences of patients and physicians regarding certain therapies and other prescription, prescriber and patient data, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other

data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. In particular, unless otherwise specified, all prescription, prescriber and patient data in this Annual Report on Form 10-K is from 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

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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®, Relday™ and Zogenix™ 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 its consolidated subsidiaries.

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Item 1. Business

Overview

We are a pharmaceutical company committed to developing and commercializing central nervous system, or CNS, therapies that address specific clinical needs for people living with orphan and other CNS disorders. Our current primary area of therapeutic focus is epilepsy and related seizure disorders.

We have worldwide development and commercialization rights to ZX008, our lead product candidate. ZX008 is a low-dose fenfluramine for the treatment of seizures associated with Dravet syndrome. Dravet syndrome is a rare and catastrophic form of pediatric epilepsy with life threatening consequences for patients and for which current treatment options are very limited. ZX008 has received orphan drug designation in the United States and the European Union (EU) for the treatment of Dravet syndrome. In January 2016, we received notification of Fast Track designation from the FDA, for ZX008 for the treatment of Dravet syndrome. We initiated Phase 3 clinical trials in North America (Study 1501) in January 2016 and in Europe and Australia in June 2016 (Study 1502). Additionally, we initiated the enrollment of patients for our study of Dravet syndrome patients who are poor responders to a stiripentol treatment regime in September 2016 in Europe and in February 2017 initiated the Phase 3 clinical efficacy portion of this study (Study 1504), which now includes sites in in the U.S. and Canada, in addition to Europe. In January 2017, we announced our plan to report top-line results from studies 1501 and 1502 via a merged study analysis approach whereby top-line results from the first half of the combined patient population of studies 1501 and 1502 would be reported initially as “Study 1”. We expect to report top-line results from Study 1 in the third quarter of 2017 and additional Phase 3 data to be released over the remainder of year.

Beginning in first quarter of 2016, we funded an open-label dose-ranging twenty-patient investigator initiated study in patients with Lennox Gastaut Syndrome, or LGS, another rare and catastrophic form of pediatric epilepsy with life threatening consequences for patients and for which current treatment options are very limited. Refractory LGS patients were treated with ZX008 as an adjunctive therapy for seizures associated with LGS. In December 2016, we presented initial data from an interim analysis of the first 13 patients to have completed at least 12 weeks of this Phase 2 open-label, dose-finding study at the American Epilepsy Society Meeting. These data demonstrated that ZX008 provided clinically meaningful improvement in major motor seizure frequency in patients with severely refractory LGS, despite not attempting to dose to maximal efficacy as per protocol, with seven out of 13 patients (54%) achieving at least a 50% reduction in the number of major motor seizures. In addition, ZX008 was generally well tolerated. This data indicate that ZX008 has the potential to be a safe and effective adjunctive treatment for LGS. Based on the strength of the LGS data generated, we plan to submit an investigational new drug, or IND, application in the first quarter of 2017 and initiate a Phase 3 program for ZX008 in LGS in the second half of 2017. In February 2017, ZX008 received orphan drug designation for the treatment of LGS in the EU.

We have an additional product candidate, Relday™ (risperidone once-monthly long-acting injectable) for the treatment of schizophrenia. Relday is a proprietary, long-acting injectable formulation of risperidone. Risperidone is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. We completed the Phase 1b multi-dose clinical study for Relday in 2015, and efforts to secure a global strategic development and commercialization partner for Relday are ongoing.

We sold our Zohydro ER® business in April 2015 to enable us to focus on development of our CNS product candidates and to enhance our financial strength. Zohydro ER (hydrocodone bitartrate) is an extended-release capsule oral formulation of hydrocodone without acetaminophen.

We sold our Sumavel® DosePro® (sumatriptan injection) Needle-free Delivery System business in May 2014 to Endo International Plc, or Endo. In connection with the sale, we entered into a supply agreement for the exclusive right, and contractual obligation, to manufacture and supply Sumavel DosePro to Endo. We and Endo have recently entered into a letter agreement acknowledging Endo’s decision to have us discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. We expect to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time.

Our Strategy

We are committed to providing therapeutic solutions for people living with rare and burdensome conditions of CNS disorders. Our strategy centers on advancing late-stage product candidates and identifying clear pathways for clinical development and regulatory approval in order to provide access to differentiated medicines that can make meaningful improvements in patients' daily lives. The key elements of our strategy are:

Rapidly advancing ZX008 through clinical development and regulatory approval. We are currently conducting three Phase 3 clinical trials to evaluate ZX008 as an adjunctive therapy for seizures associated with Dravet syndrome. The studies continue to enroll patients in the United States and internationally. We expect to announce initial top-line data in the third quarter of 2017 and additional Phase 3 data to be released over the remainder of year.

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Developing ZX008 for the treatment of Lennox-Gastaut syndrome. We are planning to initiate a Phase 3 program to evaluate ZX008 as an adjunctive therapy for seizures associated with LGS in the second half of 2017. In February 2017, ZX008 received orphan drug designation for the treatment of LGS in the EU.

Identifying differentiated, late-stage product development candidates in the therapeutic area of CNS for acquisition and further development. Our business development team continues to seek and evaluate differentiated, high-value licensing and product acquisition opportunities that would build our CNS product candidate pipeline and effectively leverage our capabilities in the United States and Europe.

Evaluating ZX008 for potential treatment of other forms of orphan pediatric epilepsy. In addition to Dravet syndrome and LGS, we believe that the unique mechanism of action of ZX008 has the potential to treat other epileptic encephalopathies where there is a significant unmet medical need. We expect to continue to evaluate its potential in additional indications.

Seeking a global development and commercialization partner for Relday. We are currently seeking a partner for Relday, our proprietary subcutaneously-injected formulation of once-monthly risperidone for the treatment of schizophrenia.

Our Product Candidates

We currently have two late-stage product candidates in our development pipeline for differentiated therapies treating central nervous system disorders.

ZX008 (Low-Dose Fenfluramine) for the Treatment of Dravet Syndrome

Dravet syndrome is a rare form of channelopathy in which intractable epilepsy is one of the most significant and devastating symptoms. Children and young adults with Dravet syndrome experience debilitating, persistent and potentially life-threatening seizures beginning in the first year of life. Seizures continue throughout their lifetime and are drug resistant, meaning that currently available medications are not able to achieve complete seizure control and, in some cases, worsen the condition. Individuals with Dravet syndrome face a higher incidence of Status Epilepticus and Sudden Unexplained Death in Epilepsy, or SUDEP. These patients suffer from severe cognitive and developmental impairment throughout life, as well as neurobehavioral disorders such as autistic-like behavior and attention deficit hyperactivity disorder. The prognosis for patients with Dravet syndrome to become seizure free is poor. There are estimated to be between 16,000 and 29,000 patients living with Dravet syndrome in the United States and Europe, respectively. A recent study by Wu et. al. published by the American Academy of Pediatrics in 2015 reported an incidence of 1 per 15,700 people in the U.S population.

There are currently no FDA-approved treatments indicated for the treatment of seizures associated with Dravet syndrome. The standard of care usually involves a combination of the following anticonvulsant drugs: clobazam, clonazepam, leviteracetam, topirimate, valproic acid, ethosuximide and zonisamide. Stiripentol is approved in Europe, Canada, Australia and Japan for the treatment of seizures associated with Dravet syndrome in conjunction with clobazam and valproate. In Europe, stiripentol was granted an orphan drug designation for the treatment of Dravet syndrome in 2001. In the United States, stiripentol is not FDA-approved and can only be obtained via the FDA's Personal Importation Policy, or PIP. Sodium channel blocking anticonvulsant drugs often used to treat most other epilepsy conditions increase seizure frequency in patients with Dravet syndrome. Management of this disease may also include a nonpharmacologic treatments, including ketogenic diet and vagal nerve stimulation.

Fenfluramine was originally developed and approved as an anorectic agent for the treatment of adult obesity. However, pre-clinical and clinical evidence of the drug's ability to treat epileptic seizures was first described in the 1980s. When fenfluramine was withdrawn from the market in 1997 because of an unacceptable risk of the occurrence of serious heart valve defects and pulmonary hypertension in the treated adult obese patient population, academic pediatric neurologists in Belgium continued to evaluate low doses of fenfluramine in a small number of Dravet syndrome patients under a government approved protocol. Their open-label study, which continues today, evaluated the safety and effectiveness of low-dose fenfluramine to reduce seizures in refractory Dravet syndrome patients. In December 2016, we presented the most recent analyses of these Dravet syndrome patients being treated in Belgium

under this government approved protocol at the American Epilepsy Society Meeting. There are ten original patients who started treatment with fenfluramine prior to 2010 and now have been treated with low-dose fenfluramine for a mean of 17.5 years (range: 7-28 years). Low-dose fenfluramine continues to provide these patients with long-term, durable seizure control. For the most immediate past six years of treatment, three patients were seizure-free for the entire six years and four patients experienced seizure-free intervals of at least two years. None of these patients has developed any clinically meaningful signs or symptoms of cardiac valvulopathy or pulmonary hypertension, while two patients had mild and stable cardiac valve thickening on the most recent cardiac echocardiogram that was deemed to be clinically unimportant. After 2010, an additional nine Dravet syndrome patients started adjuvant treatment with low-dose fenfluramine and have been treated for an average duration of 2.1 years (range, 0.8-5.6 years). For these additional nine patients, the median reduction in major motor seizures has been 76% and there has been no evidence of cardiac valvulopathy or pulmonary

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hypertension in any patient. For all Dravet syndrome patients treated with low dose fenfluramine in this Belgian study, no patient has stopped treatment for any adverse event.

Because of the known cardiac side effects of fenfluramine, the ongoing study requires periodic evaluations of the heart and, in particular, the heart valves using echocardiography. Overall, low-dose fenfluramine has been shown to be well tolerated and side-effects of treatment have been mild and transient over the entire 28-year study period. There have been no clinically significant findings related to cardiac valvulopathy. In addition, there have been no reports of pulmonary hypertension and there have been no deaths.

ZX008 has received orphan drug designation in the United States and EU for the treatment of Dravet syndrome. In January 2016, we received notification of Fast Track designation from the FDA for ZX008 for the treatment of Dravet syndrome.

Formal meetings have been held with the regulatory agencies in the United States and EU to obtain concurrence on remaining pre-clinical and clinical requirements for approval. Based upon this information, we believe two successful pivotal placebo-controlled Phase 3 studies in Dravet syndrome will support regulatory approval of ZX008 in the United States and one pivotal study will support regulatory approval in Europe. Our IND application for ZX008 for the treatment of Dravet syndrome became effective in December 2015. The Phase 3 program for ZX008 includes three randomized, double-blind placebo-controlled studies of ZX008 as adjunctive therapy for patients with uncontrolled seizures who have Dravet syndrome: identical Studies 1501 and Study 1502, which are evaluating two dose levels of ZX008 (0.2 mg/kg/day and 0.8 mg/kg/day, up to a maximum daily dose of 30 mg), and Study 1504, that is evaluating a single dose a ZX008 (0.5 mg/kg/day, up to a maximum daily dose of 20 mg, which has been shown to be equivalent to 0.8mg/kg/day in patients not taking stiripentol), in patients taking stiripentol, clobazam and valproate. The primary objective of the clinical trials will be to compare the reduction in convulsive seizures experienced by participants after treatment with ZX008 compared to treatment with a placebo. We have recently modestly expanded the target number of subjects for studies 1501 and 1502 and now intend to enroll 120 subjects in each of the two studies, with 40 subjects in each treatment arm rather than the originally planned 35/arm, due to results from a Dravet syndrome study that reported high variability between the treated group and placebo. Study 1501 commenced in January 2016 and is being conducted in North America. Study 1502 is a multi-national study commenced in June 2016 and is being conducted primarily in western Europe. Study 1504 is also a multi-national study commenced in the third quarter 2016 and is being conducted in western Europe and North America. In February 2017, we announced our plan to report top-line results from studies 1501 and 1502 via a merged study analysis approach whereby top-line results from the first half of the combined patient population of studies 1501 and 1502 would be reported as “Study 1”. We expect to report top-line results from Study 1 in the third quarter of 2017 and additional Phase 3 data to be released over the remainder of year. Patients completing the Phase 3 trials are given the opportunity to enroll in an open label long-term extension safety study.

We are conducting the study 1504 in Dravet syndrome patients who are poor responders to a stiripentol treatment regimen not only as a pivotal Phase 3 trial, but to also demonstrate the potential incremental benefit of ZX008 as compared to stiripentol, which is required to maintain ZX008 orphan drug status in the EU. We also expect that this study will be important for future market positioning and reimbursement of ZX008 in Europe.

We are currently developing the appropriate elements of a specific risk evaluation and mitigation strategy, or REMS, to support and maintain a long-term favorable benefit-risk profile for ZX008 in the United States, as well as a similar risk mitigation plan (RMP) for Europe. This is consistent with other drugs with known safety issues that are approved for serious diseases with high unmet need. We intend to submit an NDA and marketing authorization application for ZX008 for the treatment of Dravet syndrome in 2018.

ZX008 for the Treatment of Lennox-Gastaut Syndrome

Lennox-Gastaut syndrome (LGS) is a severe form of epilepsy that typically becomes apparent during infancy or early childhood. Affected children experience generalized tonic-clonic seizures, tonic seizures, atonic seizures, and tonic/atonic seizures, all of which most often can result in “drop attacks.” Other seizure types that occur in some LGS patients include atypical absences, non-convulsive seizures, focal seizures, and myoclonic seizures. Children with LGS also develop cognitive dysfunction, delays in reaching developmental milestones and behavioral problems. LGS can be caused by a variety of underlying conditions, but in some cases no cause can be identified.

LGS has an estimated prevalence of 15 per 100,000. It affects over 30,000 children and adults in the U.S and over 50,000 individuals in the EU. There is no specific therapy for LGS that is effective in all cases and the disorder has proven particularly resistant to most therapeutic options. The three main therapeutic options for the treatment of LGS are anti-epileptic drugs (AEDs), dietary therapy (typically the ketogenic diet) or surgery (VNS therapy or corpus callosotomy). AEDs are usually given

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to individuals with LGS, but the individual response is highly variable. However, because individuals with LGS rarely respond successfully to one AED, they most often require therapy with multiple types of AEDs. Although a variety of specific drugs have been approved by the FDA and/or EMA for the treatment of LGS including Topiramate, Lamotrigine, Clobazam, Rufinamide, Felbamate and Clonazepam, these medications typically have limited success and in addition, are often associated with significant side effects, especially in individuals who receive multidrug, high-dose regimens. Similarly, a non-FDA/EMA approved AED, valproate (valproic acid), while generally considered the first-line therapy for LGS, rarely results in significant seizure reduction and often causes side effects as well. Furthermore, all current AEDs can also become less effective over time.

Beginning in first quarter of 2016, we funded an open-label dose-ranging twenty-patient investigator initiated study in patients with LGS. Refractory LGS patients were treated with ZX008 as an adjunctive therapy for seizures associated with LGS. In December 2016, we presented initial data from an interim analysis of the first 13 patients to have completed at least 12 weeks of this Phase 2 open-label, dose-finding study at the American Epilepsy Society Meeting. These data demonstrated that ZX008 provided clinically meaningful improvement in major motor seizure frequency in patients with severely refractory LGS, despite not attempting to dose to maximal efficacy as per protocol, with seven out of 13 patients (54%) achieving at least a 50% reduction in the number of major motor seizures. In addition, ZX008 was generally well tolerated. This data indicate that ZX008 has the potential to be a safe and effective adjunctive treatment for LGS. Based on the strength of the LGS data generated, we plan to submit an IND application in the first quarter of 2017 and initiate a Phase 3 program for ZX008 in LGS in the second half of 2017. In February 2017, ZX008 received orphan drug designation for the treatment of LGS in the EU.

We also intend to evaluate additional indications in other orphan pediatric epilepsy conditions in the future.

Relday for the Treatment of Schizophrenia

Relday is a proprietary, long-acting injectable formulation of risperidone using Durect Corporation's SABER™ controlled-release formulation technology. If successfully developed and approved, we believe Relday may be the first subcutaneous antipsychotic product with once-monthly dosing. We believe Relday's simplified dosing regimen, improved pharmacokinetic profile and significant reduction in injection volume versus currently marketed long-acting injectable antipsychotics could 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, and in July 2012, we initiated our first clinical trial for Relday. This Phase 1 clinical trial was a single-center, open-label, safety and pharmacokinetic trial of 30 patients with chronic, stable schizophrenia or schizoaffective disorder. We announced positive single-dose pharmacokinetic results from the Phase 1 clinical trial 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 announced positive top-line results from the extended Phase 1 clinical trial in May 2013. The results from the extended Phase 1 clinical trial showed risperidone blood concentrations in the therapeutic range were achieved on the first day of dosing and maintained throughout the one-month period. In addition, dose proportionality was demonstrated across the full dose range studied.

In September 2015, we announced the results of our Phase 1b multi-dose parallel group clinical trial which was conducted as a single-center, open-label, safety and pharmacokinetic trial of 60 patients with chronic, stable schizophrenia or schizoaffective disorder across a dose range of 60, 90 and 120 mg every four weeks. The study included a comparator arm of Risperdal Consta, a form of risperidone that requires oral supplementation for the first three weeks following dosing initiation, and at least four Risperdal Consta doses are required to reach steady state. The results for Relday demonstrated that risperidone plasma concentrations in the therapeutic range were achieved on the first day of dosing, reached steady state levels following the second dose and consistently maintained therapeutic levels throughout the four-month period. In addition, dose proportionality was confirmed across the dose range intended for clinical practice (60 to 120 mg). Relday was generally safe and well-tolerated, with results consistent

with the profile of risperidone and our previous Phase 1 single-dose clinical trial. The results of this trial and activities regarding manufacturing scale-up will put us in position to have an end of Phase 2 meeting with the FDA. Efforts to secure a global strategic development and commercialization partner for Relday are ongoing.

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.

First line therapy for most schizophrenia patients today are drugs generally known as atypical or second generation antipsychotics. Patient compliance with medication has been a long-standing problem in the treatment of schizophrenia. Results from the Clinical Antipsychotic Trials in Intervention Effectiveness conducted between 2001 and 2004, and published in The

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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.

In an attempt to improve patient compliance, physicians increasingly administer antipsychotic drugs through long-acting injections. Long-acting 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, Invega Sustenna and Invega Trinza, marketed by Janssen Pharmaceuticals; Zyprexa Relprevv, marketed by Eli Lilly & Co; Abilify Maintena, marketed by Otsuka America Pharmaceutical, Inc.; and Aristada, marketed by Alkermes plc. These drugs provide between two weeks and three months of therapy per dose.

According to data from IMS (Source: IMS Midas US Manufacturer Dollars, January 2014-December 2014), the global long acting atypical injectable antipsychotic market was $3.28 billion in 2014. The existing long-acting injectable risperidone product, Risperdal Consta, achieved global net sales of $1.24 billion in 2014, according to IMS, and has a wholesale acquisition cost of approximately $397 per bi-weekly dose, or approximately $795 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 25,700 total prescribers of long-acting injectable products, including approximately 13,500 psychiatrists in 2016 (Source: PHAST Prescription, January 2016–December 2016).

Market research conducted on our behalf by bioStrategies Group in 2013 and 2015 indicates that psychiatrists in the United States and Europe see significant potential advantages for Relday over the currently marketed long-acting risperidone injectable. We believe on the basis of our clinical development work and market research that, if successfully developed and approved, Relday could potentially provide a significant improvement over existing treatment options for patients suffering from schizophrenia as a result of:

- Therapeutic plasma levels on first day: Relday has demonstrated in two Phase 1 studies in schizophrenic patients the ability to achieve therapeutic plasma levels of risperidone within 24 hours of initial dosing with an acceptable initial burst (i.e., plasma levels similar to or less than the comparable oral dose). Achieving first-day therapeutic plasma levels avoids the need for oral supplementation in connection with the initiation of therapy or following a missed or delayed dose. Risperdal Consta 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.
- Once-monthly dosing: Relday has demonstrated in two Phase 1 studies in schizophrenic patients a pharmacokinetic profile that will allow for once-monthly dosing with dose proportionality across the therapeutic range. Risperdal Consta provides therapy for only two weeks, resulting in more frequent physician visits and a greater number of annual injections, as well as more opportunities for patients to miss or delay a dose.
- 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 serious adverse events, and in addition can also result in slow, painful and/or difficult injections.
- 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. Risperidone is now the third most commonly prescribed oral atypical antipsychotic compound in the United States, accounting for 19% of total prescriptions in 2016 (Source: PHAST Prescription, January 2016–November 2016).

We are working to identify potential worldwide development and commercialization partner or partners for Relday.

Our Contract Manufacturing Services

In May 2014, we divested our Sumavel DosePro Needle-free Delivery System business to Endo. In connection with the sale, we also entered into a manufacturing and supply agreement to supply Sumavel DosePro to Endo. Under the supply agreement, Endo agreed to purchase all Sumavel DosePro manufactured by us at cost, plus a mark-up. The initial term of the supply agreement was for a minimum of eight years. We and Endo have recently entered into a letter agreement acknowledging Endo's decision to have us discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. We expect to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel

DosePro following such time.

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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 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, manufacturing capabilities, experience in obtaining regulatory approvals for product candidates and other resources than us. We will face competition not only in the commercialization of 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.

ZX008

There are currently no FDA-approved treatments indicated for the treatment of seizures associated with for Dravet syndrome. The standard of care usually involves a combination of the following anticonvulsant drugs: clobazam, clonazepam, leviteracetam, topirimate, valproic acid, ethosuximide and zonisamide. Stiripentol is approved in Europe, Canada, Australia and Japan for the treatment of Dravet syndrome when used in conjunction with clobazam and valproate. In Europe, stiripentol was granted an orphan drug designation for the treatment of Dravet syndrome in 2001. In the United States, stiripentol is not FDA approved and can only be obtained via the FDA's Personal Important Policy or under an Expanded Access IND. The FDA's PIP is meant to help people with life threatening illnesses obtain drugs when FDA approved drugs have failed. The FDA does not consider the PIP a license to import drugs for personal use, including for life threatening illnesses. In 2013, the FDA mandated that all new patients obtaining stiripentol must have a patient specific IND application submitted to the FDA by the prescribing physician, who is most often an academic pediatric neurologist. The manufacturer of stiripentol, Biocodex, may in the future seek and receive FDA approval for stiripentol for the treatment of Dravet syndrome.

ZX008 has a distinctive mechanism of action (selective serotonin activity and possibly sigma-1 activity) that is different from the other antiepileptic drugs currently available and in clinical development in the United States and EU for the treatment of Dravet syndrome. Two other drugs in clinical development for the treatment of Dravet syndrome are cannabinoids. We do not expect that their successful development and approval in the United States or Europe would block the FDA from granting approval of ZX008 even if they are approved prior to ZX008.

GW Pharmaceuticals' Epidiolex is a liquid drug formulation of plant-derived purified cannabidiol, or CBD, a component of marijuana. Published open-label clinical data and anecdotal evidence has suggested that patients with Dravet syndrome experience a reduction in seizures when CBD is prescribed to them. In March 2016, GW Pharmaceuticals announced positive results from its first Phase 3 clinical trial for Epidiolex for the treatment of Dravet syndrome, and in June and September 2016 announced positive results from its two Phase 3 clinical trials for Epidiolex for the treatment of LGS, with drug achieving its primary study endpoints in all three trials. GW Pharmaceuticals is currently conducting an additional Phase 3 study in Dravet syndrome and has announced that it intends to file an NDA for both indications in 2017. Insys Therapeutics, or Insys, is also developing a synthetic CBD for the treatment of Dravet syndrome. Insys has advanced its synthetic CBD program, which has received orphan drug designation and Fast Track status by the FDA for use of CBD as a potential treatment for Dravet syndrome, into a Phase 1/2 clinical trial. Insys intends to initiate Phase 3 development of its CBD product candidate for Dravet syndrome and LGS in 2017.

Sage Therapeutics has completed a Phase 1/2 clinical trial for its lead compound SAGE-547, an allosteric modulator of GABA receptors, for the acute treatment of super-refractory status epilepticus, which is status epilepticus (prolonged nonstop seizure) that continues or recurs 24 hour or more after the onset of anesthetic therapy. Status epilepticus is associated with many epilepsy conditions, including Dravet syndrome.

Several other companies, including Xenon Pharmaceuticals, Inc. have disclosed that they are developing preclinical drug candidates for the potential treatment of Dravet syndrome.

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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, Invega Sustenna and Invega Trinza marketed by Janssen Pharmaceuticals; Zyprexa Relprevv marketed by Eli Lilly & Company; Aristada marketed by Alkermes plc; and 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 Janssen Pharmaceuticals, 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 Vanda Pharmaceuticals, 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 Braeburn Pharmaceuticals, Laboratorios Farmaceuticos Rovi SA and Indivior PLC, each of which has announced they are developing long-acting antipsychotic product candidates. In May 2015, Janssen Pharmaceuticals announced that the FDA approved Invega Trinza, a three-month long-version of paliperidone palmitate, for the treatment of schizophrenia in patients adequately treated with Invega Sustenna for at least four months. Also in May 2015, Indivior PLC announced positive top-line results from its Phase 3 clinical trial of RBP-7000, an investigational drug formulation of risperidone for the treatment of schizophrenia that is intended to require once-monthly dosing. In October 2015, Alkermes plc announced that the FDA approved Aristada (aripiprazole lauroxil) extended-release injectable suspension for the treatment of schizophrenia which offers once-monthly and six-week dosing options.

Distribution

Since May 2014, we have been the exclusive supplier of Sumavel DosePro to Endo under a supply agreement. We and Endo have recently entered into a letter agreement acknowledging Endo’s decision to have us discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. We expect to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time. Prior to May 2014, we sold Sumavel DosePro to wholesale pharmaceutical distributors, who, in turn, sold the products to pharmacies, hospitals and other customers.

Manufacturing and Supply

In May 2014, we entered into a supply agreement to exclusively manufacture and supply Sumavel DosePro to Endo for an initial term expiring May 2022. To fulfill our obligation, we manage the supply chain for Sumavel DosePro and have various supply agreements with third parties for raw materials, component parts and contract manufacturing services for the production of Sumavel DosePro.

We and Endo have recently entered into a letter agreement acknowledging Endo’s decision to have us discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. We expect to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time.

Based on the stage of production in our supply chain for the products to be delivered, we expect to obtain the remaining raw materials and component parts from our existing suppliers, including Patheon UK Limited, or Patheon, to fulfill our obligation to Endo. Thereafter, we intend to terminate or not renew our agreements with our third-party suppliers, including Patheon.

In fulfilling our obligation to supply Sumavel DosePro to Endo, we rely on the following third-party manufacturer.

Patheon UK Limited

We have entered into a manufacturing services agreement with Patheon, located in Swindon, United Kingdom, a specialist in the aseptic fill/finish of injectables and other sterile pharmaceutical products that will expire on April 30, 2017. Under the terms of the agreement, Patheon serves as our exclusive manufacturer for the aseptic capsule assembly, filling and inspection, final system 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

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pay Patheon a monthly manufacturing fee over the remaining term. Under the agreement, we are also required to pay support and service fees, with the level of service fees increasing if annual production exceeds a specified volume. Under the 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.

ZX008 and Relday

We do not own or operate, and currently have no plans to establish any manufacturing facilities with respect to the manufacture of ZX008 or Relday. We currently rely, and expect to continue to rely, on third-party manufacturers to produce sufficient quantities of our product candidates and their component raw materials for use in our internal research efforts and clinical trials and in relation to any future commercialization of our product candidates. Our third-party manufacturers are responsible for obtaining the raw materials necessary to manufacture our product candidates, which we believe are readily available from more than one source. Additional third-party manufacturers are and will be used to fill, label, package and distribute investigational drug products. This approach allows us to maintain a more efficient infrastructure while enabling us to focus our expertise on developing our product candidates. Although we believe we have multiple potential sources for the manufacture of our product candidates and the related raw materials, we currently rely on single manufacturers for different aspects of ZX008 and Relday.

Collaborations, Commercial and License Agreements

Zogenix International Limited Sales and Purchase Agreement

Under the terms of our agreement to acquire Zogenix International Limited, pursuant to a sale and purchase agreement with Brabant Pharma Limited (Brabant), we agreed to make future milestone payments to the former principals of Brabant of up to $95.0 million in the event we achieve contractually specified regulatory and sales milestones with respect to ZX008. We agreed to use commercially reasonable efforts to develop and commercialize ZX008 and to achieve the milestones.

Endo Asset Purchase Agreement

In May 2014, we entered into an asset purchase agreement, the Endo Asset Purchase Agreement, with Endo Ventures Bermuda Limited and Endo Ventures Limited to sell our Sumavel DosePro business to Endo and concurrently entered into the supply agreement for with Endo.

We and Endo have recently entered into a letter agreement acknowledging Endo’s decision to have us discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. We expect to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time.

Aradigm Corporation Asset Purchase Agreement

In August 2006, we entered into an asset purchase agreement with Aradigm Corporation whereby Aradigm assigned and transferred to us all of its right, title and interest to tangible assets and intellectual property related to the DosePro needle-free drug delivery system. Aradigm also granted to us a license under all other intellectual property of Aradigm that is necessary or useful to the DosePro delivery system. Aradigm also retained a license 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.

Under terms of the agreement, if 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 royalty on net sales of each non-sumatriptan product commercialized, or a percentage of the royalty revenues received by us from the licensee, if any. 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.

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Durect Corporation Development and License Agreement

In July 2011, we entered into a development and license agreement with Durect Corporation, or Durect. Under the terms of the agreement, we are responsible for the clinical development and commercialization of Relday. Durect is responsible for pre-clinical, formulation and chemistry, manufacturing and controls, or CMC, development responsibilities of Relday. Durect will be reimbursed by us for its research and development efforts on the product. We paid an upfront fee to Durect and may be obligated to pay up to $103.0 million in total future milestone payments based on specified development, regulatory and sales targets. We are also required to pay a royalty on annual net sales of the product. 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. We are also required to pay Durect a tiered percentage of fees received in connection with any sublicense of the licensed rights.

Durect granted to us an exclusive license to intellectual property rights related to Durect's proprietary polymeric and non-polymeric controlled-release formulation technology to make 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.

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.

ZX008

We acquired rights to four pending U.S. patent applications directed to methods of treating Dravet syndrome in connection with our acquisition of Zogenix International Limited. On January 24, 2017, we were issued U.S. Patent No. 9,549,909 from the U.S. Patent and Trademark Office. The patent, entitled "Method for the Treatment of Dravet Syndrome", covers claims related to a method for the adjunctive treatment of seizures associated with Dravet syndrome with ZX008. This patent is expected to provide protection of the associated claims through 2033. There are currently 10 pending U.S. patent applications (which includes two provisional applications); and 11 pending foreign applications (which includes four Patent Cooperation Treaty applications) in the ZX008 series of patent cases. Our pending patent applications may not result in the issuance of any additional patents.

Relday

We have licensed a number of U.S. 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 ongoing 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 Federal Food, Drug, and Cosmetic Act, or 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-

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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 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 GLP, regulations;
- submission to the FDA of an IND for human clinical testing which must become effective before human clinical trials may begin in the United States;
- performance of adequate and well-controlled human clinical trials in accordance with current good clinical practice, or GCP, regulations, to establish the safety and efficacy of the proposed drug product for each intended use;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the product is produced to assess compliance with current Good Manufacturing Practice, or cGMP, requirements; 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 a trial on 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.

Clinical trials involve the administration of an investigational 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. 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.
- Phase 3: When Phase 2 evaluations demonstrate that a dose range of the product appears to be effective and has an acceptable safety profile, Phase 3 "pivotal" trials are undertaken in large patient populations to obtain additional evidence of clinical efficacy and safety in an expanded patient population at multiple, geographically-dispersed clinical trial sites.

In some cases, the FDA may condition the approval of the NDA 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 clinical trials are typically referred to as Phase 4 or Post Marketing clinical trials.

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, the FDA may determine that a REMS is necessary to ensure that the benefits of the drug outweigh the risks of the drug, and may require submission of a REMS as a condition of approval. The submission of an NDA 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

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whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission has been accepted for filing, the FDA begins an in-depth substantive review.

During the FDA's review of 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 (for medical device components), 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 requirements before approving an NDA. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully when making decisions.

Once the FDA's NDA review process is substantially complete, it may issue an approval letter, or it may issue a complete response letter, or CRL, to indicate that the review cycle for an application is complete and that the application is not ready for approval. CRLs generally outline the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when the deficiencies have been addressed to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Once issued, the FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems are identified after the product reaches the market. 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 a post-market REMS requirement. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the sponsor may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require the development of additional data or conduct of 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 Administration, or DEA, regulations applicable to marketed controlled substances. 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 or QSR 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 or QSR 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 or QSR 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, though the FDA must provide an application holder with notice and an opportunity for a hearing in order to withdraw its approval of an application. 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 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.

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The FDA strictly regulates the marketing, labeling, advertising and promotion of drug and device products that are placed on the market. While physicians may prescribe drugs and devices 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, and associated FDA regulations, which governs 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. With the enactment of the Drug Quality and Security Act in November 2013, drug manufacturers will also be subject to new requirements for identifying and tracking prescription drugs as they are distributed in the United States. The requirements of the new law will be phased in over a ten-year period, including requirements for unique product identifiers and provision of product handling information to the FDA.

The FDA may require post-approval studies and clinical trials if the FDA finds they are appropriate based on scientific data, including information regarding related drugs. 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 that the benefits of a drug outweigh its risks. In determining whether a REMS is necessary, the FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. If the FDA determines a REMS is necessary for a new drug, the drug sponsor must submit a proposed REMS as part of its NDA prior to 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 continue to outweigh its risks. 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 and 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 a minimum, at 18 months, three years, and seven years after the strategy's approval.

Concurrently with our clinical development program for ZX008, we plan to develop the appropriate elements of a REMS program to support and monitor the long-term favorable benefit-risk profile for ZX008. We expect that the FDA will require a REMS for ZX008 including elements to assure safe use, among other requirements, as a condition of approval, consistent with other drugs with known safety issues and that are approved for serious diseases with high unmet need. We will be solely responsible for the costs of development of any REMS for ZX008 and will continue to be responsible for all costs associated with implementation and operation of the REMS if ZX008 is approved.

With respect to post-market product advertising and promotion, the FDA imposes a number of complex requirements 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 and social media. 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.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United States. Orphan drug

designation must be requested before submitting an NDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan drugs are eligible for certain incentives, including tax credits for qualified clinical testing and waiver of application fees.

If the FDA approves a sponsor's marketing application for a designated orphan drug for use in the rare disease or condition for which it was designated, the sponsor is eligible for a seven-year period of marketing exclusivity, during which the

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FDA may not approve another sponsor's marketing application for a drug with the same active moiety and intended for the same use or indication as the approved orphan drug, except in limited circumstances, such as if a subsequent sponsor demonstrates its product is clinically superior. During a sponsor's orphan drug exclusivity period, competitors, however, may receive approval for drugs with different active moieties for the same indication as the approved orphan drug, or for drugs with the same active moiety as the approved orphan drug, but for different indications. Orphan drug exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for a drug with the same active moiety intended for the same indication before we do, unless we are able to demonstrate that grounds for withdrawal of the orphan drug exclusivity exist, or that our product is clinically superior. Further, if a designated orphan drug receives marketing approval for an indication broader than the rare disease or condition for which it received orphan drug designation, it may not be entitled to exclusivity.

ZX008 has received orphan drug designation in the United States and the EU for the treatment of Dravet syndrome and in the EU for the treatment of LGS. We may seek orphan drug designation for ZX008 for a different indication, or other product candidates, but the FDA may disagree with our analysis of the prevalence of the particular disease or condition or other criteria for designation and refuse to grant orphan status. We cannot guarantee that we will obtain orphan drug designation or approval for any product candidate, or that we will be able to secure orphan drug exclusivity if we do obtain approval.

Section 505(b)(2) New Drug Applications

An applicant may submit an NDA under Section 505(b)(2) of the FFDCA to seek approval for modifications or new uses of products previously approved by the FDA. 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 previous findings of safety and effectiveness for an approved product based on the prior pre-clinical or clinical trials conducted for the approved product. The FDA may also require companies to perform new 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 FDA's current list of "Approved Drug Products with Therapeutic Equivalence Evaluations," known as 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 based on the Paragraph IV certification. Under the FFDCA, if a patent infringement lawsuit is filed against the 505(b)(2) NDA applicant within 45 days of receipt of the Paragraph IV certification notice, an automatic stay of approval is imposed, which prevents the FDA from approving the Section 505(b)(2) NDA for 30 months, or until a court decision or settlement finding that the patent is invalid, unenforceable or not infringed, whichever is earlier. The court also has the ability to shorten or lengthen the 30 month stay if either party is found not to be reasonably cooperating in expediting the litigation. Thus, the 505(b)(2) NDA 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 may be eligible for its own regulatory exclusivity period, such as three-year new product 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 trials, 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 is 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 expired. Additional exclusivities may also apply, such as an added six-month pediatric exclusivity period based on studies conducted in pediatric patients under a written request from the FDA.

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Additionally, the 505(b)(2) NDA applicant may list its own relevant patents in the Orange Book, and if it does, it can initiate patent infringement litigation against subsequent applicants that challenge such patents, which could result in a 30-month stay delaying those applicants.

DEA Regulation

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.

Fenfluramine, the active ingredient in ZX008, is currently regulated as a Schedule IV drug in the United States. Substances in Schedule IV are considered to have a low potential for abuse relative to substances in Schedule III. A prescription for controlled substances in Schedules III, IV, and V issued by a practitioner, may be communicated either orally, in writing, or by facsimile to the pharmacist, and may be refilled if so authorized on the prescription or by call-in. Many commonly prescribed sleep aids (e.g., Ambien®, Sonata®), most benzodiazepines (e.g., Ativan®, Valium®, Versed®, Diastat®, Onfi®) and some weight loss drugs (e.g., Belviq®, Qsymia®) are also regulated as Schedule IV drugs.

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. Reports must also be made for thefts or losses of any controlled substance, and authorization must be obtained to destroy any controlled substance. In addition, special authorization and notification requirements apply to imports and exports.

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 and respective 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 EU 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 EU member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the

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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.

Healthcare Fraud and Abuse Laws

We are subject to various federal, state and local laws targeting fraud and abuse in the healthcare industry. These laws are 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. Moreover, the lack of uniform court interpretation of the Anti-Kickback Statute makes compliance with the law difficult. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the 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.

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. 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. 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 and improper promotion of off-label uses (i.e., uses not expressly approved by FDA in a drug's label). 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.

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. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the PPACA, also imposes new reporting and disclosure requirements on drug manufacturers for any "transfer of

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value" made or distributed to prescribers and other healthcare providers, and any ownership or 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. Manufacturers are required to report such data to the government by the 90th day of each calendar year.

Under California law, pharmaceutical companies must adopt a comprehensive compliance program that is in accordance with both the 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 have imposed restrictions on the types of interactions that pharmaceutical 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, including the final omnibus rule published on January 25, 2013, 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 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, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, 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. 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 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 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2025 unless additional Congressional action is taken.

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On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations.
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 our product candidates, if approved, 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 established even if coverage is 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, 2016, we employed 67 full-time employees. Of the full-time employees, 33 were engaged in product development, quality assurance and clinical and regulatory activities, 9 were engaged in manufacturing operations, 6 were engaged in sales and marketing and 19 were engaged in general and administrative activities (including business and corporate development).
None of our employees are represented by a labor union, and we consider our employee relations to be good. We currently utilize two employer services companies to provide human resource services. These service companies are the employer of record for payroll, benefits, employee relations and other employment-related administration.

Research and Development

We invested $41.8 million, $27.9 million and $11.9 million in research and development in 2016, 2015 and 2014, respectively.

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About Zogenix

We were formed as a Delaware corporation on May 11, 2006 as SJ2 Therapeutics, Inc. We changed our name to Zogenix, Inc. on August 28, 2006. Our principal executive offices are located at 5858 Horton Street, Suite 455, Emeryville, California 94608, and our telephone number is 1-866-ZOGENIX (1-866-964-3649). We conduct our research and development activities, general and administrative functions and our contract manufacturing services primarily from our Emeryville, California location.

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. Zogenix International Limited is a wholly-owned subsidiary of Zogenix Europe Limited which was acquired in October 2014.

Financial Information about Segments

We manage our business as one segment which includes all activities related to the development and commercialization of pharmaceutical products. For financial information related to our one segment, see "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included in this Annual Report on 10-K.

Available Information

We file our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K electronically with the Securities and Exchange Commission, or SEC, pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended. We make copies of these reports available on our website at www.zogenix.com, free of charge, 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

Our success depends substantially on our product candidates, ZX008 and Relday. We cannot be certain that any product candidate will receive regulatory approval or be successfully commercialized.

We have only a limited number of product candidates in development, and our business depends substantially on their successful development and commercialization. Following the completion of the sale of our Zohydro ER business in April 2015, we have no drug products approved for sale, and we may not be able to develop marketable drug products in the future. All of our product candidates will require additional clinical and pre-clinical development, regulatory review and approval in multiple jurisdictions, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenues from product sales. The research, testing, manufacturing, labeling, approval, sale, marketing, distribution and promotion of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, whose regulations differ from country to country.

We are not permitted to market our product candidates in the United States until we receive approval of an NDA from the FDA, or in any foreign countries until we receive the requisite approval from the regulatory authorities of such countries, and we may never receive such regulatory approvals. Obtaining regulatory approval for a product candidate is a lengthy, expensive and uncertain process, and may not be successful. Any failure to obtain regulatory approval of any of our product candidates, or failure to obtain such approval for all of the indications and labeling claims we deem desirable, would limit our ability to generate future revenues, would potentially harm the development prospects of our product candidates and would have a material and adverse impact on our business.

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Even if we successfully obtain regulatory approvals to market our product candidates, our revenues will be dependent, in part, on our ability to commercialize such products as well as the size of the markets in the territories for which we gain regulatory approval. If the markets for our product candidates are not as significant as we estimate, our business and prospects will be harmed.

Our clinical trials may fail to demonstrate acceptable levels of safety and efficacy for ZX008, Relday or any of our other product candidates, which could prevent or significantly delay their regulatory approval.

ZX008, Relday and any of our other product candidates are prone to the risks of failure inherent in drug development. Before obtaining U.S. regulatory approval for the commercial sale of ZX008, Relday or any other product candidate, we must gather substantial evidence from well-controlled clinical trials that demonstrate to the satisfaction of the FDA that the product candidate is safe and effective, and similar regulatory approvals would be necessary to commercialize our product candidates in other countries. Failure can occur at any stage of our clinical trials, and we could encounter problems that cause us to abandon or repeat clinical trials.

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 ZX008, Relday or any of our other product candidates are not shown to be safe and effective in clinical trials, the programs could be delayed or terminated, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Delays in the commencement or completion of clinical testing for ZX008, Relday or pre-clinical or clinical testing for any of our other product candidates could result in increased costs to us and delay or limit our ability to pursue regulatory approval for, or generate revenues from, such product candidates.

Clinical trials are very expensive, time consuming and difficult to design and implement. Delays in the commencement or completion of clinical testing for ZX008, Relday or pre-clinical or clinical testing for any of our other product candidates could significantly affect our product development costs and business plan.

Our Phase 3 program for ZX008 includes three randomized, double-blind placebo-controlled studies of ZX008 as adjunctive therapy for patients with uncontrolled seizures who have Dravet syndrome: identical Studies 1501 and Study 1502, which are evaluating two dose levels of ZX008 (0.2 mg/kg/day and 0.8 mg/kg/day, up to a maximum daily dose of 30 mg), and Study 1504, that is evaluating a single dose a ZX008 (0.5 mg/kg/day, up to a maximum daily dose of 20 mg, which has been shown to be equivalent to 0.8mg/kg/day in patients not taking stiripentol), in patients taking stiripentol, clobazam and valproate. The primary objective of the clinical trials will be to compare the reduction in convulsive seizures experienced by participants after treatment with ZX008 compared to treatment with a placebo. We have recently modestly expanded the target number of subjects for studies 1501 and 1502 and now intend to enroll 120 subjects in each of the two studies, with 40 subjects in each treatment arm rather than the originally planned 35/arm, due to results from a Dravet syndrome study that reported high variability between the treated group and placebo. Study 1501 commenced in January 2016 and is being conducted in North America. Study 1502 is a multi-national study commenced in June 2016 and is being conducted primarily in western Europe. Study 1504 is also a multi-national study commenced in the third quarter 2016 and is being conducted in western Europe and North America. In February 2017, we announced our plan to report top-line results from studies 1501 and 1502 via a merged study analysis approach whereby top-line results from the first half of the combined patient population of studies 1501 and 1502 would be reported as “Study 1”. We expect to report top-line results from Study 1 in the third quarter of 2017 and additional Phase 3 data to be released over the remainder of year. Notwithstanding the aforementioned plans, we may not be able to identify and enroll sufficient number of study participants and interpret results on these time frames, and consequently the completion of our Phase 3 clinical trials may be delayed.

Beginning in first quarter of 2016, we funded an open-label dose-ranging twenty-patient investigator initiated study in patients with LGS. Refractory LGS patients were treated with ZX008 as an adjunctive therapy for seizures associated with LGS. In December 2016, we presented initial data from an interim analysis of the first 13 patients to have completed at least twelve weeks in the study at the American Epilepsy Society meeting. These data demonstrated that ZX008 provided clinically meaningful improvement in major motor seizure frequency in patients with severely refractory LGS, despite not attempting to dose to maximal efficacy as per protocol, with seven out of 13 patients (54%) achieving at least a 50% reduction in the number of major motor seizures. In addition, ZX008 was generally well tolerated. This data indicate that ZX008 has the potential to be a safe and effective adjunctive treatment for LGS.

Based on the strength of the LGS data generated, we plan to submit an IND application in the first quarter of 2017 and initiate a Phase 3 program for ZX008 in LGS in the second half of 2017. The initial results of this on-going study may not be indicative of future results and negative results could increase our costs or limit our ability to pursuant regulatory approval of ZX008 in patients with LGS or other indications.

We initiated clinical testing for Relday in patients with schizophrenia in July 2012 and announced positive single-dose pharmacokinetic results from the Phase 1 clinical trial in January 2013. Based on the favorable safety and pharmacokinetic profile demonstrated in the Phase 1 trial, we extended the study to include an additional dose of the same formulation and announced positive top-line results in May 2013. The results for the extended Phase 1 clinical trial showed risperidone blood

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concentrations in the assumed therapeutic range were achieved on the first day of dosing and maintained throughout the one-month period. In addition, dose proportionality was demonstrated across the full dose range studied. In March 2015, we began a multi-dose clinical trial, which we believe will provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies. On September 30, 2015, we announced positive top-line pharmacokinetic results from our Phase 1b multi-dose clinical trial of Relday. Based on this data, we are seeking to secure a global strategic development and commercialization partner for Relday to support the continued development of Relday. If we are unable to secure such a partner on favorable terms, or at all, we will evaluate the continued development of Relday.

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

In addition, if a significant number of patients fail to stay enrolled in any of our current or future clinical trials of ZX008, Relday or any of our other product candidates and such failure is not adequately accounted for in our trial design and enrollment assumptions, our clinical development program could be delayed. Clinical trials may also be delayed or repeated as a result of ambiguous or negative interim results or unforeseen complications in testing. In addition, a clinical trial may be suspended or terminated by us, the FDA or EMA, 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:

- inability to design appropriate clinical trial protocols;
- inability by us, our employees, our CROs or their employees to conduct the clinical trial in accordance with all applicable FDA, drug enforcement administration, or 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;
- inability 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 the FDA, EMA and IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical

trial. If we experience delays in the completion of, or if we terminate, any of our clinical trials, the commercial prospects for ZX008, 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.

Fast Track designation for ZX008 may not lead to a faster development or review process.

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We have been granted a Fast Track designation for ZX008 in the United States. The Fast Track program is intended to expedite or facilitate the process for reviewing new drug candidates that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended, alone or in combination with one or more drugs, to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the drug candidate and the specific indication for which it is being studied. With a Fast Track drug candidate, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable and the sponsor pays any required user fees upon submission of the first section of the NDA. Obtaining a Fast Track designation does not change the standards for product approval, but may expedite the development or approval process. Even though the FDA has granted such designation for ZX008, it may not actually result in faster clinical development or regulatory review or approval. Furthermore, such a designation does not increase the likelihood that ZX008 will receive marketing approval in the United States.

If we do not secure collaborations with strategic partners to develop and commercialize Relday, we may not be able to successfully develop Relday and generate meaningful revenues from it.

Our current strategy is to selectively enter into a strategic collaboration with one or more third parties to conduct clinical testing for, seek regulatory approval for and to commercialize Relday. We may not be successful in securing a strategic partner on favorable terms, or at all. If we are able to identify and reach an agreement with one or more collaborators, our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. Collaboration agreements typically call for milestone payments that depend on successful demonstration of efficacy and safety in required clinical trials and obtaining regulatory approvals. Collaboration revenues are not guaranteed, even when efficacy and safety are demonstrated.

Even if we succeed in securing collaborators, the collaborators may fail to develop or effectively commercialize Relday. Collaborations involving Relday pose a number of risks, including the following:

- collaborators may not have sufficient resources or may decide not to devote the necessary resources due to internal constraints such as budget limitations, lack of human resources, or a change in strategic focus;
- collaborators may believe our intellectual property is not valid or is unenforceable or the product candidate infringes on the intellectual property rights of others;
- collaborators may dispute their responsibility to conduct development and commercialization activities pursuant to the applicable collaboration, including the payment of related costs or the division of any revenues;
- collaborators may decide to pursue a competitive product developed outside of the collaboration arrangement;
- collaborators may not be able to obtain, or believe they cannot obtain, the necessary regulatory approvals;
- collaborators may delay the development or commercialization of our product candidates in favor of developing or commercializing their own or another party's product candidate; or
- collaborators may decide to terminate or not to renew the collaboration for these or other reasons.

As a result, collaboration agreements may not lead to development or commercialization of Relday in the most efficient manner or at all.

We also face competition in seeking out collaborators. If we are unable to secure a collaboration that achieves the collaborator's objectives and meets our expectations, we may be unable to advance Relday and may not generate meaningful revenues.

We have limited sales and marketing resources, and we may not be able to effectively market and sell our products.

As a result of the sale of our Zohydro® ER business in April 2015, we do not currently have all the necessary components of an organization for sales, marketing and distribution of pharmaceutical products, and therefore we must build this organization or make arrangements with third parties to perform these functions in order to commercialize any products that we successfully develop and for which we obtain regulatory approvals. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. We will also face competition in our search for collaborators and potential co-promoters, if we choose such an option. To the extent we may rely on third parties to co-promote or otherwise commercialize any

product candidates in one or more regions 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 candidates, they may be unable to devote the resources necessary to realize the full commercial potential of our products.

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Further, we may lack the financial and managerial resources to establish a sales and marketing organization to adequately promote and commercialize any product candidates that may be approved. The establishment of a sales force will result in an increase in our expenses, which could be significant before we generate revenues from any newly approved product candidate. Even though we may be successful in establishing future 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, and could have a material adverse effect on our business, results of operations, financial condition and prospects.

We face intense competition, and if our competitors market and/or develop treatments for Dravet syndrome or psychiatric 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 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 we do.

If approved for the chronic treatment of Dravet syndrome, ZX008 may compete against other products and product candidates. In the EU, Canada, Australia and Japan, Diacomit (stiripentol) by Laboratoires Biocodex has been approved and is being commercialized as an adjunctive therapy (in combination with sodium valproate and clobazam) for the treatment of Dravet syndrome; stiripentol, while not yet approved by FDA, is available to patients in the United States via the FDA's Personal Importation Policy and Expanded Access IND. Epidiolex®, a cannabinoid drug, which is being developed by GW Pharmaceuticals, has received an orphan designation by the EMA for the treatment of Dravet syndrome and by the FDA for the treatment of Dravet and Lennox-Gastaut syndromes, as well as Fast Track status by the FDA for the treatment of Dravet syndrome. In March 2016, GW Pharmaceuticals announced positive results from its first Phase 3 clinical trial for Epidiolex for the treatment of Dravet syndrome, and in June and September 2016 announced positive results from its two Phase 3 clinical trials for Epidiolex for the treatment of Lennox-Gastaut syndromes, with the drug achieving its primary study endpoints in all three trials. GW Pharmaceuticals is currently conducting an additional Phase 3 study in Dravet syndrome and has announced it intends to file an NDA for both indications in 2017. Insys Therapeutics has advanced its pharmaceutical cannabinoid program, which has received orphan drug designation and Fast Track status by the FDA for use of cannabidiol as a potential treatment for Dravet syndrome. Sage Therapeutics has completed a Phase 1/2 clinical trial for its lead compound SAGE-547, an allosteric modulator of GABA receptors, for the acute treatment of super-refractory status epilepticus, which is status epilepticus (prolonged nonstop seizure) that continues or recurs 24 hour or more after the onset of anesthetic therapy. Status epilepticus is associated with many epilepsy conditions, including Dravet syndrome.

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, Invega Sustenna and Invega Trinza marketed by Janssen Pharmaceuticals, Zyprexa Relprevv marketed by Eli Lilly & Company, Aristada marketed by Alkermes plc and 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 Janssen Pharmaceuticals, 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 Vanda Pharmaceuticals, Inc., 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 Teva, Braeburn Pharmaceuticals, Laboratorios Farmaceuticos Rovi SA, Indivior PLC and Luye Pharma Group, Ltd., each of which has announced they are developing long-acting antipsychotic product candidates. In May 2015, Janssen Pharmaceuticals announced that the FDA approved Invega Trinza, a three-month long-version of paliperidone palmitate, for the treatment of schizophrenia in patients adequately treated with Invega Sustenna for at least four months. Also in May 2015, Indivior PLC announced positive top-line results from its Phase 3 clinical trial of RBP-7000, an investigational drug formulation of risperidone for the treatment of schizophrenia that is intended to require once-monthly dosing. In October 2015, Alkermes plc announced that the FDA approved Aristada (aripiprazole lauroxil) extended-release injectable suspension for the treatment of schizophrenia, which offers once-monthly and six-week dosing options.

We expect ZX008, Relday and any of our other product candidates, if approved, to compete on the basis of, among other things, product efficacy and safety, time to market, price, coverage and reimbursement by third-party payors, extent of adverse side effects and convenience of treatment procedures. One or more of our competitors may develop other products that compete with ours, obtain necessary approvals for such products from the FDA, or other agencies, if required, more rapidly than we do

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or develop alternative products or therapies that are safer, more effective and/or more cost effective than any products developed by us. The competition that we will encounter with respect to any of our product candidates that receive the requisite regulatory approval and classification and are marketed will have an effect on our product prices, market share and results of operations. We may not be able to successfully differentiate any products that we are able to market from those of our competitors, successfully develop or introduce new products that are less costly or offer better results than those of our competitors or offer purchasers of our products payment and other commercial terms as favorable as those offered by our competitors. In addition, competitors may seek to develop alternative formulations of our product candidates and/or alternative drug delivery technologies that address our targeted indications.

The commercial opportunity for 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, expertise 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 we are 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 effectively compete with any of our product candidates that are approved, our business, results of operations, financial condition and prospects may be materially adversely affected.

If ZX008, Relday or any other product candidate receives regulatory approval but does not achieve broad market acceptance or coverage by third-party payors, the revenues that we generate will be limited.

The commercial success of ZX008, Relday or any other product candidates, if approved by the FDA or other regulatory authorities will depend upon the acceptance of these products by physicians, patients, healthcare payors and the medical community. Adequate coverage and reimbursement of our approved product by third-party payors will also be critical for commercial success. The degree of market acceptance of any product candidates for which we may receive regulatory approval will depend on a number of factors, including:

- acceptance by physicians and patients of the product as a safe and effective treatment;
- any negative publicity or political action related to our or our competitors' products;
- the relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- demonstration to authorities of the pharmacoeconomic benefits;
- demonstration to authorities of the improvement in burden of illness;
- limitations or warnings contained in a product's FDA-approved or European Medicines Agency, or EMA, approved labeling;
- the clinical indications for which a product is approved;
- availability and perceived advantages of alternative treatments;
- the effectiveness of our or any current or future collaborators' sales, marketing and distribution strategies;
- pricing and cost effectiveness;
- our ability to obtain sufficient U.S. third-party payor coverage and reimbursement;
- our ability to obtain European countries' pricing authorities' coverage and reimbursement; and
- the willingness of patients to pay out of pocket in the absence of third-party payor coverage.

Our efforts to educate the medical community, U.S. third-party payors and European countries' health authorities on the benefits of ZX008, Relday or any of our other product candidates for which we obtain marketing approval from the FDA or other

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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, pharmacists, patients, and the medical community, we may not generate sufficient revenue from these products to become or remain profitable.

We have a history of significant net losses and negative cash flow from operations. We cannot predict if or when we will become profitable and anticipate that our net losses and negative cash flow from operations will continue for next year.

We were organized in 2006, began commercialization of Sumavel DosePro in January 2010 and launched the commercial sale of Zohydro ER in the United States in March 2014. We sold our Sumavel DosePro business in April 2014 and sold our Zohydro ER business in April 2015. Our business and prospects must be considered in light of the risks and uncertainties frequently encountered by pharmaceutical companies developing and commercializing new products.

Excluding gains from two discrete business divestitures, we have incurred significant net losses from its operations since its inception and has an accumulated deficit of $445.2 million as of December 31, 2016. In 2016, the Company used $72.9 million of cash in operations. We expect to continue to incur operating losses and negative cash flow from operating activities for at least the next year primarily as a result of the development of ZX008. Additionally, in the event that ZX008 is approved in the United States or EU, we will owe milestone payments under the Zogenix International Limited Sales and Purchase Agreement for ZX008. Our ability to generate revenues from any of our product candidates will depend on a number of factors including 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 are subject to the risk that the marketplace will not accept our products.

Because of the numerous risks and uncertainties associated with our commercialization and product development efforts, we are unable to predict the extent of our future losses or when or if we will become profitable and it is possible we will never become profitable. If we do not generate significant sales from any of our product candidates that may receive regulatory approval, there would likely be a material adverse effect on our business, results of operations, financial condition and prospects which could result in our inability to continue operations.

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

We have agreements with third-party CROs to conduct our ongoing Phase 3 program for ZX008. We rely heavily on these parties for the execution of our clinical trials 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 and regulatory requirements. We and our CROs are required to comply with good clinical practice, or GCP, requirements for clinical studies of our product candidates, and good laboratory practice, or GLP, requirements for certain pre-clinical studies. The FDA enforces these regulations through periodic inspections of trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable regulations, the data generated in our pre-clinical studies and clinical trials may be deemed unreliable and the FDA may require us to perform additional pre-clinical studies or 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 practice, or cGMP, regulations, and require a large number of test subjects. Our inability 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 terminates, we may not be able to enter into arrangements with alternative CROs on commercially reasonable terms, or at all. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory

approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate additional revenues could be delayed.

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

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

We commenced our operations on August 25, 2006. Our operations to date have included 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 products and product candidates, in-licensing rights to Zohydro ER and Relday, acquiring rights to ZX008, commercializing Sumavel DosePro and Zohydro ER and divesting Sumavel DosePro and Zohydro ER. In January 2010, we launched Sumavel DosePro and began generating revenues, and we launched Zohydro ER in March 2014. We sold our Sumavel DosePro business in April 2014 and sold our Zohydro ER business in April 2015. Consequently, any predictions about our future performance may not be as accurate as they would be if we had a longer history of developing and commercializing pharmaceutical products.

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. For example, in October 2014, we completed the acquisition of Brabant, which owns worldwide development and commercialization rights to ZX008 for the treatment of Dravet syndrome, and in October 2016, we completed an asset purchase agreement to acquire the global rights to a preclinical development program for orphan CNS disorders. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- significant or 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, personnel 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 additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

We are dependent on numerous third parties in our supply chain, all of which are currently single source suppliers, for the supply of Sumavel DosePro to Endo and for the clinical supply of ZX008 and Relday, and if we experience problems with any of these suppliers, the manufacturing of Sumavel DosePro, ZX008 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, ZX008, Relday or any other product candidates. Our DosePro system 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 addition to Patheon's manufacturing services, Nypro Limited, located in Bray, Ireland, manufactures the actuator assemblies and injection molded components for our DosePro system and Nipro PharmaPackaging, Germany GmbH (formerly MGlas AG), located in Münnerstadt, Germany, manufactures the specialized glass capsule (cartridge) that houses the

sumatriptan active pharmaceutical ingredients, or API, in our DosePro system. Each of these manufacturers and each other company that supplies, fabricates or manufactures any component used in our DosePro system 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 ZX008 and Relday to third parties.

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Similarly, Durect is the exclusive manufacturer of the risperidone formulation using Durect's SABER™ controlled-release technology for all Relday clinical trials through Phase 3 and, if approved, has the option to supply the same formulation for commercial production. ZX008, if approved, would require process validation, for which there can be no assurance of success. We may never be able to establish additional sources of supply for ZX008 or Relday's risperidone formulation.

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

Reliance on third-party manufacturers and suppliers entails risks to which we would not be subject if we manufactured Sumavel DosePro 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 are unable to provide the quantities of our product candidates required for our clinical trials and, if approved, for commercial sale, on a timely basis and at commercially reasonable prices, and we are unable to find one or more replacement manufacturers or suppliers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality, and on a timely basis, we would likely be unable to meet demand for our products and would have to delay or terminate our pre-clinical or clinical trials, and we would lose potential revenue. It may also take a significant period of time to establish an alternative source of supply for our products, product candidates and components and to have any such new source approved by the FDA or any applicable foreign regulatory authorities. Furthermore, any of the above factors could cause the delay or suspension of initiation or completion of clinical trials, regulatory submissions or required approvals of our product candidates, cause us to incur higher costs and could prevent us from commercializing our product candidates successfully.

We may encounter delays in the manufacturing of Sumavel DosePro for Endo or fail to generate contract manufacturing 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 system will be adversely affected and our ability to meet the distribution requirements for any Sumavel DosePro purchase orders from Endo and the resulting contract manufacturing 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 contract manufacturing revenue from Sumavel DosePro or our ability to generate revenue from any potential future DosePro products, which in turn could have a material adverse effect on our business, results of operations, financial condition and prospects.

We and Endo have recently entered into a letter agreement acknowledging Endo's decision to have us discontinue the manufacturing and supply of Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. We expect to fulfill currently open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time.

Based on the stage of production in our supply chain for the products to be delivered, we expect to obtain the remaining raw materials and component parts from our existing suppliers, including Patheon UK Limited, or Patheon, to fulfill our obligation to Endo. Thereafter, we intend to terminate our agreements with our third-party suppliers, including Patheon.

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We may not realize the full economic benefit from the sale of our Sumavel DosePro business and Zohydro ER business.

Pursuant to the Endo Asset Purchase Agreement that we entered into in April 2014, in addition to the $89.6 million upfront cash payment, we may receive contingent payments, based on Endo's achievement of pre-determined sales and gross margin milestones, in an amount up to $20.0 million. Our ability to receive these contingent payments under our supply agreement with Endo is dependent upon Endo successfully maintaining and increasing market demand for, and sales of, Sumavel DosePro. We and Endo have recently entered into a letter agreement acknowledging Endo's decision to have us discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. We expect to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time. As a result, we do not expect to receive any further milestone payments under this agreement.

Pursuant to the asset purchase agreement with Pernix that we entered into in March 2015, we may receive contingent payments of up to $283.5 million, based on Pernix's achievement of pre-determined milestones. These milestones include a $12.5 million payment upon approval by the FDA of an abuse-deterrent extended-release hydrocodone tablet and up to $271.0 million in potential sales milestones. Our ability to receive these contingent payments is dependent upon Pernix successfully maintaining and increasing market demand for, and sales of, Zohydro ER in a manner in which the requisite sales of the product will be achieved and devoting the resources necessary to achieve the manufacturing milestone.

We have also agreed to indemnify Pernix and its affiliates against losses suffered as a result of our material breach of representations and warranties and our other obligations in the asset purchase agreement. In addition, we have agreed to indemnify Pernix for certain indemnification matters up to an aggregate amount of $5.0 million. We cannot provide any assurance that we will receive all or any portion of the contingent milestone payments.

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

Our success depends on our continued ability to attract, retain and motivate highly qualified management and key clinical development, regulatory, sales and marketing and other personnel. As of December 31, 2016, we employed 67 full-time employees. Of the full-time employees, 33 were engaged in product development, quality assurance and clinical and regulatory activities, 9 were engaged in manufacturing operations, 6 were engaged in sales and marketing and 19 were engaged in general and administrative activities (including business and corporate development). If we are not able to retain our employee base, we may not be able to effectively manage our business or be successful in commercializing our products.

We are highly dependent on the development, regulatory, commercial and financial expertise of our senior management team. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the areas in Southern and Northern California, where we currently operate. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercialization objectives, our ability to raise additional capital, our ability to implement our business strategy and our ability to maintain effective internal controls for financial reporting and disclosure controls and procedures as required by the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act. The loss of the services of any members of our senior management team, especially our Chief Executive Officer and President, Stephen J. Farr, Ph.D., could delay or prevent the development and commercialization of any of our product candidates, including ZX008 and 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.

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

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disasters, terrorism, war and telecommunication and electrical failures. For example, we have in the past experienced failures in our information systems and computer servers, which may have been the result of a cyber-attack. These failures resulted in an interruption of our normal business operations and required substantial expenditure of financial and administrative resources to remedy. We cannot be sure that similar failures will not occur in the future. System failures, accidents or security breaches can cause interruptions in our operations, and can result in a material disruption of our commercialization activities, drug development programs and our business operations. The loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval and post-market study compliance efforts and significantly increase our costs to recover or reproduce the data. Similarly, we rely on a large number of third parties to supply components for and manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of ZX008, Relday or any of our other product candidates could be delayed or otherwise adversely affected.

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

We conduct research and development activities in the United Kingdom and other European countries and some of the payments for these activities are denominated in Euros and U.K. pounds sterling. As a result, we are exposed to foreign exchange risk, and our results of operations may be impacted by fluctuations in the exchange rate between the U.S. dollar and the Euro or U.K. pound sterling, such as the decline in value of the U.K. pound sterling following the results of the United Kingdom's referendum on withdrawal from the EU. 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.

If we are unable to achieve and maintain adequate levels of coverage and reimbursement for 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 any product candidates for which we may receive regulatory approval will 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 are critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

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

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

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

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

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

The commercial use of our products and clinical use of our products and product candidates expose us to the risk of product liability claims. This risk exists even if a product or product candidate is approved for commercial sale by the FDA and manufactured in facilities regulated by the FDA such as the case with Zohydro ER, or an applicable foreign regulatory authority. Our products and product candidates are designed to affect important bodily functions and processes. Any side effects, manufacturing defects, misuse or abuse associated with Zohydro ER or our product candidates could result in injury to a patient or even death. For example, 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. Although we no longer sell Zohydro ER following the sale of the Zohydro ER business in April 2015, we retain all liabilities associated with the Zohydro ER business arising prior to such sale, including possible product liability exposure in connection with sales of Zohydro ER made prior to the sale of the Zohydro ER business. In addition, a liability claim may be brought against us even if our products or product candidates merely appear to have caused an injury.

Product liability claims may be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products or product candidates, if approved, 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 candidates;
- decreased demand for our product candidates, if approved;
- 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 $20 million per occurrence and 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 approval of ZX008 or Relday, or otherwise, we may be unable to obtain this increased product liability insurance on commercially reasonable terms or at all. Large judgments have been awarded in class action or individual lawsuits based on drugs that had unanticipated side effects, including side effects that are less severe than those of Zohydro ER and our product candidates. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and have a material adverse effect on our business, results of operations, financial condition and prospects.

We may never receive regulatory approval or commercialize our product candidates outside of the United States.

We intend to market certain of our product candidates outside of the United States, if approved. For example, ZX008 has received orphan drug designation in the EU, and we commenced a Phase 3 clinical trial in Europe and Australia in June 2016 to support a European marketing authorization application. In order to market our products outside of the United States, we, or any potential partner, must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our products. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed in these "Risk Factors" regarding FDA approval in the United States, as well as other risks.

For example, in the European Economic Area, or EEA (comprised of 28 EU member states plus Iceland, Liechtenstein, and Norway), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of MAs:

- The Community MA, which is issued by the European Commission through the Centralized · Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicines that contain a new active substance

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indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the Centralized Procedure the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when the authorization of a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. Under the accelerated procedure the standard 210-day review period is reduced to 150 days.

- National MAs, which are issued by the competent authorities of the member states of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure.
- Where a product has already been authorized for marketing in a member state of the EEA, this National MA can be recognized in other member states through the Mutual Recognition Procedure. If the product has not received a National MA in any member state at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

In the EEA, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity and qualify for data exclusivity.

In the EEA we can take advantage of the hybrid application pathway of the EU Centralized Procedure, which is similar to the FDA's 505(b)(2) pathway. Hybrid applications may rely in part on the results of pre-clinical tests and clinical trials contained in the authorization dossier of the reference product, but must be supplemented with additional data. In territories where data is not freely available, we or our partners may not have the ability to commercialize our products without negotiating rights from third parties to refer to their clinical data in our regulatory applications, which could require the expenditure of significant additional funds. We, or any potential partner, may be unable to obtain rights to the necessary clinical data and may be required to develop our own proprietary safety effectiveness dossiers. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Inability to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed in these "Risk Factors" regarding FDA approval in the United States. As described above, such effects include the risks that our product candidates may not be approved at all or for all requested indications, which could limit the uses of our product candidates and have an adverse effect on their commercial potential or require costly, post-marketing studies. In addition, we, or any potential partner, may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution if we are unable to comply with applicable foreign regulatory requirements.

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 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 research and development efforts and business operations, injury to our employees and others, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the

use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources. We do not currently carry biological or hazardous waste insurance coverage.

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

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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. 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.

Generally accepted accounting principles in the United States 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.

The results of the United Kingdom's referendum on withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business.

We are a company with worldwide operations, which includes significant business operations in Europe, and our wholly owned subsidiary Zogenix Europe Limited is incorporated under the laws of England and Wales. In June 2016, a majority of voters in the United Kingdom elected to withdraw from the EU in a national referendum. The referendum was advisory, and the terms of any withdrawal are subject to a negotiation period that could last at least two years after the government of the United Kingdom formally initiates a withdrawal process. Nevertheless, the referendum has created significant uncertainty about the future relationship between the United Kingdom and the EU, and has given rise to calls for certain regions within the United Kingdom to preserve their place in the EU by separating from the United Kingdom as well as for the governments of other EU member states to consider withdrawal.

These developments, or the perception that any of them could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates and credit ratings may be especially subject to increased market volatility. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU laws to replace or replicate in the event of a withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict our access to capital. If the United Kingdom and the EU are unable to negotiate acceptable withdrawal terms or if other EU member states pursue withdrawal, barrier-free access between the United Kingdom and other EU member states or among the European economic area overall could be diminished or eliminated. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and affect our strategy in the European pharmaceutical market.

Risks Related to Our Financial Position and Capital Requirements

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

We launched our first approved product, Sumavel DosePro, in January 2010 and subsequently sold the business in April 2014. We launched our approved product, Zohydro ER, in March 2014 and subsequently sold the business in April 2015. We have financed our operations primarily through the proceeds from the issuance of equity securities, the sale of the Sumavel DosePro and Zohydro ER businesses, and debt, and have incurred negative cash flow from operations in each year since our inception. For the years ended December 31, 2016, 2015 and 2014, we incurred net (loss) income of $(69.7) million, $26.1 million and $8.6 million, respectively, and our cash used in operating activities was $72.9 million, $64.6 million and $80.8 million, respectively. As of December 31, 2016, we had an accumulated deficit of $445.2 million. The losses and negative cash flow from operations have had a material adverse effect on our stockholders' equity and working capital.

We expect to continue to incur net losses and negative cash flow from operating activities for at least the next year to conduct clinical trials to support regulatory approval of our product candidates. As a result, we will remain dependent upon external sources of financing to fund our business and the development and commercialization of any approved products and product candidates. To the extent we need to raise additional capital in the future, we cannot ensure that debt or equity financing will be available to us in amounts, at times or on terms that will be acceptable to us, or at all. Any shortfall in our cash resources could require that we delay or abandon certain development and commercialization activities and could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

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We will require additional funding to carry out our plan of operations and if we are unable to raise capital when needed, we may be forced to delay, reduce or eliminate our product development programs or future commercialization efforts.

Our operations have consumed substantial amounts of cash since inception. Based on our operating plans, we believe our cash and cash equivalents will be sufficient to fund our operations through the end of 2017. We will need to obtain additional funds to finance our operations beyond that point in order to:

- fund our operations, including further development of ZX008 and development of any other product candidates to support potential regulatory approval; and
- commercialize any of our product candidates, or any products or product candidates that we may develop, in-license or otherwise acquire, if any such product candidates receive regulatory approval.

In addition, our estimates of the amount of cash necessary to fund our business and development 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 rate of progress and cost of our clinical trials and other product development programs for ZX008 and our other product candidates and any other product candidates that we may develop, in-license or acquire;
- the timing of regulatory approval for any of our other product candidates and the commercial success of any approved products;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with ZX008, Relday and any of our other product candidates;
- the costs of establishing or outsourcing sales, marketing and distribution capabilities, should we elect to do so;
- the costs, terms and timing of completion of outsourced commercial manufacturing supply arrangements for any product candidate;
- the effect of competing technological and market developments;
- the terms and timing of any additional collaborative, licensing, co-promotion or other arrangements that we may establish, including our ability to secure a global strategic development and commercialization partner for Relday or ZX008; and
- the receipt of contingent payments from the sale of our Zohydro ER business, which are based on the achievement of pre-determined regulatory and sales milestones by Pernix

Until we can generate a sufficient amount of product revenue and cash flow from operations and achieve profitability, we expect to finance future cash needs through public or private equity offerings, debt financings, receivables financings or corporate collaboration and licensing arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unsuccessful in raising additional required funds, we may be required to significantly delay, reduce the scope of or eliminate one or more of our development programs or our commercialization efforts, or cease operating as a going concern. We also may be required to relinquish, license or otherwise dispose of rights to product candidates or products that we would otherwise seek to develop or commercialize ourselves on terms that are less favorable than might otherwise be available. If we raise additional funds by issuing equity securities, substantial dilution to existing stockholders would likely 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 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.

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

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In its report accompanying our audited consolidated financial statements for the year ended December 31, 2016, our independent registered public accounting firm included an explanatory paragraph stating that our recurring losses from operations and negative cash flows from operating activities 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.

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. For example, in May 2016, we entered into a Controlled Equity Offering^{SM} sales agreement with Cantor Fitzgerald & Co. for the offer and sale of up to $25 million of shares of our common stock from time to time. 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.

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. We had a third ownership change as defined by IRC Sections 382 and 383, which occurred in January 2014. There was no forfeiture in federal and California net operating loss carryforwards or research and development income tax credits as a result of the third 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. 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.

The terms of our credit facility place restrictions on our operating and financial flexibility.

We have entered into a loan and security agreement, or the credit facility, with Oxford Finance LLC, or Oxford, as collateral agent, and the lenders party thereto from time to time, or the lenders, including Oxford and Silicon Valley Bank, or SVB, that is secured by substantially all of our personal property other than our intellectual property. The outstanding principal balance under the credit facility was $20.0 million at December 31, 2016.

The credit facility includes affirmative and negative covenants applicable to us and any subsidiaries we create in the future. The affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, maintain insurance coverage and satisfy certain requirements regarding accounts receivable. The negative covenants include, among others, restrictions on our transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, selling assets and undergoing a change in control, in each case subject to certain exceptions.

The credit facility also includes events of default, the occurrence and continuation of which could cause interest to be charged at the rate that is otherwise applicable plus 5.0% and would provide Oxford, as collateral agent, with the right to exercise remedies against us and the collateral securing the credit facility, including foreclosure against our properties securing

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the credit facilities, including our cash. These events of default include, among other things, our failure to pay any amounts due under the credit facility, a breach of covenants under the credit facility, our insolvency, a material adverse change, the occurrence of any default under certain other indebtedness in an amount greater than $400,000 and one or more judgments against us in an amount greater than $400,000 individually or in the aggregate.

Our ability to make scheduled payments on or to refinance our indebtedness depends on our future performance and ability to raise additional sources of cash, which is subject to economic, financial, competitive and other factors beyond our control. If we are unable to generate sufficient cash to service our debt, we may be required to adopt one or more alternatives, such as selling assets, restructuring our debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. If we desire to refinance our indebtedness, our ability to do so will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

Risks Related to Regulation of our Product and Product Candidates

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

We currently are developing ZX008 for the treatment of seizures associated with Dravet syndrome and LGS, and Relday for the treatment of the symptoms of schizophrenia. The research, testing, manufacturing, labeling, approval, sale, marketing, distribution and promotion of drug products, among other things, are subject to extensive regulation by the FDA and other regulatory authorities in the United States. We are not permitted to market ZX008, 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 any of our product candidates, or that any such product candidates will be successfully commercialized.

Under the policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA is subject to a two-tiered system of review times for new drugs: standard review and priority review. For drugs that do not contain a new molecular entity, such as Relday, a standard review means the FDA has a goal to complete its review of the NDA and respond to the applicant within ten months from the date of receipt of an NDA. The review process and the PDUFA target action date may be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission. The FDA's review goals are subject to change, and the duration of the FDA's review may depend on the number and type of other NDAs that are submitted to the FDA around the same time period.

The FDA may also refer applications for novel products or products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. Although the FDA is not bound by the recommendation of an advisory committee, the matters discussed at the advisory committee meeting, and in particular any concerns regarding safety, could limit our ability to successfully commercialize our product candidates subject to advisory committee review.

As part of its review of an NDA, the FDA may inspect the facility or facilities where the drug is manufactured. If the FDA's evaluations of the NDA and the clinical and manufacturing procedures and facilities are favorable, the FDA will issue an action letter, which will be either an approval letter, authorizing commercial marketing of the drug for a specified indication, or a Complete Response letter containing the conditions that must be met in order to secure approval of the NDA. These conditions may include deficiencies identified in connection with the FDA's evaluation of the NDA submission or the clinical and manufacturing procedures and facilities. Until any such conditions or deficiencies have been resolved, the FDA may refuse to approve the NDA. If and when those conditions have been met to the FDA's satisfaction, the FDA will issue an approval letter. The FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. For example:

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

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

Product candidates such as ZX008 and Relday, and any of our other product candidates, 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

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the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates. Approval may also be contingent on a risk evaluation and mitigation strategy, or REMS program, which can limit the labeling and distribution of a drug product.

ZX008, Relday and any of our other product candidates may not achieve their specified endpoints in clinical trials.

The safety and effectiveness of ZX008 has been evaluated in a single, continuing, long-term, open-label, study in patients with Dravet syndrome in Belgium. In January 2016, we initiated a Phase 3 clinical trial in North America for ZX008 as an adjunctive treatment of seizures in children with Dravet syndrome. This followed FDA acceptance of our IND application for ZX008 in December 2015. The Phase 3 program for ZX008 includes two randomized, double-blind placebo-controlled studies Study 1501 and Study 1502, that will evaluate two dose levels of ZX008 (0.2 mg/kg/day and 0.8 mg/kg/day, up to a maximum daily dose of 30 mg), as well as placebo and an additional randomized, double-blind placebo-controlled study, Study 1504, that will evaluate a single dose of ZX008 (0.5 mg/kg/day, up to a maximum daily dose of 20 mg, which has been shown to be equivalent to 0.8mg/kg/day in patients not taking stiripentol), as well as placebo as adjunctive antiepileptic therapy to a drug regimen that includes stiripentol, clobazam and valproate. Thus for Study 1, we intend to have 120 subjects randomized with 40 subjects per treatment arm. We intend to enroll 80 subjects in Study 1504 with 40 subjects in each treatment arm. Study 1501 commenced in January 2016 and is being conducted in North America. Study 1502 is a multi-national study commenced in June 2016 and is being conducted primarily in Western Europe. Study 1504 is also a multi-national study commenced in the third quarter 2016 and is being conducted in Western Europe and North America. In January 2017, we announced our plan to report top-line results from studies 1501 and 1502 via a merged study analysis approach whereby top-line results from the first half of the combined patient population of studies 1501 and 1502 would be reported as “Study 1”. We expect to report top-line results from Study 1 in the third quarter of 2017 and additional Phase 3 data later in the year. Notwithstanding the aforementioned plans, we may not be able to identify and enroll sufficient study participants and interpret results on these time frames, and consequently the completion of our Phase 3 clinical trials may be delayed.

Beginning in first quarter of 2016, we funded an open-label dose-ranging twenty-patient investigator initiated study in patients with LGS. Refractory LGS patients were treated with ZX008 as an adjunctive therapy for seizures associated with LGS. In December 2016, we released data from an interim analysis of the first 13 patients to have completed at least 12 weeks in the study. The initial results of this on-going study may not be indicative of future results and negative results could increase our costs or limit our ability to pursuant regulatory approval of ZX008 in patients with LGS or other indication.

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 ten patients at a 100 mg dose of the same formulation and announced positive top-line results from the extended Phase 1 clinical trial in May 2013. The positive results from this study extension positioned us to begin a multi-dose clinical trial, which will provide the required steady-state pharmacokinetic and safety data prior to initiating Phase 3 development studies. We started this multi-dose clinical trial in the first half of 2015, and we announced positive top-line pharmacokinetic data in September 2015. Based on this data, we are seeking to secure a global strategic development and commercialization partner for Relday to support the continued development of Relday. If we are unable to secure such a partner on favorable terms, or at all, we will evaluate the continued development of Relday.

If we are unable to obtain regulatory approval for ZX008, Relday or any other product candidates on the timeline we anticipate, we may not be able to execute our business strategy effectively and our ability to generate revenues may be limited.

We may not be able to maintain orphan drug designation or obtain or maintain orphan drug exclusivity for ZX008.

We have obtained orphan drug designation for ZX008 for treatment of Dravet syndrome in the United States and Europe. In the United States, under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition affecting fewer than 200,000 individuals in the United States or, if it affects more than 200,000 people, there is no reasonable expectation that costs of research and development of the

drug for the indication can be recovered by sales in the United States. In the EU, a drug may receive orphan designation if the prevalence of the condition in the EU is of no more than five in 10,000 or it if is unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development. Orphan drug designation in the United States confers certain benefits, including tax incentives and waiver of the applicable application fee upon submission of the product for approval in the rare disease or condition. In the EU, sponsors who obtain orphan designation benefit from a number of incentives, including protocol assistance and fee reductions.

If a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is eligible for a period of marketing exclusivity, which precludes the FDA or EMA from approving another marketing application for the same drug to treat the same rare disease or condition for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in Europe. Also, we are only able to attain orphan drug status in Europe if we are able to demonstrate to EMA that ZX008 has incremental benefit over

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any other approved product for that orphan disorder. Our planned study, 1504, to show incremental benefit over stiripentol may not show any benefit. Currently, only stiripentol has orphan drug status in Europe for treatment of seizures in Dravet syndrome, but others could be approved.

The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Orphan drug exclusivity may not effectively protect the product from competition in the United States because different drugs can be approved for the same condition. Even after an orphan drug is approved and granted exclusivity, the FDA and EMA can subsequently approve the same or a similar drug for the same condition during the exclusivity period if the FDA or the EMA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Any of our 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 implementation of a REMS program. We may 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 any approved product. These requirements may include submissions of safety and other post-marketing information and reports, establishment registration and drug listing, as well as continued compliance with cGMP for our marketed and investigational products, and with GCP and GLP requirements, 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 any product candidates containing controlled substances, we and our contract manufacturers will also be subject to ongoing DEA regulatory obligations, including, among other things, annual registration renewal, security, recordkeeping, theft and loss reporting, periodic inspection and annual quota allotments for the raw material for commercial production of our products. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations, QSR requirements for medical device components or similar requirements, if applicable. If we or a regulatory agency discovers previously unknown problems with an approved 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.

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

- impose restrictions on the marketing or manufacturing of a 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.

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In addition, labeling, advertising and promotion of any approved products 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 Food and Drug Administration Safety and Innovation Act, enacted in 2012, required the FDA to issue new guidance describing its policy regarding internet and social media promotion of regulated medical products, and the FDA has since released several draft guidance documents enumerating new regulatory obligations and restrictions with respect to this type of promotion. In addition, in December 2016, the 21st Century Cures Act was signed into law, which is intended, among other things, to modernize the regulation of drugs and biologics and to spur innovation. 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.

ZX008, Relday and our other product candidates may cause undesirable side effects or have other unexpected properties that could delay or prevent approval or 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, during development or after obtaining U.S. regulatory approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may not permit us to initiate our studies or could put them on hold;
- regulatory authorities may not approve, or may withdraw their approval of the product;
- regulatory authorities may require us to recall the product;
- regulatory authorities may add new limitations for distribution and marketing of the 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;
- we may be required to implement a REMS program;
- 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.

In our Phase 1b multi-dose clinical trial for Relday with 59 enrolled subjects, there was one report of elevated liver enzymes in a subject taking Relday considered a serious and unexpected adverse event. Increases in hepatic enzymes were noted to affect < 2% of Risperdal Consta subjects in clinical trials for registration. High levels of liver enzymes may indicate liver problems or damage, which may have been part of the subject's underlying disease, or an unrelated disease, or it may have been related to Relday.

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, if approved, and could substantially increase the costs of commercializing our product candidates.

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

The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the Federal Food, Drug, and Cosmetic Act. 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 safety and effectiveness data not developed by the filer of the NDA. We plan to submit an NDA for Relday under Section 505(b)(2), and as such, the NDA will rely, in part, on the FDA's previous findings of safety and effectiveness for risperidone. If the FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as anticipated, we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for these product candidates, and complications and risks associated with these product candidates, would likely substantially increase. Moreover, inability to pursue the Section 505(b)(2) regulatory pathway could result in new competitive products reaching the market more quickly than our product candidates, which would likely materially adversely impact our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization.

Even though we may be able to take advantage of Section 505(b)(2) to support potential U.S. approval for Relday, the FDA may still require us to perform additional studies or measurements to support approval. In addition, the FDA's interpretation and use of Section 505(b)(2) has been controversial and has previously been challenged in court, but without a definitive ruling on the propriety of the FDA's approach. Future challenges, including a direct challenge to the approval of our products and product candidates, may be possible and, if successful, could limit or eliminate our ability to rely on the Section 505(b)(2) pathway for the approval of Relday and our other product candidates. Such a result could require us to conduct additional testing and costly clinical trials, which could substantially delay or prevent the approval and launch of Relday and our other product candidates, such as ZX008.

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

In the United States, there have been a number of legislative and regulatory changes to the healthcare system in ways that could affect our future results of operations and the future results of operations of our customers. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established a new Part D prescription drug benefit, which became effective January 1, 2006. Under the prescription drug benefit, Medicare beneficiaries can obtain prescription drug coverage from private sector plans that are permitted to limit the number of prescription drugs that are covered in each therapeutic category and class on their formularies. If 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, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the PPACA, was signed into law, 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 methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as

a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability;

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- 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. Manufacturers are required to report such data to the Centers for Medicare & Medicaid Services, or CMS, by the 90th day of each calendar year;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- 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 has authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and
- establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

There have been judicial and Congressional challenges to certain aspects of the PPACA, and we expect there will be additional challenges and amendments to the PPACA in the future, particularly in light of the new presidential administration and U.S. Congress. In addition, Congress could consider subsequent legislation to replace repealed elements of the PPACA. At this time, the full effect that the PPACA and any subsequent legislation would have on our business remains unclear.

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 2% per fiscal year, which went into effect on April 1, 2013, and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012 which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Recently, there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. These new laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations. Given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform, the cost of prescription drugs and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to market our product candidates, if approved, and generate revenues. In addition, legislation has been introduced in Congress that, if enacted, would permit more widespread importation or re-importation of pharmaceutical products from foreign countries into the United States, including from countries where the products are sold at lower prices than in the United States. Such legislation, or similar regulatory changes, could lead to a decision to decrease our prices to better compete, which, in turn, could adversely affect our business, results of operations, financial condition and prospects. Alternatively, in response to legislation such as this, we might elect not to seek approval for or market our products in foreign jurisdictions in order to minimize the risk of re-importation, which could also reduce the revenue we generate from sales of any approved product candidates. 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.

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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 do not 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, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are 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, in cash or in kind, 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, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- federal "sunshine" requirements that require drug manufacturers to report and disclose any "transfer of value" made or distributed to physicians and teaching hospitals, and any investment or ownership interests held by such physicians and their immediate family members. Manufacturers are required to report data to the government by the 90th day of each calendar year; 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. In addition, recent health care reform legislation has strengthened these laws. For example, the PPACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

In addition, there has been a recent trend of increased state regulations that require drug manufacturers to file reports with states regarding pricing and marketing information, and require the tracking and reporting of gifts, compensation and other remuneration to physicians. Certain states mandate implementation of commercial compliance programs to ensure compliance with these laws and impose restrictions on drug manufacturer marketing practices and tracking and reporting of gifts, compensation and other remuneration to physicians. The shifting commercial compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions

with different compliance and/or reporting requirements increases the possibility that a healthcare company may be found out of compliance of one or more of the requirements.

To the extent that any product we make is sold in a foreign country, we may be subject to similar foreign laws and regulations. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in U.S. federal or state health care programs, and the curtailment or restructuring of our operations. Any

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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 any 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 depends in large part on obtaining and maintaining patent, trademark and trade secret protection of our current product candidates, including ZX008 and Relday, and any future product candidates, their respective components, formulations, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing 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-licensed certain intellectual property for Relday from Durect. We rely on this licensor 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 agreement with Durect, we cannot be certain that such activities by 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. 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 non-infringement, 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 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. We also in-licensed certain data from a continuing, long-term, open-label study in 15 Dravet syndrome patients, as well as certain intellectual property related to fenfluramine for the treatment of Dravet syndrome from the Universities of Antwerp and Leuven in Belgium, or the Universities.

Prior to the recent issuance of U.S. Patent 9,549,909 on January 24, 2017, we owned no issued patents covering ZX008. There is no guarantee that any of our pending applications will issue as patents. The patents covering the active pharmaceutical ingredient, or API, in ZX008 have expired and therefore it is not subject to patent protection. The initial applications covering methods of treatment using ZX008 were acquired by us and not written by our attorneys. Neither we nor our licensors had control over the drafting and initial prosecution of these applications. Further, the counsel previously handling the matter might not have given the same attention to the drafting and prosecution to these applications as we would have if we had been the owners and originators of the applications and had control over the drafting and prosecution. In addition, the former counsel handling the matter may not have been completely familiar with U.S. patent law or the patent law in various countries, possibly resulting in inadequate disclosure and/or filing of applications at times which do not meet appropriate priority requirements. The named inventors on the pending applications and others involved in the protection of the intellectual property related to ZX008 did not and may still not have sufficient knowledge relating to preferred procedures related to the protection of intellectual property. They published papers which adversely affected our rights. Although they have been advised with respect to procedures going forward, we cannot directly control their actions. All of these factors and others

could result in the inability to obtain the issuance of these applications in the United States or elsewhere in the world. 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 U.S. Patent and Trademark Office, or USPTO, and Congress have recently made significant changes to the patent system. There have been three U.S. Supreme Court decisions that now show a trend of the Supreme Court which is distinctly negative on patents. The trend of these decisions along with

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resulting changes in patentability requirements being implemented by the USPTO could make it increasingly difficult for us to obtain and maintain patents on our products. 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 the same or similar to the pharmaceutical compounds used in our product candidates but that are not covered by the claims of our patents or our in-licensed patents;
- the APIs in ZX008 and Relday are, or may 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 our owned or in-licensed U.S. patents or patent applications are not Orange-Book eligible;
- it is possible that there are dominating patents to ZX008 or Relday of which we are not aware;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' inventions, as the case may be, or parts of our or their inventions of which we or they are not aware;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- it is possible that the U.S. government may exercise any of its statutory rights to our owned or in-licensed patents or applications that were developed with government funding;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our system or products or our system 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 administrative 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, state laws in the Unites States vary, and their courts as well as 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.

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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.

Our existing licenses with Durect and the Universities impose various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate the license, in which event we would not be able to develop or market the affected products. If we lose such license rights, our business, results of operations, financial condition and prospects may be materially adversely affected. We may enter into additional licenses in the future and if we fail to comply with obligations under those agreements, we could suffer similar consequences.

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

If we or our collaborators or licensors choose to go to court to stop a third party from using the inventions claimed in our owned or in-licensed patents, that third party may ask the court to rule that the patents are not infringed, 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 or other post-grant proceeding before the USPTO, or during litigation, under the revised criteria which make it more difficult to obtain patents. We are not entitled to control the manner in which Durect may defend certain of the intellectual property that is licensed to us, either in a reexamination or other post-grant proceeding before the USPTO, or during the litigation, and it is possible that their defense activities may be less vigorous than had we conducted the defense ourselves.

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, 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 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 ZX008 and Relday. As the medical device, biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert that our products or product candidates infringe the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of medical devices, drugs, products or their methods of use. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our products, product candidates, technology or methods.

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 candidate or proprietary technologies. Because some patent applications in the

United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until eighteen months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our product candidates 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

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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 USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such proceedings may be decided against us 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. In addition, 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 USPTO 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, Australian Patent Office or other jurisdictions 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 our efforts would be unsuccessful. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. These lawsuits are costly and could adversely affect our results of operations and divert the attention of managerial and technical personnel. There is a risk that a court would decide that we or our commercialization partners are infringing the third party's patents and would order us or our partners to stop the activities covered by the patents. In addition, there is a risk that a court will order us or our partners to pay the other party damages for having violated the other party's patents.

If a third-party's patent was found to cover our 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 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 order prohibiting us from selling or licensing the product unless the third party licenses its patent rights to us, which it is not required to do;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and/or grant cross-licenses to intellectual property rights for our products; and
- redesigning our products or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

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

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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 USPTO 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 USPTO 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 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 our product candidates, if approved by the FDA or other regulatory authorities, 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, 2016, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price of $7.33 to a high sale price of $14.60. 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:

- FDA or international regulatory actions and whether and when we receive regulatory approval for any of our product candidates;
- the development status of ZX008, Relday or any of our other product candidates, including the results from our clinical trials;
- variations in the level of expenses related to ZX008, 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;

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

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 success and costs of our ZX008, 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:

- variations in the level of development and/or regulatory expenses related to ZX008, Relday or other development programs;
- results of clinical trials for ZX008, Relday or any other of our product candidates;
- any intellectual property infringement lawsuit in which we may become involved;
- the level of underlying demand for any of our product candidates that may receive regulatory approval;
- our ability to control production spending and underutilization of production capacity;
- 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 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.

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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, 2016, 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.

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, 2016, we had 24,813,169 shares of common stock outstanding. The majority of these shares 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 1,973,025 shares of our common stock issuable upon the exercise of the warrants we issued in July 2012, which warrants became exercisable on July 27, 2013 at an exercise price of $20.00 per share (subject to restrictions on exercise set forth in such warrants). As of December 31, 2016, warrants were still outstanding to exercise 1,901,918 shares of this registered common stock, 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. 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;

- 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

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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. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. In addition, our ability to pay dividends is currently restricted by the terms of the credit facility with Oxford and SVB. 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. We are subject to the reporting requirements of the Exchange Act, 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. We currently do not have an internal audit function, and we may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Implementing any appropriate changes to our internal controls may require specific compliance training for our directors, officers and employees, entail substantial costs to modify our existing accounting systems, and take a significant period of time to complete. Such changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate consolidated financial statements or other reports on a timely basis, could increase our operating costs and could materially impair our ability to operate our business. Moreover, effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent fraud. If we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal controls that are deemed to be material weaknesses, the

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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

None.

Item 2. Properties

Our corporate headquarters, which includes research and development and business operations and executive offices, is located in Emeryville, California. It consists of approximately 22,000 square feet of office and laboratory space under an operating lease that expires in 2022. We also lease limited office space in Maidenhead, United Kingdom under a month-to-month arrangement. 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.

We believe that our facilities are adequate to meet our needs for the immediate future, and that, should it be needed, suitable additional space will be available to accommodate expansion of our operations.

Item 3. Legal Proceedings

We are currently not a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not Applicable.

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PART II

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

Market Information

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

	High	Low
2016		
Fourth Quarter	$13.70	$7.50
Third Quarter	$11.59	$7.74
Second Quarter	$11.98	$7.33
First Quarter	$14.60	$7.90
2015		
Fourth Quarter	$16.56	$10.41
Third Quarter	$21.65	$12.20
Second Quarter	$14.32	$10.56
First Quarter	$15.68	$9.36

Holders of Common Stock

According to the records of our transfer agent, there were 22 holders of record of our common stock on March 6, 2017. Because many of such shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

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Performance Graph

The following stock performance graph illustrates a comparison of the total cumulative stockholder return on our common stock over the five year period ended December 31, 2016 to the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of $100 on December 31, 2011, and that all dividends were reinvested. The comparisons in the graph are required by the Securities and Exchange Commission and are not intended to forecast or be indicative of possible future performance of our common stock.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. We expect to retain available cash to finance ongoing operations and the potential growth of our business. Any future determination to pay dividends on our common stock will be at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant. In addition, our ability to pay dividends is currently restricted by the terms of the credit facility with Oxford Finance LLC and Silicon Valley Bank.

Equity Compensation Plan Information

See Part III, Item 12, “Security Ownership of Certain Beneficial Owners and Management and related Stockholder Matters” for information regarding securities authorized for issuance under equity compensation plans.

Recent Sales of Unregistered Securities

None.

Issuer Repurchases of Equity Securities

None.

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Item 6. Selected Financial Data.

The following table summarizes certain of our selected financial data. The selected statement of operations data for the years ended December 31, 2016, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016 and 2015 should be read in conjunction with the audited financial statements and related notes, Management's Discussion and Analysis of Financial Condition and Results of Operations and other financial information presented elsewhere in this Form 10-K. The selected statements of operations data for the years ended December 31, 2013 and 2012 and the consolidated balance sheet data as of December 31, 2014, 2013 and 2012 have been derived from audited financial statements not included herein.

Our historical results for any prior period do not necessarily indicate our results to be expected for any future period.

	Year Ended December 31,				
	2016	2015	2014	2013	2012
	(In Thousands, Except Per Share Amounts)				
Statement of Operations Data					
Revenue:					
Contract manufacturing revenue [1]	$28,525	$24,369	$15,392	$—	$—
Net product revenue	—	—	9,840	31,699	35,826
Contract revenue	—	—	—	—	8,462
Service and other product revenue	325	2,813	3,715	1,313	38
Total revenue	28,850	27,182	28,947	33,012	44,326
Operating expenses:					
Cost of contract manufacturing [1]	22,173	22,356	14,342	—	—
Cost of goods sold	—	—	5,263	21,241	19,496
Royalty expense	295	345	591	1,242	1,353
Research and development	41,840	27,860	11,893	8,372	9,871
Selling, general and administrative	26,996	26,347	34,639	46,218	47,562
Change in fair value of contingent consideration [2]	1,800	(2,000)	—	—	—
Restructuring costs	—	—	—	876	—
Impairment charges [3][10]	8,431	—	838	—	—
Net gain on sale of business [1]	—	—	(79,980)	—	—
Total operating expenses (income)	101,535	74,908	(12,414)	77,949	78,282
Loss from operations	(72,685)	(47,726)	41,361	(44,937)	(33,956)
Other income (expense):					
Interest expense, net	(2,382)	(2,959)	(3,070)	(6,592)	(10,260)
Loss on sale of investments [4]	—	(5,746)	—	—	—
Loss on extinguishment of debt[5]	—	—	(1,254)	—	—
Change in fair value of common stock warrant liabilities [6]	5,387	(1,103)	25,332	(21,927)	11,811
Change in fair value of embedded derivatives [7]	—	—	(14)	759	(147)
Other income (expense)	46	(71)	(784)	96	(1,354)
Total other income (expense)	3,051	(9,879)	20,210	(27,664)	50
(Loss) income from continuing operations before income taxes	(69,634)	(57,605)	61,571	(72,601)	(33,906)
Income tax benefit (expense) [8]	948	15,901	(84)	—	(5)
Net (loss) income from continuing operations	$(68,686)	$(41,704)	$61,487	$(72,601)	$(33,911)
Net (loss) income from discontinued operations	(1,021)	67,848	(52,900)	(8,255)	(13,475)
Net (loss) income	$(69,707)	$26,144	$8,587	$(80,856)	$(47,386)
Net (loss) income per share, continuing operations, basic[9]	$(2.77)	$(1.94)	$3.45	$(5.35)	$(3.37)
Net (loss) income per share, continuing operations, diluted[9]	$(2.77)	$(1.94)	$3.44	$(5.35)	$(3.37)

(1) Amounts in connection with our sale of Sumavel DosePro to Endo. See Note 6 to our consolidated financial statements included in this Form 10-K.

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(2) Represents change in contingent consideration liability acquired with purchase of Zogenix International Limited. See Note 7 to our consolidated financial statements included in this Form 10-K.

(3) Represents the impairment of long-lived assets in connection with the sale of our Sumavel DosePro business in 2014. See Note 2 to our consolidated financial statements included in this Form 10-K.

(4) Represents loss on sale of stock acquired in connection with sale of Zohydro ER business. See Note 5 to our consolidated financial statements included in this Form 10-K.

(5) Loss recognized upon early termination of the financing agreement entered into with Healthcare Royalty Partners.

(6) Represents change in fair value of warrant liabilities. See Note 2 and Note 10 to our consolidated financial statements included in this Form 10-K.

(7) Represents change in fair value of embedded derivatives related to the financing agreement entered into with Healthcare Royalty Partners.

(8) Benefit related to sale of Zohydro ER. See Note 13 to our consolidated financial statements included in this Form 10-K.

(9) See Note 2 to our consolidated financial statements included in this Form 10-K 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.

(10) See Note 6 for additional information related to the circumstances that resulted in an impairment charge in 2016.

	As of December 31,				
	2016	2015	2014	2013	2012
	(In Thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments[11]	$91,551	$155,349	$42,205	$72,021	$41,228
Working capital	99,604	154,517	33,741	34,981	30,179
Total assets	231,505	305,822	202,835	108,288	80,297
Long-term debt, less current portion	18,824	15,899	21,703	28,802	28,481
Accumulated deficit	(445,223)	(375,516)	(401,660)	(410,247)	(329,391)
Total stockholders' equity	120,756	182,760	55,279	18,426	14,473

(11) Cash balance as of December 31, 2015 included approximately $92.0 million in net proceeds from a public offering.

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

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with "Selected Financial Data" and our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including, but not limited, to those set forth under "Item 1A — Risk Factors" and elsewhere in this Annual Report on Form 10-K.

Overview

We are a pharmaceutical company committed to developing and commercializing central nervous system, or CNS, therapies that address specific clinical needs for people living with orphan and other CNS disorders who need innovative treatment alternatives to help them improve their daily functioning. Our current primary area of focus is epilepsy and related seizure disorders.

We have worldwide development and commercialization rights to ZX008, our lead product candidate. ZX008 is a low-dose fenfluramine for the treatment of seizures associated with Dravet syndrome. Dravet syndrome is a rare and catastrophic form of pediatric epilepsy with life threatening consequences for patients and for which current treatment options are very limited. ZX008 has received orphan drug designation in the United States and European Union, or the EU, for the treatment of Dravet syndrome. In January 2016, we received notification of Fast Track designation from the U.S. Food and Drug Administration, or FDA, for ZX008 for the treatment of Dravet syndrome. We initiated Phase 3 clinical trials in North America (Study 1501) in January 2016 and in Europe and Australia in June 2016 (Study 1502). Additionally, we initiated the enrollment of patients for our study of Dravet syndrome patients who are poor responders to a stiripentol treatment regime in September 2016 in Europe and in February 2017 initiated the Phase 3 clinical efficacy portion of this study (Study 1504), which now includes sites in in the U.S. and Canada in addition to Europe. In January 2017, we announced our plan to report top-line results from studies 1501 and 1502 via a merged study analysis approach whereby top-line results from the first half of the combined patient population of studies 1501 and 1502 would be reported initially as "Study 1". We expect to report top-line results from Study 1 in the third quarter of 2017 and additional Phase 3 data to be released over the remainder of year.

Beginning in first quarter of 2016, we funded an open-label dose-ranging twenty-patient investigator initiated study in patients with LGS. In December 2016, we presented initial data from an interim analysis of the first 13 patients to have completed at least 12 weeks of this Phase 2 open-label, dose-finding study at the American Epilepsy Society Meeting. These data demonstrated that ZX008 provided clinically meaningful improvement in major motor seizure frequency in patients with severely refractory LGS, despite not attempting to dose to maximal efficacy as per protocol, with seven out of 13 patients (54%) achieving at least a 50% reduction in the number of major motor seizures. In addition, ZX008 was generally well tolerated. This data indicate that ZX008 has the potential to be a safe and effective adjunctive treatment for LGS. Based on the strength of the LGS data generated, we plan to submit an investigational new drug, or IND, application in the first quarter of 2017 and initiate a Phase 3 program for ZX008 in LGS in the second half of 2017. In February 2017, ZX008 received orphan drug designation for the treatment of LGS in the EU.

We have an additional product candidate, Relday™ (risperidone once-monthly long-acting injectable) for the treatment of schizophrenia. Relday is a proprietary, long-acting injectable formulation of risperidone. Risperidone is used to treat the symptoms of schizophrenia and bipolar disorder in adults and teenagers 13 years of age and older. We completed the Phase 1 program for Relday in 2015, and efforts to secure a global strategic development and commercialization partner for Relday are ongoing.

Sale of Sumavel DosePro Business and Contract Manufacturing Supply Agreement

Divestiture

On May 16, 2014, the Company completed the sale of its Sumavel DosePro business to Endo International plc, or Endo, which included registered trademarks, regulatory and all rights to market, sell and distribute Sumavel DosePro

under the trademark and commercialization rights under a specified subset of our technology patents. We retained all rights to the DosePro technology patents and know-how for use with other products. We received $85.0 million in cash, subject to an escrow holdback of $8.5 million, and $4.6 million in cash for the purchase of Sumavel DosePro finished goods inventory on hand at our standard cost. The escrow period expired in May 2015.

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As part of the transaction, we entered into a supply agreement with Endo Ventures Limited for the exclusive right, and contractual obligation, to manufacture and supply Sumavel DosePro to Endo. Endo agreed to purchase all Sumavel DosePro from the Company at cost, plus a 2.5% mark-up and reimburse us for the royalty obligations due Aradigm Corporation on sales of Sumavel DosePro. The agreement provides for an initial term of eight years. To support our Sumavel DosePro manufacturing operations, Endo provided us with an interest-free working capital advance of $7.0 million under a promissory note (see Note 9). The working capital advance is collateralized by liens on materials and unreleased finished Sumavel DosePro inventory and matures upon termination of the supply agreement.

Pending Termination of Contract Manufacturing Supply Agreement

We and Endo have recently entered into a letter agreement acknowledging Endo's decision to have us discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. We expect to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time.

Sale of Zohydro ER Business

On March 10, 2015, we entered into an asset purchase agreement with Pernix Ireland Limited and Pernix Therapeutics, or collectively, Pernix, whereby we agreed to sell our Zohydro ER business to Pernix, and on April 24, 2015, we completed the sale to Ferrimill, an Irish corporation and subsidiary of Pernix, as a substitute purchaser. The divested Zohydro ER business included the registered patents and trademarks, certain contracts, the new drug application, or NDA, and other regulatory approvals, documentation and authorizations, the books and records, marketing materials and product data relating to Zohydro ER. We received consideration of $80.0 million in cash, $10.0 million of which has been deposited in escrow to fund potential indemnification claims for a period of 12 months, and $10.6 million in Pernix Therapeutics common stock. Further, Ferrimill purchased $0.9 million of Zohydro ER inventory from us. We agreed to indemnify the purchaser for certain intellectual property matters up to an aggregate amount of $5.0 million.

In addition to the cash payment paid at closing, we are eligible to receive cash payments of up to $283.5 million based on the achievement of certain regulatory and sales milestones. As of December 31, 2016, we have not received and do not expect to receive any additional cash payments.

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. We evaluate our estimates and assumptions on an ongoing basis. Our estimates are based on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Actual results could differ from those estimates.

We believe that the assumptions and estimates associated with revenue recognition, the impairment assessments related to goodwill, indefinite-lived intangible assets and other long-lived assets, business combinations, discontinued operations, fair value measurements, clinical trials expense accrual and stock-based compensation have the greatest potential impact on our consolidated financial statements. Therefore, we consider these to be our critical accounting policies and estimates. For further information on all of our significant accounting policies, see Note 2 to our consolidated financial statements included in this Form 10-K.

Revenue Recognition

We historically generated revenue from contract manufacturing, service fees earned on collaborative arrangements and product revenue related to Sumavel DosePro prior to the sale of the business in May 2014. We also generate revenue from the sale of Zohydro ER, which is included in net income (loss) from discontinued operations in the consolidated statement of operations and comprehensive income (loss). 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 (a) our price to the buyer is substantially fixed or determinable at the date of sale, (b) the buyer has paid us, or the buyer is obligated to pay us and the obligation is not

contingent on resale of the product, (c) the buyer's obligation to us would not be changed in the event of theft or physical destruction or damage of the product, (d) the buyer acquiring the product for resale has economic substance apart from that provided by us, (e) we do not have significant obligations for future performance to directly bring about resale of the product by the buyer, and (f) the amount of future returns can be reasonably estimated. We deferred recognition of revenue on product shipments of Zohydro ER until the right of return lapsed, as we were not able to reliably estimate expected returns of the product at the time of shipment given the limited sales and return history of Zohydro ER.

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Revenue arrangements with multiple elements are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the customer. The consideration received is allocated among the separate units based on their respective fair values, and the applicable revenue recognition criteria are applied to each of the separate units. The application of the multiple element guidance requires subjective determinations, and requires us to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (1) the delivered item(s) has value to the customer on a stand-alone basis and (2) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in our control. In determining the units of accounting, we evaluate certain criteria, including whether the deliverables have stand-alone value, based on the consideration of the relevant facts and circumstances for each arrangement. In addition, we consider whether the buyer can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s), and whether there are other vendors that can provide the undelivered element(s).

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria, as described above, are applied to each of the separate units of accounting in determining the appropriate period or pattern of recognition. We determine the estimated selling price for deliverables within each agreement using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or management’s best estimate of selling price, or BESP, if neither VSOE nor TPE is available. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs.

Contract Manufacturing Revenue

We record deferred revenue when we receive payments in advance of the delivery of products or the performance of services. As part of the sale of our Sumavel DosePro business in May 2014 to Endo, we allocated a portion of the total consideration received as payments in advance of the delivery of product under a supply agreement that was concurrently entered into with the asset sale. We initially recorded $9.1 million of deferred revenue, which is being recognized as contract manufacturing revenue when earned on a “proportional performance” basis as product is delivered. As a result, a portion of our contract manufacturing revenue reported includes deferred revenue from this transaction being recognized when earned.

Under the proportional performance method, revenue recognition is based on products delivered to date relative to the total expected products to be delivered over the performance period as this is considered to be representative of the delivery of service under the arrangement. The performance period under the supply agreement was initially estimated to be 8 years, the minimum contractual term under the agreement. Changes in estimates of total expected products to be delivered or service obligation time period are accounted for prospectively as a change in estimate. In the fourth quarter of 2016, as a result of Endo’s intent to terminate the supply agreement by the first half of 2017, we revised our estimates of total expected products to be delivered under the arrangement and recognized revenue for the inception-to-date effect of the change in estimate. The effect of this change in estimate resulted in an increase to 2016 revenue by $4.9 million.

In addition, we follow the authoritative accounting guidance when reporting revenue as gross when we act as a principal versus reporting revenue as net when we act as an agent. For transactions in which we act as a principal, have discretion to choose suppliers, bear credit risk and perform a substantive part of the services, revenue is recorded at the gross amount billed to a customer and costs associated with these reimbursements are reflected as a component of cost of sales for contract manufacturing services.

Business Combinations

Under the acquisition method of accounting, we allocate the fair value of the total consideration transferred to the tangible and identifiable intangible assets acquired and liabilities assumed based on their estimated fair values on the date of acquisition. The fair values assigned, defined as the price that would be received to sell an asset or paid to

transfer a liability in an orderly transaction between willing market participants, are based on estimates and assumptions determined by management. We record the excess consideration over the aggregate fair value of tangible and intangible assets, net of liabilities assumed, as goodwill. These valuations require us to make significant estimates and assumptions, especially with respect to intangible assets.

In connection with some of our acquisitions, additional contingent consideration is earned by the sellers upon completion of certain future performance milestones. In these cases, a liability is recorded on the acquisition date for an estimate of the acquisition date fair value of the contingent consideration by applying the income approach utilizing variable inputs such as anticipated future cash flows, risk-free adjusted discount rates, and nonperformance risk. Any change in the fair value of the contingent consideration subsequent to the acquisition date is recognized in other income (expense) in our

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consolidated statements of operations. Changes in the fair value of the contingent consideration obligations can result from adjustments to the discount rates, payment periods and adjustments in the probability of achieving future development steps, regulatory approvals, market launches, sales targets and profitability. These fair value measurements represent Level 3 measurements, as they are based on significant inputs not observable in the market. See Note 2 for further information regarding changes recorded to contingent consideration.

Management typically uses the discounted cash flow method to value our acquired intangible assets. This method requires significant management judgment to forecast future operating results and establish residual growth rates and discount factors. The estimates we use to value and amortize intangible assets are consistent with the plans and estimates that we use to manage our business and are based on available historical information and industry estimates and averages. If the subsequent actual results and updated projections of the underlying business activity change compared with the assumptions and projections used to develop these values, we could experience impairment charges.

Goodwill and Indefinite-Lived Intangibles

Goodwill and indefinite-lived intangible assets are reviewed for impairment at least annually in the fourth quarter, and more frequently if events or other changes in circumstances indicate that the carrying amount of the assets may not be recoverable. Impairment of goodwill and indefinite-lived intangibles is determined to exist when the fair value is less than the carrying value of the net assets being tested.

Goodwill

We determined that we have only one operating segment and reporting unit under the criteria in ASC 280, Segment Reporting. Accordingly, our review of goodwill impairment indicators is performed at the entity-wide level. The goodwill impairment test consists of a two-step process. The first step of the goodwill impairment test, used to identify potential impairment, compares the fair value of the reporting unit to its carrying value. If the fair value of the reporting unit exceeds its carrying amount, goodwill of the reporting unit is considered not impaired, and the second step of the impairment test is not required. We use our market capitalization as an indicator of fair value. We believe that since our reporting unit is publicly traded, the ability of a controlling shareholder to benefit from synergies and other intangible assets that arise from control might cause the fair value of our reporting unit as a whole to exceed our market capitalization. However, we believe that the fair value measurement need not be based solely on the quoted market price of an individual share of our common stock, but also can consider the impact of a control premium in measuring the fair value of its reporting unit. Should our market capitalization be less than our total stockholder's equity as of our annual test date or as of any interim impairment testing date, we would also consider market comparables, recent trends in our stock price over a reasonable period and, if appropriate, use an income approach (discounted cash flow) to determine whether the fair value of our reporting unit is greater than our carrying amount. If we were to use an income approach, we would establish a fair value by estimating the present value of our projected future cash flows expected to be generated from our business. The discount rate applied to the projected future cash flows to arrive at the present value would be intended to reflect all risks of ownership and the associated risks of realizing the stream of projected future cash flows. Our discounted cash flow methodology would consider projections of financial performance for a period of several years combined with an estimated residual value. The most significant assumptions we would use in a discounted cash flow methodology are the discount rate, the residual value and expected future revenues, gross margins and operating costs, along with considering any implied control premium. The second step, if required, compares the implied fair value of the reporting unit goodwill with the carrying amount of that goodwill. If the carrying amount of the reporting unit's goodwill exceeds its implied fair value, an impairment charge is recognized in an amount equal to that excess. Implied fair value is the excess of the fair value of the reporting unit over the fair value of all identified assets and liabilities. Based on our goodwill impairment tests for 2016, 2015 and 2014, we concluded that the fair value of the reporting unit exceeded the carrying value and no impairment existed.

Indefinite-Lived Intangibles

Our indefinite-lived intangible asset consists of in-process research and development (IPR&D) acquired in a business combination (see Note 7) that are used in research and development activities but have not yet reached technological feasibility, regardless of whether they have alternative future use. The primary basis for determining the technological

feasibility or completion of these projects is obtaining regulatory approval to market the underlying products in an applicable geographic region. We classify in-process research and development acquired in a business combination as an indefinite-lived intangible asset until the completion or abandonment of the associated research and development efforts. Upon completion of the associated research and development efforts, we will determine the useful life of the technology and begin amortizing the assets to reflect their use over their remaining lives. Upon permanent abandonment, we would write-off the remaining carrying amount of the associated in-process research and development intangible asset. We use the income approach to determine the fair value of our IPR&D. This approach calculates fair value by estimating the after-tax cash flows attributable to an in-process project over its useful life and then discounting these after-tax cash flows back to a present value. We base our revenue assumptions on estimates of relevant market sizes, expected market growth rates, expected trends in technology and expected

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levels of market share. In arriving at the value of the in-process projects, we consider, among other factors: the in-process projects' stage of completion; the complexity of the work completed as of the acquisition date; the costs already incurred; the projected costs to complete; the contribution of other acquired assets; the expected regulatory path and introduction dates by region; and the estimated useful life of the technology. We apply a market-participant risk-adjusted discount rate to arrive at a present value as of the date of acquisition. Based on our IPR&D impairment tests for 2016, 2015 and 2014, we concluded that the fair value of the indefinite-lived intangible asset exceeded the carrying value and no impairment existed.

For asset purchases outside of business combinations, we expense any purchased research and development assets as of the acquisition date if they have no alternative future uses.

Impairment of Long-Lived Assets

We evaluate long-lived assets, consisting of property and equipment, periodically for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset (group) may not be recoverable. If the sum of our estimated undiscounted future cash flows is less than the asset's (group) carrying value, we then estimated the fair value of the asset (group) to measure the impairment, if any.

We and Endo have recently entered into a letter agreement acknowledging Endo's decision to have us discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. As a result, we performed an analysis to estimate cash flows from equipment used in the production of Sumavel DosePro. Based on this analysis, we determined its fair value exceeded the carrying value by $6.4 million and recognized an impairment charge for long-lived assets in the fourth quarter of 2016. No impairment charges for long-lived assets were recorded in 2015.

Discontinued Operations

On April 24, 2015, we sold the Zohydro ER business. As a result of this sale, our Zohydro ER activity has been excluded from continuing operations for all periods herein and reported as discontinued operations. See Note 5, Sale of Zohydro ER business, for additional information on the divestiture.

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, such as our acquired in-process research and development, contingent purchase consideration and warrants for common stock 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.

Research and Development Expense and Accruals

Research and development costs include personnel-related costs, outside contracted services including clinical trial costs, facilities costs, fees paid to consultants, milestone payments prior to FDA approval, license fees prior to FDA approval, professional services, travel costs, dues and subscriptions, depreciation and materials used in clinical trials and research and development. Research and development costs are expensed as incurred unless there is an alternative future use in other research and development projects. 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.

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 estimated time to satisfy the performance criteria, or vesting period, on a straight-line basis. Equity awards issued to non-employees are recorded at their fair value on the grant date

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and are periodically remeasured 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, 2016, 2015 and 2014

Revenue

	Year Ended December 31,			2015 to 2016		2014 to 2015	
(Dollars in thousands)	2016	2015	2014	$ change	% change	$ change	% change
Contract manufacturing revenue	$28,525	$24,369	$15,392	$4,156	17 %	$8,977	58 %
Net product revenue	—	—	9,840	—	— %	(9,840)	(100)%
Service and other product revenue	325	2,813	3,715	(2,488)	(88)%	(902)	(24)%
Total revenue	$28,850	$27,182	$28,947	$1,668	6 %	$(1,765)	(6)%

We recognize contract manufacturing revenue in connection with the supply agreement with Endo. Contract manufacturing revenue includes a portion of deferred revenue recognized under the “proportional performance” method. Prior to the divestiture of our Sumavel DosePro business to Endo, we recognized net product sales upon the shipment of product to wholesale pharmaceutical distributors and retail pharmacies. The increase in contract manufacturing revenue in 2016 as compared to 2015 was primarily due to a change in estimate in the performance period under the proportional performance method. As a result of the impending termination of our contract manufacturing supply agreement with Endo, the performance period and the total expected products to be delivered under the arrangement were revised, which resulted in an increase to 2016 revenue by $4.9 million. Once the termination agreement is finalized, we will no longer have a source of recurring revenue and expect to have limited revenue in the foreseeable future. The increase in contract manufacturing revenue in 2015 as compared to 2014 was primarily due to the inclusion of a full year of contract manufacturing revenue in 2015, while 2014 only included a partial year’s contract manufacturing revenue as the agreement was executed in May 2014.

Net product revenue in 2014 consisted of sale of Sumavel DosePro products, which we divested in May 2014.

Service and other product revenue was comprised primarily of co-promotion fees earned for our Migranal ® Nasal Spray sales efforts under our agreement with Valeant Pharmaceuticals North America LLC until it was terminated in June 2015, as well as adjustments to Sumavel DosePro returns reserves subsequent to the sale of the business in May 2014. For 2016, service and other product revenue resulted from the true-up of reserves to reflect actual Sumavel DosePro returns. For 2015, service and other product revenue were comprised of Migranal co-promotion fees earned through June 2015, $0.5 million received for a contract termination payment and $2.0 million from true-up of reserves to reflect actual returns for product whose return period had lapsed. Service and other product revenue in 2014 was comprised primarily of fees generated by Migranal co-promotion activity.

Cost of Contract Manufacturing and Cost of Goods Sold

	Year Ended December 31,			2015 to 2016		2014 to 2015	
(Dollars in thousands)	2016	2015	2014	$ change	% change	$ change	% change
Cost of contract manufacturing	$22,173	$22,356	$14,342	$(183)	(1)%	$8,014	56 %
Cost of goods sold	$—	$—	$5,263	$—	— %	$(5,263)	(100)%

Costs of contract manufacturing consists primarily of materials, third-party manufacturing costs, freight in and indirect personnel and other overhead costs associated with Sumavel DosePro based on units sold to Endo, as well as the effect of changes in reserves for excess, dated or obsolete commercial inventories and production manufacturing variances. It represents the cost of units recognized as contract manufacturing revenues in the period and the impact of underutilized production capacity and other manufacturing variances. Cost of contract manufacturing in 2016 was flat compared to 2015 while the corresponding contract manufacturing revenue increased. This resulted from a change in estimate under the proportional performance method of revenue recognition, which had no impact to cost of contract manufacturing. The increase in cost of contract manufacturing in 2015 compared to 2014 corresponds to the increase in units delivered.

Cost of goods sold consisted primarily of materials, third-party manufacturing costs, freight in and indirect personnel and other overhead costs associated with sales of Sumavel DosePro based on product dispensed to units sold to patients until the

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sale of the business to Endo in May 2014. Subsequent to the divestiture, we no longer sold the Sumavel DosePro commercially and manufacturing costs under the supply agreement were recorded as cost of contract manufacturing.

Royalty Expense

	Year Ended December 31,			2015 to 2016		2014 to 2015	
(Dollars in thousands)	2016	2015	2014	$ change	% change	$ change	% change
Royalty expense	$295	$345	$591	$(50)	(14)%	$(246)	(42)%

Prior to our divestiture of the Sumavel DosePro business in May 2014, we incurred royalty expense on product sales of Sumavel DosePro, either by us or one of our licensees. Royalty expense incurred subsequent to our divestiture represent the amortization of a royalty prepayment over the contractual term to supply Sumavel DosePro to Endo. In the fourth quarter of 2016, approximately $2.0 million of unamortized prepaid royalties were written off as a result of the impending termination of our supply agreement and were included in impairment charges in operating expense.

Research and Development Expenses

	Year Ended December 31,			2015 to 2016		2014 to 2015	
(Dollars in thousands)	2016	2015	2014	$ change	% change	$ change	% change
Research and development	$41,840	$27,860	$11,893	$13,980	50 %	$15,967	134 %

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 program. We recognize the expenses associated with the services provided by CROs based on the percentage complete 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.

	Year Ended December 31,		
	2016	2015	2014
	(In Thousands)		
Research and development expenses:			
ZX008	$29,133	$10,782	$391
Relday	439	9,625	5,515
Other (1)	12,268	7,453	5,987
Total	$41,840	$27,860	$11,893

(1) Other research and development expenses include employee and infrastructure resources that are not tracked on a program-by-program basis.

The increase in ZX008 expense in 2016 as compared to 2015 was primarily attributable to increased development activities related to our Phase 3 clinical trials in Dravet syndrome and funding of an open-label dose-ranging twenty-patient investigator initiated study in patients with LGS. In addition, 2016 research and development expense included a $1.5 million asset acquisition for a project that had not yet reached technological feasibility, was deemed to have no alternative use, and was immediately expensed. The increase in ZX008 expense in 2015 compared to 2014 was due to the timing of the acquisition of ZX008, which was in October 2014. The decrease in Relday expense in 2016 compared to 2015 reflects our decision to seek a strategic partner for the ongoing clinical development of Relday

and focus our resources on ZX008, our lead product candidate.

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The increase in Relday expense in 2015 compared to 2014 was attributable to costs incurred to complete a Phase 1b multi-dose parallel group clinical trial for Relday in 2015.

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 anticipate research and development costs in 2017 to increase over our 2016 levels as we plan to submit an investigational new drug, or IND, application in the first quarter of 2017 and initiate a Phase 3 program for ZX008 in LGS in the second half of 2017 in addition to our ongoing Phase 3 clinical trials for ZX008.

Selling, General and Administrative Expenses

	Year Ended December 31,			2015 to 2016		2014 to 2015	
(Dollars in thousands)	2016	2015	2014	$ change	% change	$ change	% change
Selling expense	$6,002	$3,935	$13,872	$2,067	53 %	$(9,937)	(72)%
General and administrative expense	20,994	22,412	20,767	(1,418)	(6)%	1,645	8 %
Total	$26,996	$26,347	$34,639	$649	2 %	$(8,292)	(24)%

Selling expense consists primarily of salaries and benefits of sales and marketing management and sales representatives, marketing and advertising costs, service fees under our co-promotion agreement and product sample costs. The increase in selling expense in 2016 as compared to 2015 resulted from our increased spend on marketing infrastructure, marketing research and participation in industry conferences raising awareness of our lead product candidate ZX008 and its potential to treat LGS. The decrease in selling expense in 2015 compared to 2014 was due to the sale of our Sumavel DosePro business in May 2014, which had a dedicated sales force.

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 professional fees for legal, public relations, patent protection and accounting services.

The decrease in general and administrative expense in 2016 compared to 2015 was primarily attributable to lower personnel-related expense due to reduced headcount. The increase in general and administrative expense in 2015 compared to 2014 was primarily the result of additional professional service fees incurred for patent defense of $0.9 million and additional rent expense of $0.6 million for the expansion of our San Diego facility in the second half of 2014.

We anticipate that our selling, general and administrative expense in 2017 to be comparable to our 2016 levels.

Change in Fair Value of Contingent Consideration, Impairment Charges and Net Gain on Sale of Business

	Year Ended December 31,			2015 to 2016		2014 to 2015	
(Dollars in thousands)	2016	2015	2014	$ change	% change	$ change	% change
Change in fair value of contingent consideration	$1,800	$(2,000)	—	$3,800	n/m	$(2,000)	— %
Impairment charges	$8,431	$—	838	$8,431	— %	$(838)	(100)%
Net gain on sale of business	$—	$—	(79,980)	$—	— %	$79,980	(100)%

The contingent consideration liability resulted from our acquisition of Zogenix International Limited in October 2014 where we agreed to pay additional consideration if certain future regulatory and commercial milestones are met for ZX008. The changes in the fair value of the contingent acquisition consideration payable were primarily attributable to changes in the estimated time frame necessary to achieve the developmental milestones, changes in market interest rates as well as the passage of time.

As a result of the sale of the Sumavel DosePro business to Endo, we recorded an impairment charge of $0.8 million in 2014 for the disposal of construction in progress equipment that will no longer be placed into service. In the fourth quarter of 2016, as a result of Endo’s intention to discontinue Sumavel DosePro (See Note 6), we recorded impairment charges of $8.4 million consisting of $6.4 million for long-lived assets associated with the production of Sumavel DosePro and $2.0 million in prepaid royalties.

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In 2014, we recognized a net gain on sale of $80.0 million in the consolidated statements of operations in connection with the sale of our Sumavel DosePro business within operating income. The divestiture did not qualify for discontinued operations presentation based on the accounting guidance in effect in 2014.

Other income (expense)

(Dollars in thousands)	Year Ended December 31, 2016	2015	2014	2015 to 2016 $ change	2015 to 2016 % change	2014 to 2015 $ change	2014 to 2015 % change
Interest income	$443	$101	$20	$342	339 %	$81	405 %
Interest expense	$(2,825)	$(3,060)	$(3,090)	$235	(8)%	$30	(1)%
Loss on sale of short-term investments	$—	$(5,746)	$—	$5,746	(100)%	$(5,746)	— %
Loss on extinguishment of debt	$—	$—	$(1,254)	$—	— %	$1,254	(100)%
Change in fair value of warrant liabilities	$5,387	$(1,103)	$25,332	$6,490	n/m	$(26,435)	n/m
Change in fair value of embedded derivatives	$—	$—	$(14)	$—	— %	$14	(100)%
Other income (expense)	$46	$(71)	$(784)	$117	n/m	$713	(91)%
Total other income (expense)	$3,051	$(9,879)	$20,210	$12,930	n/m	$(30,089)	n/m

n/m—not meaningful

Interest Income

Interest income increased in 2016 as compared to 2015. The increase is from interest earned from higher average cash and cash equivalents balances resulting from proceeds of our public offering in August 2015. Interest income increased in 2015 as compared to 2014. The increase is from interest earned from higher average cash and cash equivalents balances resulting from proceeds of our Zohydro business divestiture in April 2015 and our public offering in August 2015.

Interest Expense

Interest expense decreased slightly in 2016 as compared to 2015. In 2016, interest expense was incurred primarily in connection with our term debt and amortization of imputed interest on our interest-free working capital advance from Endo. In 2016, we refinanced out term debt and extended its maturity from its original maturity date of December 1, 2018 to July 1, 2020. In 2015, interest expense relates to our term debt, working capital advance from Endo, as well as our revolving line of credit for a portion of the year. In 2014, interest expense was incurred in connection with our Healthcare Royalty financing agreement, which was terminated on May 16, 2014, and amortization of the related imputed interest on our interest-free working capital advance from Endo.

We expect interest expense in 2017 to decrease as compared to 2016 as we expect the working capital advance to be repaid upon maturity, which is triggered once the termination of the supply agreement with Endo is finalized. Subsequent to repayment, amortization of imputed interest will cease.

Loss on sale of short-term investments

We received short-term investments as part of the sales consideration related to the divestiture of our Zohydro ER business in 2015. We sold these investments in 2015 and recognized a loss of $5.7 million.

Change in Fair Value of Warrant Liabilities

The change in fair value of warrant liabilities results from the periodic remeasurement of the estimated fair value of our warrant liabilities as discussed in Note 10 to our consolidated financial statements. The (income) expense in 2016, 2015 and 2014 resulted from fluctuations in our stock price between the measurement date as well as the decreased expected term from the passage of time.

The income or expense realized as a change in the valuation will continue to fluctuate based upon changes to inputs used to estimated fair value of our warrant liabilities while the warrants remain outstanding.

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Other Income (Expense)

Other income (expense) in 2016 and 2015 was comprised primarily of foreign currency transaction gains and losses. Other income (expense) in 2014 was comprised of fees incurred to register our Zogenix International Limited stock of $0.7 million and net foreign exchange losses of $0.1 million.

Income Taxes

	Year Ended December 31,			2015 to 2016		2014 to 2015	
(Dollars in thousands)	2016	2015	2014	$ change	% change	$ change	% change
Tax benefit (expense)	$948	$15,901	$(84)	$(14,953)	(94)%	$15,985	n/m

n/m—not meaningful

We are required to allocate the provision for income taxes between continuing operations and other categories of earnings, such as discontinued operations. In 2016, we recognized a tax benefit to continuing operations primarily related to the tax rate reductions enacted in the United Kingdom in September 2016 which resulted in a decrease in our deferred tax liability. In 2015, we recognized net income from discontinued operations, and, as a result, we recorded a tax expense of $14.1 million in discontinued operations and a corresponding tax benefit from continuing operations. The remaining tax benefit to continuing operations primarily relates to tax rate reductions enacted in the United Kingdom in November 2015 which resulted in a decrease in our deferred tax liability. In 2014, tax expense of $0.1 million was primarily related to the taxable foreign income generated by our wholly-owned subsidiary, Zogenix Europe Limited.

Discontinued Operations

In the first quarter of 2015, we reached a decision to sell our Zohydro ER business. On March 10, 2015, we entered into an asset purchase agreement with Pernix whereby we sold our Zohydro ER business to Pernix, and on April 24, 2015, we completed the sale to Ferrimill, a subsidiary of Pernix, as a substitute purchaser.

The sale, including the related gain on the transaction, was reflected in net income from discontinued operations in 2015, as discussed in Note 5 to our consolidated financial statements. As a result of our strategic decision to sell the Zohydro ER business and focus on clinical development of ZX008 and Relday, our consolidated statements of operations and consolidated balance sheets have been retrospectively revised to reflect the financial results from the Zohydro ER business as discontinued operations for all periods presented.

Net Operating Loss and Tax Credit Carryforwards

As of December 31, 2016, we had available federal, California and foreign net operating loss carryforwards of approximately $208.9 million, $191.3 million and $63.5 million, respectively. If not utilized, the net operating loss carryforwards will begin expiring in 2026 for federal tax purposes and 2016 for state tax purposes. As of December 31, 2016, we had federal and state research and development tax credit carryforwards of approximately $3.0 million and $3.6 million, respectively. If not utilized, the federal research and development income tax credit carryforwards will begin to expire in 2026. The California research and development income tax credit carryforwards do not expire and can be carried forward indefinitely.

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, 2016 we had three 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 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 net

operating loss carryforwards as of December 31, 2011 by $121.1 million and research and development income tax credits as of December 31, 2011 by $3.0 million. We also reduced our California net operating loss carryforwards as of December 31, 2011 by $53.3 million as a result of the second ownership change. We had a third ownership change as defined by IRC Sections 382 and 383, which occurred in January 2014. There was

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no forfeiture in federal and California net operating loss carryforwards or research and development income tax credits as a result of the third ownership change.

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 statements of operations.

LIQUIDITY AND CAPITAL RESOURCES

We have experienced net losses and negative cash flow from operations since inception. We expect to continue to incur net losses and negative cash flow from operating activities for at least the next year primarily as a result of the expenses incurred in connection with the clinical development of ZX008.

Since inception, our operations have been financed primarily through equity and debt financings and proceeds from two business divestitures—Sumavel DosePro and Zohydro ER. Through December 31, 2016, we received aggregate net cash proceeds of approximately $512.0 million from the sale of shares of our preferred and common stock, including the following financing transactions:

- in July 2012, we issued and sold a total of 4,382,287 shares of common stock and warrants to purchase 1,973,025 shares of common stock in a public offering for aggregate net proceeds of $65.4 million;
- in 2013, we issued and sold a total of 844,138 shares of common stock under our controlled equity offering program for aggregate net proceeds of $10.8 million;
- in November 2013, we issued and sold a total of 3,833,333 shares of common stock in a follow-on public offering for aggregate net proceeds of $64.5 million; and
- in August 2015, we issued and sold a total of 5,462,500 shares of common stock in a follow-on public offering for aggregate net proceeds of $92.0 million.

Excluding the above mentioned business divestitures, we have incurred recurring losses from operations and negative cash flows from operating activities. As of December 31, 2016, we had an accumulated deficit of $445.2 million. We held cash and cash equivalents of $91.6 million as of December 31, 2016. Our loan agreement with Oxford Finance LLC and Silicon Valley Bank includes a material adverse change clause (see Note 9). In the event that ZX008 is approved in the United States or the EU, we will owe milestone payments under our purchase agreement for ZX008 (see Note 7). Based on our operating plans, we do not expect that our existing capital resources will be sufficient to fund our operations beyond the first half of 2018. These factors raise substantial doubt about our ability to continue as a going concern. Our independent registered public accounting firm included an explanatory paragraph highlighting this uncertainty in its “Report of Independent Registered Public Accounting Firm” dated March 9, 2017 included in “Part IV, Item 15—Exhibits, Financial Statement Schedules” in this Annual Report on Form 10-K (see Note 1).

We intend to raise additional capital through public or private equity offerings, including debt financings. However, we may not be able to secure such financing in a timely manner or on favorable terms, if at all. Furthermore, if we issue equity or debt securities to raise additional funds, our existing stockholders may experience dilution, and the new equity or debt securities may have rights, preferences and privileges senior to those of our existing stockholders. If we raise additional funds through collaboration, licensing or other similar arrangements, it may be necessary to relinquish valuable rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us. Without additional funds, we may be forced to delay, scale back or eliminate some of our research and development activities, or other operations and potentially delay product development in an effort to provide sufficient funds to continue its operations. If any of these events occurs, our ability to achieve the development and commercialization goals would be adversely affected.

Cash and Cash Equivalents. Cash and cash equivalents totaled $91.6 million and $155.3 million at December 31, 2016 and 2015, respectively.

A summary of our cash flow activity was as follows:

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	Year Ended December 31,		
	2016	2015	2014
	(In Thousands)		
Cash provided by (used in):			
Operating activities	$(72,880)	$(64,602)	$(80,816)
Investing activities	9,899	85,545	61,002
Financing activities	(817)	92,201	(10,002)
Net increase (decrease) in cash and cash equivalents	$(63,798)	$113,144	$(29,816)

Operating Activities

Net cash used in operating activities of $72.9 million in 2016 primarily reflects a net loss of $69.7 million, adjusted for non-cash charges including a $8.4 million impairment charge related to long-lived assets associated with the production of Sumavel DosePro and the write-down of prepaid royalties (see Note 6), $7.4 million of stock based compensation and $1.8 million increase in the fair value of contingent consideration offset by $5.4 million change in fair value of warrant liabilities. The primary use of cash from changes in working capital was attributable to an $11.2 million increase in trade accounts receivable due to the timing of shipments and collections. Other uses of cash in operating activities include personnel-related costs, research and development costs for ZX008, other professional services, including legal and accounting, and increases in our accounts payable and accrued expenses due to the timing of payments. Cash provided by changes in working capital items was primarily attributable to lower inventory purchases of Sumavel DosePro raw materials due to the anticipated wind down of our manufacturing supply agreement with Endo (see Note 6).

Net cash used in operating activities of $64.6 million in 2015 primarily reflects the use of cash for operations, adjusted for non-cash charges including the $89.5 million pre-tax gain on the sale of our Zohydro ER business, a $5.7 million loss on our short-term investments, recognition of $8.5 million of deferred revenue and $7.7 million in stock-based compensation. Significant working capital uses of cash in 2015 include personnel-related costs, research and development costs (primarily for ZX008 and Relday), other professional services, including legal and accounting, and reduction of our accounts payable and accrued expense balances totaling $14.4 million, offset by lower accounts receivable balances of $7.5 million.

Net cash used in operating activities of $80.8 million in 2014 primarily reflects the use of cash for operations, adjusted for non-cash charges including the $80.0 million gain on the sale of our Sumavel DosePro business, a $25.3 million change in fair value of warrant liabilities and $9.5 million of stock-based compensation. Significant working capital uses of cash in 2014 include personnel-related costs, advertising and promotion, professional fees and required monitoring expenses associated with the launch of Zohydro ER.

Investing Activities

Investing activities resulted in net cash inflows of $9.9 million in 2016 primarily due to $10.0 million released from escrow funds related to the sale of Zohydro ER business.

Investing activities resulted in a cash inflow of $85.5 million in 2015. The primary inflows of cash associated with investing activities were primarily attributable to the proceeds from the sale of our Zohydro ER business, including $4.4 million of proceeds from the sale of short-term investments that was acquired as part of the sales consideration.

Investing activities resulted in a cash inflow of $61.0 million in 2014. The primary inflows of cash associated with investing activities were proceeds received from the sale of our Sumavel DosePro business for $89.6 million, of which $8.5 million was required to be placed in escrow and accounted for as restricted cash. The primary outflow of cash associated with investing activities was the acquisition of Zogenix International Limited for $20.0 million.

Financing Activities

Net cash used in financing activities of $0.8 million in 2016 consisted of $1.2 million for net debt repayment, offset by $0.3 million of cash receipts from exercises of employee stock options and employee stock purchase plan.

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Net cash provided by financing activities was $92.2 million in 2015. The primary inflows of cash associated with financing activities were net proceeds from our public offering of $92.2 million and $1.4 million of cash receipts from exercises of employee stock options and employee stock purchase plan. The primary outflow of cash associated with financing activities was $1.4 million for the repayment of all outstanding indebtedness under the revolving credit facility with Oxford and SVB.

Net cash used in financing activities was $10.0 million in 2014. The primary outflow of cash associated with financing activities was $40.0 million for the repayment of all outstanding indebtedness under a financing arrangement with Healthcare Royalty Partners. The primary inflows of cash associated with financing activities included $21.0 million of net proceeds from our term loan and revolving line of credit with Oxford and SVB, a working capital advance from Endo of $7.0 million and proceeds of $1.5 million from the exercise of warrants and stock options.

Debt Obligations

Term Debt

In December 2014, we entered into a Loan and Security Agreement (the Loan Agreement) with Oxford Finance LLC (Oxford) and Silicon Valley Bank (SVB), collectively, the Lenders, under which we borrowed a $20.0 million term loan. In addition, the Loan Agreement provided for a revolving credit facility of up to $4.0 million. The obligations under the Loan Agreement were secured by liens on our personal property and we have agreed to not encumber any of our intellectual property.

The term loan bore interest at an annual rate equal to the greater of (i) 8.75% or (ii) the sum of the prevailing prime rate (as report by the Wall Street Journal) plus 5.25%. Payments under the loan were interest-only until January 1, 2016, followed by equal monthly payments of principal and interest through the scheduled maturity date of December 1, 2018. The Loan Agreement includes a material adverse change clause, which enables the Lenders to require immediate repayment of the outstanding debt if certain subjective acceleration provisions are triggered. The material adverse change clause covers provisions including a material impairment of underlying collateral, change in business operations or condition or material impairment of our prospects for repayment of any portion of the remaining debt obligation (see Note 9).

On April 23, 2015, in connection with the sale of the Zohydro ER business, we and the Lenders entered into an amendment to the Loan Agreement, which terminated all encumbrances on our personal property related to its Zohydro ER business.

On June 17, 2016, we entered into a second amendment (the Second Amendment) to the Loan Agreement with the Lenders. The Second Amendment modified the loan repayment terms to be interest-only from July 1, 2016 to February 1, 2018, followed by equal monthly payments of principal and interest through the new maturity date of July 1, 2020. Under the terms of the Second Amendment, the interest rate applicable to the term loan bears interest at an annual rate equal to the greater of (i) 7.00% or (ii) the sum of the prevailing prime rate (as report by the Wall Street Journal) plus 3.25%. In addition, the Second Amendment terminated the revolving credit facility previously available under the Loan Agreement. In connection with the Second Amendment, we paid (i) the end of term fee of $1.0 million due under the Loan Agreement as a result of this refinancing transaction and (ii) the end of term fee of $0.1 million with respect to the termination of the revolving credit facility. The Second Amendment also includes an end of term fee of $1.4 million payable on July 1, 2020, or upon early repayment of the term loan. An early repayment will be subject to a prepayment penalty of $0.2 million.

The Loan Agreement required us to establish a controlled deposit account with SVB containing at least 85% of our account balances at all financial institutions which can be utilized by the Lenders to satisfy the obligations in the event of default. The Second Amendment permitted us to maintain collateral account balances exceeding the greater of (i) $50.0 million, or (ii) 50% of our total collateral account balances (other than specifically excluded accounts), with financial institutions other than the Lenders; provided that, if our total collateral account balances are below$50.0 million, all such balances will be maintained with the Lenders. Other affirmative covenants include, among others, requiring us to maintain legal existence and governmental approvals, deliver certain financial reports, maintain insurance coverage and satisfy certain requirements regarding accounts receivable. Negative covenants include, among others, restrictions on transferring collateral, incurring additional indebtedness, engaging in mergers or

acquisitions, paying dividends or making other distributions, making investments, creating liens, selling assets and suffering a change in control, in each case subject to certain exceptions. We were in compliance with these covenants at December 31, 2016 and 2015.

Note Payable for Working Capital Advance

In connection with the sale of the Sumavel DosePro business, Endo provided us with an interest-free working capital advance of $7.0 million, which is evidenced by a promissory note. The note payable is secured by a lien on our Sumavel DosePro raw materials and unreleased finished inventory. The note payable does not have a stated maturity date, but matures

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upon the termination of the related supply agreement. The supply agreement executed with Endo was for a minimum eight-year term.

We and Endo have recently entered into a letter agreement acknowledging Endo's decision to have us discontinue the manufacturing and the supply of Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. We expect to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time.

As a result, we changed the balance sheet classification of the note payable from long-term to current as the note payable matures in the event the termination of the supply agreement is finalized.

Contractual Obligations and Commitments

The following table describes our contractual obligations and commitments as of December 31, 2016:

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	4-5 Years	More than 5 Years
	(In Thousands)				
Debt obligations (1)	$27,000	$ 7,000	$ 16,000	$ 4,000	$ —
Debt interest (2)	4,721	1,420	3,301	—	—
Operating lease obligations (3)	8,872	1,838	5,085	1,949	—
Purchase obligations (4)	3,042	3,042	—	—	—
Other (5)	570	570	—	—	—
Total	$44,205	$ 13,870	$ 24,386	$ 5,949	$ —

(1) Represents principal payments due in connection with our term debt and working capital advance note. See Note 9 to our consolidated financial statements included in this Form 10-K. The $7.0 million working capital advance matures upon the termination of the Endo supply agreement.

(2) Represents the estimated interest on scheduled debt payments under the term debt.

(3) Represents the minimum lease payments for our Emeryville and San Diego, California offices pursuant to leases which expire in March 2020 and November 2022.

(4) Primarily represents non-cancellable purchase orders for the production of key components of Sumavel DosePro and a minimum manufacturing fee payable to Patheon UK Limited through the remaining term of our manufacturing services agreement. These purchase obligations are based on the exchange rate at December 31, 2016.

(5) Represents asset retirement obligations related to our production equipment at the sites of our suppliers.

We may also be required, in connection with in-licensing or asset acquisition agreements, to make certain royalty and milestone payments and we cannot, at this time, determine when or if the related milestones will be achieved or whether the events triggering the commencement of payment obligations will occur. Therefore, such payments are not included in the table above. See Note 3 and Note 7 to our consolidated financial statements in this Form 10-K for a description of the agreements that include these royalty and milestone payment obligations.

Recent Accounting Pronouncements

For the summary of recent accounting pronouncements applicable to our consolidated financial statements, see Note 2, Summary of Significant Accounting Policies, in Part IV, Item 15, Notes to Consolidated Financial Statements, which is incorporated herein by reference.

Off-Balance Sheet Arrangements

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

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Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

As of December 31, 2016, we had cash and cash equivalents of $91.6 million. A portion of our cash equivalents, which are in money market funds, may be subject to interest rate risk and could fall in value if market interest rates increase. However, because our cash equivalents are primarily short-term in duration, we believe that our exposure to interest rate risk is not significant and a 100 basis points movement in market interest rates would not have a significant impact on the total value of our portfolio.

Our term loan bears interest at an annual rate equal to the greater of (i) 7.00% or (ii) the sum of the prevailing prime rate (as report by the Wall Street Journal) plus 3.25%. As a result, we are exposed to interest rate risk from fluctuations in the prime rate. Based on our outstanding principal balance of $20.0 million at December 31, 2016 and historical interest rate volatility, we believe that our exposure to interest rate risk is not significant and a 100 basis points movement in market interest rates would not have a significant impact on our consolidated financial statements.

Foreign Exchange Risk

Our material suppliers and contract manufacturers are primarily in the U.K. which requires payments denominated in the Euro and the British Pound Sterling. As a result, we face foreign exchange risk for such expenditures. Due to the uncertain timing of expected payment in foreign currencies, we do not utilize any forward exchange contracts. While we have not experienced significant gains and/or losses from such transactions to date, an adverse movement in foreign exchange rates could have a material effect on payments made to foreign suppliers and contract manufacturers in the future. In 2016, the effect of foreign exchange rate fluctuations was not material to our consolidated financial statements. A hypothetical 10% change in the average exchange rate of the Euro or the British Pound Sterling during 2016 would not have had a material impact on our consolidated financial statements. We will continue to monitor and evaluate various options to mitigate the foreign exchange risk as a result of entering into transactions denominated in currencies other than the U.S. Dollar.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements and the report of our independent registered public accounting firm are included in this report on pages F-1 through F-35.

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

None.

Item 9A. Controls and Procedures

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

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

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, 2016 at the reasonable assurance level.

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.

Management’s Annual Report on Internal Control Over Financial Reporting

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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 (2013)" published by the Committee of Sponsoring Organizations of the Treadway Commission to evaluate the effectiveness of our internal control over financial reporting. Based on this evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2016, 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, 2016, which is included below.

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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, 2016, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (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 Annual 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 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, 2016, 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, 2016 and 2015, and the related consolidated statements of operations, comprehensive (loss) income, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2016 of Zogenix, Inc. and our report dated March 9, 2017 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 9, 2017

Item 9B. Other Information

None.

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PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information required by this item will be contained in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission in connection with our 2017 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, 2016, under the headings “Election of Directors,” “Corporate Governance and Other Matters ,” “Executive Officers,” and “Section 16(a) Beneficial Ownership Reporting Compliance,” and is incorporated herein by reference .

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

Item 11. Executive Compensation

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

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

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

Item 13. Certain Relationships, Related Transactions and Director Independence

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

Item 14. Principal Accounting Fees and Services

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

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PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) Documents filed as part of this report.

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

2. Financial Statement Schedules.

All 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.

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

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Zogenix, Inc.
Index to Consolidated Financial Statements

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Zogenix, Inc.

We have audited the accompanying consolidated balance sheets of Zogenix, Inc. as of December 31, 2016 and 2015, and the related consolidated statements of operations, comprehensive (loss) income, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements 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, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

The accompanying consolidated 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 has recurring losses from operations and has negative cash flows from operating activities that raise substantial doubt about its ability to continue as a going concern. Management's plans as to these matters are also described in Note 1. The 2016 consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may 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, 2016, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 9, 2017 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP
San Diego, California
March 9, 2017

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

	December 31,	
	2016	2015
Assets		
Current assets:		
Cash and cash equivalents	$91,551	$155,349
Restricted cash	—	10,002
Trade accounts receivable	12,577	1,396
Inventory	7,047	12,030
Prepaid expenses	7,404	1,707
Other current assets	1,335	3,811
Current assets of discontinued operations	—	208
Total current assets	119,914	184,503
Property and equipment, net	1,710	9,254
Intangible assets	102,500	102,500
Goodwill	6,234	6,234
Other assets	1,147	3,331
Total assets	$231,505	$305,822
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$4,549	$5,290
Accrued expenses	6,374	4,617
Common stock warrant liabilities	809	6,196
Accrued compensation	3,652	3,711
Working capital advance note payable, net of discount of $3,733	3,267	—
Current portion of long-term debt	—	6,321
Deferred revenue	1,245	945
Current liabilities of discontinued operations	414	2,906
Total current liabilities	20,310	29,986
Long-term debt	18,824	15,899
Deferred revenue, noncurrent	—	6,139
Contingent purchase consideration	52,800	51,000
Deferred tax liability	17,425	18,450
Other long-term liabilities	1,390	1,588
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.001 par value; 50,000 shares authorized; 24,813 and 24,772 shares issued and outstanding at December 31, 2016 and 2015, respectively.	25	25
Additional paid-in capital	565,954	558,251
Accumulated deficit	(445,223)	(375,516)
Total stockholders' equity	120,756	182,760
Total liabilities and stockholders' equity	$231,505	$305,822

See accompanying notes.

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

	Year Ended December 31,		
	2016	2015	2014
Revenue:			
Contract manufacturing revenue	$28,525	$24,369	15,392
Net product revenue	—	—	9,840
Service and other product revenue	325	2,813	3,715
Total revenue	28,850	27,182	28,947
Operating expenses (income):			
Cost of contract manufacturing	22,173	22,356	14,342
Cost of goods sold	—	—	5,263
Royalty expense	295	345	591
Research and development	41,840	27,860	11,893
Selling, general and administrative	26,996	26,347	34,639
Change in fair value of contingent consideration	1,800	(2,000)	—
Impairment charges	8,431	—	838
Net gain on sale of business	—	—	(79,980)
Total operating expenses (income)	101,535	74,908	(12,414)
(Loss) income from operations	(72,685)	(47,726)	41,361
Other income (expense):			
Interest income	443	101	20
Interest expense	(2,825)	(3,060)	(3,090)
Loss on sale of short-term investments	—	(5,746)	—
Loss on extinguishment of debt	—	—	(1,254)
Change in fair value of common stock warrant liabilities	5,387	(1,103)	25,332
Change in fair value of embedded derivatives	—	—	(14)
Other income (expense)	46	(71)	(784)
Total other income (expense)	3,051	(9,879)	20,210
(Loss) income from continuing operations before income taxes	(69,634)	(57,605)	61,571
Income tax benefit (expense)	948	15,901	(84)
(Loss) income from continuing operations	(68,686)	(41,704)	61,487
Discontinued operations:			
(Loss) income from discontinued operations	(1,021)	67,848	(52,900)
Net (loss) income	$(69,707)	$26,144	$8,587
Net (loss) income per share, basic and diluted			
Net (loss) income per share, basic:			
Continuing operations	$(2.77)	$(1.94)	$3.45
Discontinued operations	$(0.04)	$3.16	$(2.97)
Total	$(2.81)	$1.22	$0.48
Net (loss) income per share, diluted:			
Continuing operations	$(2.77)	$(1.94)	$3.44
Discontinued operations	$(0.04)	$3.16	$(2.96)
Total	$(2.81)	$1.22	$0.48
Weighted average shares outstanding, basic	24,785	21,449	17,825
Weighted average shares outstanding, diluted	24,785	21,449	17,855

See accompanying notes.

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Zogenix, Inc.
Consolidated Statements of Comprehensive (Loss) Income
(In Thousands)

	Year Ended December 31,		
	2016	2015	2014
Net (loss) income	$(69,707)	$26,144	$8,587
Other comprehensive (loss) income:			
Unrealized loss on available-for-sale securities	—	(5,485)	—
Reclassification of other-than-temporary loss on available-for-sale securities included in net income	—	5,485	—
Comprehensive (loss) income	$(69,707)	$26,144	$8,587

See accompanying notes.

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Zogenix, Inc.
Consolidated Statements of Stockholders' Equity
(In Thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss)/Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2013	17,365	$ 17	$ 428,656	$ —	$ (410,247)	$ 18,426
Net income	—	—	—	—	8,587	8,587
Issuance of common stock in connection with exercise of stock options	20	—	343	—	—	343
Issuance of common stock from ESPP purchase	63	—	556	—		556
Issuance of common stock in connection with exercise of warrants	58	—	2,079	—	—	2,079
Issuance of common stock in connection with vesting of restricted stock units	165	—	1	—	—	1
Issuance of common stock in connection with acquisition	1,499	2	15,235	—	—	15,237
Issuance of common stock warrants in connection with debt	—	—	558	—	—	558
Stock-based compensation	—	—	9,492	—	—	9,492
Balance at December 31, 2014	19,170	$ 19	$ 456,920	$ —	$ (401,660)	$ 55,279
Net income	—	—	—	—	26,144	26,144
Issuance of common stock in connection with public offering, net of issuance costs of $6,317	5,463	5	92,002	—	—	92,007
Issuance of common stock in connection with exercise of stock options	96	1	1,440	—	—	1,441
Issuance of common stock in connection with exercise of warrants	17	—	—	—	—	—
Issuance of common stock from ESPP purchase	26	—	203	—	—	203
Stock-based compensation	—	—	7,686	—	—	7,686
Unrealized loss on available-for-sale securities	—	—	—	5,485	—	5,485
Reclassification of other-than-temporary loss on available-for-sale securities included in net income	—	—	—	(5,485)	—	(5,485)
Balance at December 31, 2015	24,772	$ 25	$ 558,251	$ —	$ (375,516)	$ 182,760
Net loss	—	—	—	—	(69,707)	(69,707)
Issuance of common stock from stock option exercises	6	—	47	—	—	47
Issuance of common stock from ESPP purchase	35	—	303	—	—	303
Stock-based compensation	—	—	7,353	—	—	7,353
Balance at December 31, 2016	24,813	$ 25	$ 565,954	$ —	$ (445,223)	$ 120,756

See accompanying notes.

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

	Year Ended December 31,		
	2016	2015	2014
Operating activities:			
Net (loss) income	$(69,707)	$26,144	$8,587
Adjustments to reconcile net (loss) income to net cash used in operating activities:			
Stock-based compensation	7,353	7,686	9,492
Depreciation	1,402	1,621	1,625
Amortization of debt issuance costs and debt discount	991	791	457
Change in fair value of warrant liabilities	(5,387)	1,103	(25,332)
Change in fair value of embedded derivatives	—	—	14
Change in fair value of contingent consideration	1,800	(2,000)	—
Impairment charges	8,431	—	838
Loss on sale of short-term investments	—	5,746	—
Loss on extinguishment of debt	—	—	1,254
Gain on sale of business	—	(89,484)	(79,980)
Changes in operating assets and liabilities:			
Trade accounts receivable	(11,181)	7,477	(2,212)
Inventory	4,983	1,394	(3,503)
Prepaid expenses and other current assets	(3,394)	(650)	(9,200)
Other assets	471	316	(4,126)
Accounts payable and accrued expenses	(1,671)	(14,385)	5,404
Deferred revenue	(5,839)	(8,464)	15,658
Deferred tax liability	(1,025)	(2,050)	—
Deferred rent and other liabilities	(107)	153	208
Net cash used in operating activities	(72,880)	(64,602)	(80,816)
Investing activities:			
Purchases of property and equipment	(103)	(308)	(122)
Proceeds from divestiture of businesses	—	82,984	89,624
Change in restricted cash from divestiture of businesses	10,002	(1,502)	(8,500)
Proceeds from sale of short-term investments	—	4,371	—
Acquisition of business, net of cash acquired	—	—	(20,000)
Net cash provided by investing activities	9,899	85,545	61,002
Financing activities:			
Proceeds from borrowings of debt and revolving credit facility, net of issuance costs	2,167	—	27,977
Payments on borrowings of debt	(3,334)	(1,450)	(40,041)
Proceeds from issuance of common stock under employee stock plans and exercise of warrants	350	1,441	1,506
Proceeds from issuance of common stock and common stock warrants, net of issuance costs	—	92,210	556
Net cash (used in) provided by financing activities	(817)	92,201	(10,002)
Net (decrease) increase in cash and cash equivalents	(63,798)	113,144	(29,816)
Cash and cash equivalents at beginning of period	155,349	42,205	72,021
Cash and cash equivalents at end of period	$91,551	$155,349	$42,205
Supplemental disclosure of cash flow information:			
Cash paid for interest	$1,470	$1,466	$12,847
Noncash investing and financing activities:			

Issuance of common stock in connection with acquisition	$—	$—	$15,237
Issuance of common stock in connection with cashless exercise of warrants	$—	$300	$—
Purchase of property and equipment in accounts payable	$—	$—	$12
Change in common stock warrant liability associated with exercise of warrants	$—	$—	$(916)
Warrants issued in connection with debt	$—	$—	$558

See accompanying notes.

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Zogenix, Inc.
Notes to Consolidated Financial Statements

1. Organization, Basis of Presentation and Liquidity

Zogenix, Inc. and subsidiaries (the Company) is a pharmaceutical company committed to developing and commercializing central nervous system (CNS) therapies. The Company's current primary area of focus is epilepsy and related seizure disorders.

The accompanying consolidated financial statements include the accounts of Zogenix, Inc. and its wholly owned subsidiary Zogenix Europe, which was incorporated under the laws of England and Wales in June 2010. Also included is Zogenix International Limited, a wholly owned subsidiary of Zogenix Europe. All intercompany accounts and transactions have been eliminated in the preparation of the consolidated financial statements.

The accompanying consolidated balance sheets as of December 31, 2016 and 2015, and consolidated statements of operations for each of the three years in the period ended December 31, 2016 have been prepared by the Company pursuant to the rules and regulations of the Securities and Exchange Commission ("SEC") and in conformity with generally accepted accounting principles in the United States of America. The accompanying consolidated financial statements contemplate the realization of assets and the satisfaction of liabilities in the normal course of business.

As of December 31, 2016, the Company adopted Accounting Standard Update (ASU) No. 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties About an Entity's ability to Continue as a Going Concern, which requires management to evaluate whether there are conditions or events that raise substantial doubt about the Company's ability to continue as a going concern and to meet is obligations as they become due within one year from the date the financial statements are issued.

Excluding gains from two discrete business divestitures, the Company has incurred significant net losses from its operations since its inception and has an accumulated deficit of $445.2 million as of December 31, 2016. In 2016, the Company used $72.9 million of cash in operations. At December 31, 2016, the Company had cash and cash equivalents of $91.6 million. The Company's loan agreement with Oxford Finance LLC and Silicon Valley Bank includes a material adverse change clause (see Note 9.) Management expects operating losses and negative cash flows to continue for at least the next year as the Company continues to incur costs related to ongoing Phase 3 programs in Dravet syndrome in North America and EU for ZX008. Additionally, in the event that ZX008 is approved in the U.S. or EU, the Company will owe milestone payments under its Zogenix International Limited Sales and Purchase Agreement (see Note 7). Based on the Company's operating plans, management believes the Company's cash and cash equivalents will not be sufficient to fund its operations beyond the first half of 2018. As a result, there is substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued.

Management's ability to continue as a going concern is dependent upon its ability to raise additional funding. Management intends to raise additional capital through public or private equity offerings, including debt financings. However, the Company may not be able to secure such financing in a timely manner or on favorable terms, if at all. Furthermore, if the Company issues equity or debt securities to raise additional funds, its existing stockholders may experience dilution, and the new equity or debt securities may have rights, preferences and privileges senior to those of the Company's existing stockholders. If the Company raises additional funds through collaboration, licensing or other similar arrangements, it may be necessary to relinquish valuable rights to its potential products or proprietary technologies, or grant licenses on terms that are not favorable to the Company. Without additional funds, the Company may be forced to delay, scale back or eliminate some of our research and development activities, or other operations and potentially delay product development in an effort to provide sufficient funds to continue its operations. If any of these events occur, the Company's ability to achieve the development and commercialization goals would be adversely affected.

The consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or amounts and classification of liabilities that may result from the outcome of this uncertainty.

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 materially from those estimates.

Business Combinations

The Company measures all assets acquired and liabilities assumed, including contingent consideration, at fair value as of the acquisition date. Contingent purchase considerations to be settled in cash are remeasured to estimated fair value at each reporting period with the change in fair value recorded in operating expenses. In addition, the Company capitalizes in-process research and development (IPR&D) and either amortizes it over the life of the product upon commercialization, or impairs it if the carrying value exceeds the fair value or if the project is abandoned. Post-acquisition adjustments in deferred tax liabilities are recorded in current period income tax expense in the period of the adjustment.

Discontinued Operations

On April 24, 2015, the Company sold its Zohydro ER business. The operating results of the Zohydro ER business have been excluded from continuing operations for all periods herein and reported as discontinued operations. See Note 5, Sale of Zohydro ER business, for additional information on the divestiture.

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 connection with its sale of the Zohydro ER business in April 2015, the Company has $10.0 million of cash in escrow as of December 31, 2015 to fund potential indemnification claims for a period of 12 months from the closing date of the sale. The Company received the full amount from escrow in April 2016.

In connection with its sale of the Sumavel DosePro business in May 2014, the Company had $8.5 million of cash in escrow as of December 31, 2014 to fund potential indemnification claims for a period of 12 months from the closing date of the sale. The Company received the full amount from escrow in May 2015.

The Company classifies these cash flows as an investing activity in the consolidated statements of cash flows as the source of the restricted cash is related to divestitures of its businesses.

Short-term Investments

Short-term investments consisted of shares of Pernix Therapeutics common stock received as partial consideration for the sale of the Zohydro ER business in April 2015. Management classified these short-term investments as available-for-sale when acquired and evaluated such classification as of each balance sheet date until sold. Short-term investments were carried at fair value, with the unrealized gains and losses, net of tax, reported in other comprehensive loss, a component of stockholders' equity. Realized gains and losses and declines in fair value considered to be other-than-temporary are included in loss on sale of short-term investments on the consolidated statements of operations and a new accounting cost basis for the investment is established.

The Company evaluated its short-term investments to assess whether any unrealized loss position is other than temporarily impaired. Factors considered in determining whether a loss was other-than-temporary included the length of time and extent to which fair value was less than the cost basis, the financial condition and near-term prospects of the issuer, and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in market value. During 2015, the Company liquidated all of its short-term investments and recognized a loss totaling $5.7 million in the consolidated statements of operations. Also, the Company had a $0.5 million receivable from unsettled sales of the short-term investments which was included in other current assets at December 31, 2015 and received cash in 2016.

Accounts Receivable

Trade accounts receivable are recorded net of allowances for uncollectible accounts. The Company evaluates the collectability of its accounts receivable based on various factors including the length of time the receivables are past due, the financial health of the customer and historical experience. The Company reserves specific receivables if

collectability is no longer reasonably assured. Based upon the assessment of these factors, the Company did not record an allowance for uncollectible accounts at December 31, 2016 and 2015.

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

Fair Value Measurements

Certain of the Company's financial instruments, including cash and cash equivalents, restricted cash, trade accounts receivable and accounts payable are carried at cost, which approximates their fair value due to their short maturities. The carrying amount of the Company's term debt approximates fair value because it has a variable interest rate. At December 31, 2016, the estimated fair value of the Company's working capital advance note payable approximated its face amount due to its impending maturity upon finalization of a termination agreement with Endo (see Note 6). Accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

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

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

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

The Company classifies its cash equivalents within Level 1 of the fair value hierarchy because it values its cash equivalents using quoted market prices. The Company classifies its common stock warrant liabilities and contingent purchase consideration 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, 2016 and 2015 were 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, 2016				
Assets				
Cash equivalents (1)	$87,792	$—	$—	$87,792
Liabilities				
Common stock warrant liabilities (2)	$—	$—	$809	$809
Contingent purchase consideration (3)	$—	$—	$52,800	$52,800
At December 31, 2015				
Assets				
Cash equivalents (1)	$148,588	$——	——	$148,588
Liabilities				
Common stock warrant liability (2)	$—	$—	$6,196	$6,196
Contingent purchase consideration (3)	$—	$—	$51,000	$51,000

(1) Cash equivalents consists of investments in money market funds.

(2) Common stock warrant liabilities include liabilities associated with warrants issued in connection with the Company's July 2012 public offering of common stock and warrants (see Note 10) and warrants issued in connection with the financing agreement entered into with Healthcare Royalty Partners, which are measured at fair value using the Black-Scholes option pricing valuation model. The assumptions used in the Black-Scholes option pricing valuation model for both common stock warrant liabilities were: (a) a risk-free interest rate based on the

rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the remaining contractual term of the warrants; (b) an assumed dividend yield of zero based on the Company's expectation that it will not pay dividends in the foreseeable future; (c) an expected term based on the remaining contractual term of the warrants; and (d) expected volatility based upon the Company's historical volatility. The significant unobservable input used in measuring the fair value of the common stock warrant liabilities associated with the Healthcare Royalty Financing Agreement is the expected volatility. Significant increases in volatility would result in a

higher fair value measurement. The following additional assumptions were used in the Black-Scholes option pricing valuation model to measure the fair value of the warrants sold in the July 2012 public offering: (a) management's projections regarding the probability of the occurrence of an extraordinary event and the timing of such event; and for the valuation scenario in which an extraordinary event occurs that is not an all cash transaction or an event whereby a public acquirer would assume the warrants, (b) an expected volatility rate using the Company's historical volatility through the projected date of public announcement of an extraordinary transaction, blended with a rate equal to the lesser of 40% and the 180-day volatility rate obtained from the HVT function on Bloomberg as of the trading day immediately following the public announcement of an extraordinary transaction. The significant unobservable inputs used in measuring the fair value of the common stock warrant liabilities associated with the July 2012 public offering are the expected volatility and the probability of the occurrence of an extraordinary event. Significant increases in volatility would result in a higher fair value measurement and significant increases in the probability of an extraordinary event occurring would result in a significantly lower fair value measurement.

(3) Contingent purchase consideration was measured at fair value using the income approach based on significant unobservable inputs including management's estimates of the probabilities and timing of achieving specific net sales levels and development milestones and appropriate risk adjusted discount rates. Significant changes of any of the unobservable input could have a significant effect on the calculation of fair value of the contingent purchase consideration liability.

The following table provides a reconciliation of assets and liabilities measured at fair value on a recurring basis using significant unobservable inputs (Level 3) for the years ended December 31, 2016 and 2015 (in thousands):

	Short-term investments	Contingent Purchase Consideration	Common Stock Warrant Liability
Balance at December 31, 2014	$ —	$ 53,000	$ 5,093
Additions	11,926	—	—
Dispositions	(6,180)	—	—
Changes in fair value	(5,746)	(2,000)	1,103
Balance at December 31, 2015	—	51,000	6,196
Additions	—	—	—
Dispositions	—	—	—
Changes in fair value	—	1,800	(5,387)
Balance at December 31, 2016	$ —	$ 52,800	$ 809

Realized changes in fair value of the short-term investments are shown as loss on sale of short-term investments in other income (expense) in the consolidated statements of operations. Changes in fair value of contingent purchase consideration are reflected as operating expenses in the consolidated statements of operations. Changes to the warrant liabilities are recorded through a change in fair value of warrant liabilities.

Concentration of Credit Risk and Significant Customers

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains accounts in federally insured financial institutions in excess of federally insured limits. The Company also maintains investments in money market funds 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.

In 2016, substantially all of the Company's revenue were derived from a contract manufacturing service agreement with its one customer, Endo. The Company and Endo have recently entered into a letter agreement acknowledging Endo's decision to have the Company discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. The Company expects to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time (See Note 6). Once the termination agreement is finalized, the Company will no longer have a source of recurring revenue.

As of December 31, 2016, the trade accounts receivable balance of $12.6 million was due from the Company's single customer, Endo. Subsequent to year-end, the Company has collected $10.1 million of the amounts outstanding at December 31, 2016.

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 method. The Company adjusts the carrying value of inventory for potentially excess, dated or product within one year of expiration and obsolete products based on an analysis of inventory on hand and compared to forecasts of future sales. As of December 31, 2016, the entire inventory balance consists of raw materials and work-in-process related to the fulfillment of Sumavel DosePro under the supply agreement with Endo. The Company expects the procured materials are subject to reimbursement under the supply agreement. Accordingly, no reserves were deemed necessary at December 31, 2016.

Property and Equipment, Net

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

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

Depreciation expense for property and equipment was $1.4 million in 2016, $1.6 million in 2015, and $1.6 million in 2014.

Goodwill and Indefinite-Lived Intangibles

Goodwill and indefinite-lived intangible assets are reviewed for impairment at least annually in the fourth quarter, and more frequently if events or other changes in circumstances indicate that the carrying amount of the assets may not be recoverable. Impairment of goodwill and indefinite-lived intangibles is determined to exist when the fair value is less than the carrying value of the net assets being tested.

Goodwill

The Company determined it has only one operating segment and reporting unit under the criteria in ASC 280, Segment Reporting. Accordingly, the Company's review of goodwill impairment indicators is performed at the entity-wide level. The goodwill impairment test consists of a two-step process. The first step of the goodwill impairment test, used to identify potential impairment, compares the fair value of the reporting unit to its carrying value. If the fair value of the reporting unit exceeds its carrying amount, goodwill of the reporting unit is considered not impaired, and the second step of the impairment test is not required. The Company uses its market capitalization as an indicator of fair value. The Company believes that since its reporting unit is publicly traded, the ability of a controlling shareholder to benefit from synergies and other intangible assets that arise from control might cause the fair value of its reporting unit as a whole to exceed its market capitalization. However, the Company believes that the fair value measurement need not be based solely on the quoted market price of an individual share of our common stock, but also can consider the impact of a control premium in measuring the fair value of its reporting unit. Should the market capitalization be less than its total stockholder's equity as of the annual test date or as of any interim impairment testing date, the Company would also consider market comparables, recent trends in its stock price over a reasonable period and, if appropriate, use an income approach (discounted cash flow) to determine whether the fair value of its reporting unit is greater than its carrying amount. If the income approach is used, the Company would establish a fair value by estimating the present value of its projected future cash flows expected to be generated from its business. The discount rate applied to the projected future cash flows to arrive at the present value would be intended to reflect all risks of ownership and the associated risks of realizing the stream of projected future cash flows. The discounted cash flow methodology would consider projections of financial performance for a period of several years combined with an estimated residual value. The second step, if required, compares the implied fair value of the reporting unit goodwill with the carrying amount of that goodwill. If the carrying amount of the reporting unit's

goodwill exceeds its implied fair value, an impairment charge is recognized in an amount equal to that excess. Implied fair value is the excess of the fair value of the reporting unit over the fair value of all identified assets and liabilities. Based on its goodwill impairment tests for 2016, 2015 and 2014, the Company concluded that the fair value of the reporting unit exceeded the carrying value and no impairment existed.

Indefinite-Lived Intangibles

The Company's indefinite-lived intangible asset consists of in-process research and development (IPR&D) acquired in a business combination (see Note 7) that are used in research and development activities but have not yet reached technological feasibility, regardless of whether they have alternative future use. The primary basis for determining the technological feasibility or completion of these projects is obtaining regulatory approval to market the underlying products in an applicable geographic region. the Company classifies in-process research and development acquired in a business combination as an indefinite-lived intangible asset until the completion or abandonment of the associated research and development efforts. Upon completion of the associated research and development efforts, the Company will determine the useful life of the technology and begin amortizing the assets to reflect their use over their remaining lives. Upon permanent abandonment, the Company would write-off the remaining carrying amount of the associated in-process research and development intangible asset. The Company uses the income approach to determine the fair value of its IPR&D. This approach calculates fair value by estimating the after-tax cash flows attributable to an in-process project over its useful life and then discounting these after-tax cash flows back to a present value. The Company's revenue assumptions are based on estimates of relevant market sizes, expected market growth rates, expected trends in technology and expected levels of market share. In arriving at the value of the in-process projects, the Company considers, among other factors: the in-process projects' stage of completion; the complexity of the work completed as of the acquisition date; the costs already incurred; the projected costs to complete; the contribution of other acquired assets; the expected regulatory path and introduction dates by region; and the estimated useful life of the technology. The Company applies a market-participant risk-adjusted discount rate to arrive at a present value as of the date of the impairment test. Based on its IPR&D impairment tests for 2016, 2015 and 2014, the Company concluded that the fair value of its IPR&D exceeded the carrying value and no impairment existed.

For asset purchases outside of business combinations, the Company expenses any purchased research and development assets as of the acquisition date if they have no alternative future uses.

Impairment of Long-Lived Assets

The Company evaluates long-lived assets, consisting of property and equipment, periodically for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset (group) may not be recoverable. If the sum of our estimated undiscounted future cash flows is less than the asset's (group) carrying value, the Company then estimated the fair value of the asset (group) to measure the impairment, if any.

In 2014, the Company recorded an impairment charge of $0.8 million upon divestiture of Sumavel DosePro business related to the disposal of construction in progress equipment that will no longer be placed into service.

The Company and Endo have recently entered into a letter agreement acknowledging Endo's decision to have the Company discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. As a result, the Company performed an analysis to estimate cash flows from property and equipment used in the production of Sumavel DosePro. Based on this analysis, the Company determined its fair value exceeded the carrying value by $6.4 million and recognized an impairment charge for long-lived assets in the fourth quarter of 2016. See Note 6 for additional information.

Common Stock Warrants

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 or equity on the consolidated balance sheet as appropriate. The Company adjusts the carrying value of 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 statements of operations.

Revenue Recognition

The Company generates revenue from contract manufacturing, service fees earned on collaborative arrangements and product revenue related to Sumavel DosePro prior to the sale of the business in May 2014. The Company also

generates revenue from the sale of Zohydro ER, which is included in net income (loss) from discontinued operations in the consolidated statement of operations. 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 (a) the Company's price to the buyer is substantially fixed or determinable at the date of sale, (b) 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, (c) the buyer's obligation to the Company would not be changed in the event of theft or physical destruction or damage of the product, (d) the buyer acquiring

the product for resale has economic substance apart from that provided by the Company, (e) the Company does not have significant obligations for future performance to directly bring about resale of the product by the buyer, and (f) the amount of future returns can be reasonably estimated. The Company defers recognition of revenue on product shipments of Zohydro ER until the right of return no longer exists, as the Company was not able to reliably estimate expected returns of the product at the time of shipment given the limited sales history of Zohydro ER.

Revenue arrangements with multiple elements are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the customer. The consideration received is allocated among the separate units based on their respective fair values, and the applicable revenue recognition criteria are applied to each of the separate units. The application of the multiple element guidance requires subjective determinations, and requires the Company to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (1) the delivered item(s) has value to the customer on a stand-alone basis and (2) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in the Company's control. In determining the units of accounting, the Company evaluates certain criteria, including whether the deliverables have stand-alone value, based on the consideration of the relevant facts and circumstances for each arrangement. In addition, the Company considers whether the buyer can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s), and whether there are other vendors that can provide the undelivered element(s).

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria, as described above, are applied to each of the separate units of accounting in determining the appropriate period or pattern of recognition. The Company determines the estimated selling price for deliverables within each agreement using vendor-specific objective evidence (VSOE) of selling price, if available, third-party evidence (TPE) of selling price if VSOE is not available, or management's best estimate of selling price (BESP) if neither VSOE nor TPE is available. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs.

Contract Manufacturing Revenue

The Company records deferred revenue when it receives payments in advance of the delivery of products or the performance of services. As part of the sale of the Company's Sumavel DosePro business in May 2014 to Endo, the Company allocated a portion of the total consideration received as payments in advance of the delivery of product under a supply agreement with Endo that was concurrently entered into with the asset sale. The Company initially recorded $9.1 million of deferred revenue, which is being recognized as contract manufacturing revenue when earned on a "proportional performance" basis as product is delivered. As a result, a portion of our contract manufacturing revenue reported includes deferred revenue from this transaction being recognized when earned.

Under the proportional performance method, revenue recognition is based on total products delivered to date relative to the total expected products to be delivered over the performance period as this is considered to be representative of the delivery of service under the arrangement. The performance period under the supply agreement was initially estimated to be eight years, the minimum contractual term under the agreement. Changes in estimates to the total expected products to be delivered or service obligation time period are accounted for prospectively. In the fourth quarter of 2016, as a result of Endo's intent to terminate the supply agreement by mid-2017, the performance period and the total expected products to be delivered under the arrangement were revised and revenue of $4.9 million was recognized for the inception-to-date effect of the change in estimate. See Note 6 for additional information.

In addition, the Company follows the authoritative accounting guidance when reporting revenue as gross when the Company acts as a principal versus reporting revenue as net when the Company acts as an agent. For transactions in

which the Company acts as a principal, has discretion to choose suppliers, bears credit risk and performs a substantive part of the services, revenue is recorded at the gross amount billed to a customer and costs associated with these reimbursements are reflected as a component of cost of sales for contract manufacturing services.

Product Revenue, Net

The Company sold Sumavel DosePro through May 2014, and sold Zohydro ER through April 2015, in the United States to wholesale pharmaceutical distributors and retail pharmacies, or collectively the Company's customers, subject to rights of return within a period beginning six months prior to, and ending 12 months following, product expiration. The Company recognized Sumavel DosePro product sales at the time title transferred to its customer, and reduced product sales for estimated future product returns and sales allowances in the same period the related revenue was recognized.

Given the limited sales history of Zohydro ER, the Company was not able to reliably estimate expected returns of the product at the time of shipment. Accordingly, the Company deferred recognition of revenue on Zohydro ER product shipments until the right of return no longer exists, which occurs at the earlier of the time Zohydro ER is dispensed through patient prescriptions or expiration of the right of return. The Company estimates Zohydro ER patient prescriptions dispensed using an analysis of third-party syndicated data. Zohydro ER was launched in March 2014 and, accordingly, the Company did not have a significant history estimating the number of patient prescriptions dispensed. If the Company underestimated or overestimated patient prescriptions dispensed for a given period, adjustments to revenue from discontinued operations may be necessary in future periods. The deferred revenue balance does not have a direct correlation with future revenue recognition as the Company records sales deductions at the time the prescription unit was dispensed. In addition, the costs of Zohydro ER associated with the deferred revenue were recorded as deferred costs, which were included in inventory, until the time the related deferred revenue is recognized. The Company is responsible for returns for product sold prior to the sale of the business on April 24, 2015 and for rebates, chargebacks, and related fees for product sold until July 8, 2015 per the terms of the asset purchase agreement. Revenue for Zohydro ER is included in discontinued operations in the consolidated statement of operations.

The Company will continue to recognize Zohydro ER revenue upon the earlier to occur of prescription units dispensed or expiration of the right of return until it can reliably estimate product returns, at which time the Company will record a one-time increase in revenue related to the recognition of revenue previously deferred, net of estimated future product returns and sales allowances. In addition, the costs of Zohydro ER associated with the deferred revenue are recorded as deferred costs, which are included in inventory, until such time the related deferred revenue is recognized, subject to future exchange or product returns.

Product Returns. The Company is responsible for product returns for Sumavel DosePro product distributed by the Company prior to the sale of Sumavel DosePro to Endo in May 2014 up to a maximum per unit amount, as specified in the asset purchase agreement. This estimate of returns requires a high degree of judgment and is 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 reduced by a nominal fee for processing the return.

The Company has monitored and analyzed actual return history of Sumavel DosePro since product launch. The Company's analysis of actual product return history considers actual product returns on an individual product lot basis since product launch, the dating of the product at the time of shipment into the distribution channel, prescription trends, trends in customer purchases and their inventory management practices, and changes in the estimated levels of inventory within the distribution channel 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.

Service and Other Product Revenue

Service and other product revenue primarily consists of payments received for the Company's sales efforts under a co-promotion agreement with Valeant Pharmaceuticals North America LLC (Valeant) which was terminated in July 2015, and adjustments to Sumavel returns reserves subsequent to the sale of the business in May 2014. The Company recognizes service and other product revenue at the time services have been rendered or return rights have expired.

Collaborative Arrangements

The Company records certain transactions between collaborators in the consolidated statement of operations on either a gross or net basis within revenues or operating expenses, depending on the characteristics of the collaboration relationship, and provides for enhanced disclosure of collaborative relationships. The Company evaluates its collaborative agreements for proper classification of shared expenses, license fees, milestone payments and any reimbursed costs within the consolidated statement of operations based on the nature of the underlying activity. If payments to and from collaborative partners are not within the scope of other authoritative accounting literature, the statement of operations classification for the payments is based on a

reasonable, rational analogy to authoritative accounting literature that is applied in a consistent manner. For collaborations relating to commercialized products, if the Company acts as the principal in the sale of goods or services, the Company records revenue and the corresponding operating costs in its respective line items within the consolidated statement of operations based on the nature of the shared expenses. Per authoritative accounting guidance, the principal is the party who is responsible for delivering the product to the customer, has latitude with establishing price and has the risks and rewards of providing product to the customer, including inventory and credit risk.

Research and Development Expense and Accruals

Research and development costs are expensed as incurred unless there is an alternative future use in other research and development projects. Research and development costs include personnel-related costs, outside contracted services including clinical trial costs, facilities costs, fees paid to consultants, milestone payments prior to FDA approval, license fees prior to FDA approval, 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's 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 Company's contracts 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, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If possible, the Company obtains information regarding unbilled services directly from these service providers. However, the Company may be required to estimate these services based on information available to its product development or administrative staff. If the Company underestimates or overestimates 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.

Income Taxes

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

Foreign Currency Transactions

Gains or losses resulting from transactions denominated in foreign currencies are included in other expense, net in the consolidated statements of operations and were not material for all periods presented.

Stock-Based Compensation

For stock options and restricted stock units, the Company recognizes compensation cost on a straight-line basis over the awards' vesting periods for awards which contain only a service vesting feature. For awards with a performance condition vesting feature, when achievement of the performance condition is deemed probable, the Company recognizes compensation cost on a graded-vesting basis over the awards' expected vesting periods.

Net (Loss) Income per Share

Basic net (loss) income per share is calculated by dividing the net (loss) income 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 income (loss) per share is computed by dividing the net income (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.

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

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

	Year Ended December 31,					
	2016		2015		2014	
	Continuing operations	Discontinued operations	Continuing operations	Discontinued operations	Continuing operations	Discontinued operations
Numerator						
Net (loss) income, basic and diluted	$(68,686)	$ (1,021)	$(41,704)	$ 67,848	$61,487	$ (52,900)
Denominator						
Weighted average common shares outstanding, basic	24,785	24,785	21,449	21,449	17,825	17,825
Effect of dilutive securities:						
Common stock warrants	—	—	—	—	30	30
Weighted average common shares outstanding, diluted	24,785	24,785	21,449	21,449	17,855	17,855
Net (loss) income per share, basic	$(2.77)	$ (0.04)	$(1.94)	$ 3.16	$3.45	$ (2.97)
Net (loss) income per share, diluted	$(2.77)	$ (0.04)	$(1.94)	$ 3.16	$3.44	$ (2.96)

In 2015 and 2014, the Company excluded 0.5 million and 1.2 million, respectively, of potential common shares outstanding from the calculation of diluted net income per share because their effect would have been antidilutive. In 2016, all potential common shares were excluded from the diluted net loss per share calculation as their effect is antidilutive since the Company generated a net loss. The following table summarizes the potential common shares excluded from the diluted calculation (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Common stock options and restricted stock units	3,256	529	1,244
Common stock warrants	1,975	—	—
	5,231	529	1,244

Segment Reporting

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

Reclassifications

Interest income balances for prior years, which were previously combined as part of interest expense, net have been separately presented in the consolidated statements of operations to conform to current year's presentation.

Accounting Pronouncements Recently Adopted

Accounting Standards Update (ASU) 2015-03, Interest—Imputation of Interest (Subtopic 835-30): Simplifying the Presentation of Debt Issuance Costs requires debt issuance costs related to a recognized debt liability to be presented on the balance sheet as a direct deduction from the debt liability instead of as an asset. The Company adopted the guidance in the first quarter of 2016. The effect of adopting the guidance retrospectively was 1) to decrease amounts previously reported on the Company's consolidated balance sheet at December 31, 2015 for prepaid expenses and other current assets and decrease current portion of long-term debt by $0.1 million and 2) to decrease other assets, noncurrent and long term debt by $0.1 million. The balances for December 31, 2015 reflected in the Company's consolidated balance sheet in this Form 10-K reflect these reclassifications.

ASU 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties About an Entity's ability to Continue as a Going Concern provides U.S. GAAP guidance on management's responsibility in evaluating whether there is substantial doubt about a company's ability to continue as a going concern

and about related footnote disclosures. For each reporting period, management will be required to evaluate whether there are conditions or events that raise substantial doubt about a company's ability to continue as a going concern within one year from the date the financial

statements are issued. The amendments in this update are effective for the annual period ending after December 15, 2016, and for annual periods and interim periods thereafter. The Company adopted the provisions of ASU 2014-15 as of December 31, 2016 and has included the disclosures required by ASU 2014-15 in Note 1 to the consolidated financial statements.

Accounting Pronouncements Issued But Not Yet Effective

ASU 2016-09, Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting changes how companies account for certain aspects of stock-based awards to employees. Under the guidance, entities will no longer record excess tax benefits and certain tax deficiencies in additional paid-in capital (APIC). Instead, they will record all excess tax benefits and tax deficiencies as income tax expense or benefit in the income statement. In addition, entities will recognize excess tax benefits regardless of whether the benefit reduces taxes payable in the current period. Under current guidance, excess tax benefits are not recognized until the deduction reduces taxes payable. The new standard became effective for the Company on January 1, 2017. The Company has excess tax benefits for which a benefit could not be previously recognized of approximately $0.2 million. Upon adoption, the balance of the unrecognized excess tax benefits will be reversed with the impact recorded to accumulated deficit, including any change to the valuation allowance as a result of the adoption. Additionally, as permitted under the new ASU, the Company has elected to change its policy on accounting for forfeitures and recognize them as they occur. Both of these changes will be adopted using the modified retrospective transition method, which will result in a cumulative-effect adjustment to the January 1, 2017 opening accumulated deficit balance. The Company does not expect the pending adoption of this ASU to have a material impact on its consolidated financial statements.

ASU 2014-09, Revenue from Contracts with Customers (Topic 606) and subsequent amendments to the initial guidance, collectively, Topic 606, will replace all current GAAP guidance on this topic and eliminate all industry-specific guidance. The new revenue recognition standard provides a unified model to determine when and how revenue is recognized. The core principle of Topic 606 is to recognize revenues when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received for those goods or services. Topic 606 defines a five-step process to achieve this core principle and, in doing so, it is possible more judgment and estimates may be required within the revenue recognition process than are required under existing GAAP, including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each separate performance obligation, among others. This guidance will be effective for the Company January 1, 2018. The guidance permits two methods of adoption: retrospectively to each prior reporting period presented (full retrospective method), or retrospectively with the cumulative effect of initially applying the guidance recognized at the date of initial application (the modified retrospective method). In 2016, the Company generated substantially all its revenue from a single contract, the manufacturing supply agreement with Endo, which is currently undergoing termination discussions and is expected to be terminated by mid-2017. The Company cannot predict whether it will have any revenue generating contracts with customers on the date of adoption. Therefore, the Company has not yet determined the transition method by which it will adopt the standard. The Company will continue to monitor any new contracts it enters into with customers for evaluation under ASU 2014-09.

ASU 2016-02, Leases (Topic 842) requires lessees to recognize the lease assets and lease liabilities that arise from both capital and operating leases with lease terms of more than 12 months and to disclose qualitative and quantitative information about lease transactions. The guidance is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. The Company is currently evaluating the timing and impact of adopting this new accounting standard on its financial statements and related disclosures.

3. Collaboration, License and Purchase Agreements

Zogenix International Limited Sales and Purchase Agreement

On October 24, 2014, the Company acquired Zogenix International Limited, pursuant to a sale and purchase agreement with Brabant Pharma Limited (Brabant). Under the terms of the Sale and Purchase Agreement, the Company agreed to make future milestone payments to the former principals of Brabant of up to $95.0 million in the event the Company achieves certain milestones with respect to ZX008, consisting of $50.0 million in regulatory milestones and $45.0 million in sales milestones.

In September 2012, Zogenix International Limited entered into a collaboration and license agreement with the Universities of Antwerp and Leuven in Belgium (the Universities), which was amended and restated in October 2014. Under the terms of the agreement, the Universities granted Zogenix International Limited an exclusive worldwide license to use the data obtained from the study, as well as certain intellectual property related to fenfluramine for the treatment of Dravet syndrome. Zogenix International Limited is required to pay a mid-single-digit percentage royalty on net sales of fenfluramine for the treatment of Dravet syndrome or, in the case of a sublicense of fenfluramine for the treatment of Dravet syndrome, a

percentage in the mid-twenties of the sub-licensing revenues. The agreement terminates in September 2020; however, upon the commencement of Phase 3 clinical trials of fenfluramine or marketing approval by a regulatory authority, the agreement will be extended until September 2045. The agreement may be terminated by the Universities if Zogenix International Limited: (a) does not use commercially reasonable efforts to (i) develop and commercialize fenfluramine for the treatment of Dravet syndrome or related conditions stemming from infantile epilepsy, or (ii) seek approval of fenfluramine for the treatment of Dravet syndrome in the United States; or (b) if Zogenix International Limited becomes insolvent, shall make an assignment for the benefit of creditors, or shall have a petition in bankruptcy filed for or against it or if a petition for any similar relief has been filed against it. The Company can terminate the agreement upon specified prior written notice to the Universities.

Endo Ventures Limited Asset Purchase Agreement

In May 2014, the Company completed the sale of its Sumavel DosePro business to Endo Ventures Bermuda Limited and Endo Ventures Limited (collectively, Endo) and concurrently entered into a long-term supply agreement with Endo for the exclusive right, and contractual obligation, to manufacture and supply Sumavel DosePro to Endo. The agreement provides for an initial term of eight years.

The Company and Endo have recently entered into a letter agreement acknowledging Endo's decision to have the Company discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. The Company expects to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time. The Company is currently working with its suppliers to wind down activities and may incur additional costs associated with the discontinuance of Sumavel DosePro. See Note 6 for additional information.

Valeant Pharmaceuticals North America LLC Co-Promotion Agreement Termination

On June 27, 2013, the Company entered into a co-promotion agreement (the Co-Promotion Agreement) with Valeant Pharmaceuticals North America LLC (Valeant) to promote Migranal® Nasal Spray (Migranal) to a prescriber audience of physicians and other health care practitioners in the United States. The Company's sales team began promoting Migranal to prescribers in August 2013, and Valeant paid the Company a co-promotion fee on a quarterly basis that represented specified percentages of net sales generated by the Company over defined baseline amounts of net sales. The original term of the agreement was through December 31, 2015. In 2016, 2015 and 2014, the Company recognized co-promotion service revenue of zero, $0.3 million and $3.4 million, respectively, under the Valeant Agreement.

In June 2015, the Company and Valeant entered into a Termination and Mutual Release Agreement, whereby the Co-Promotion Agreement terminated on June 12, 2015. In connection with the termination, Valeant made a one-time payment to the Company totaling $0.5 million, which was recorded as service and other product revenue in the consolidated statements of operations for the year ended December 31, 2015.

Durect Development and License Agreement

On July 11, 2011, the Company entered into a development and license agreement with Durect Corporation under which the Company is responsible for the clinical development and commercialization of Relday. Durect is responsible for pre-clinical, formulation and chemistry, manufacturing and controls development. Durect will be reimbursed by the Company for its research and development efforts on the product. Total research and development expense reimbursed under this agreement for 2016, 2015 and 2014 was $0.3 million, $4.6 million, and $4.3 million, respectively.

The Company paid an upfront fee to Durect and is 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. The Company is also required to pay a mid-single-digit to low double-digit percentage patent royalty on annual net sales of the product determined on a jurisdiction-by-jurisdiction basis. Further, until an NDA for Relday has been filed in the United States, the Company is obligated to spend no less than $1.0 million in external expenses on the development of Relday in any trailing 12 month period beginning in July 2012.

The patent royalty term is equal to the later of the expiration of all Durect technology patents or joint patent rights in a particular jurisdiction, the expiration of marketing exclusivity rights in such jurisdiction, or 15 years from first commercial sale in such jurisdiction. After the patent royalty term, the Company will continue to pay royalties on annual net sales of the product at a reduced rate for so long as the Company continues to sell the product in the jurisdiction. The Company is also required to pay to Durect a tiered percentage of fees received in connection with any sublicense of the licensed rights.

Durect granted 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.

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 transferred all of its tangible assets and intellectual property related to the DosePro needle-free drug delivery system to the Company. Aradigm also granted the Company a non-exclusive license under all of its other intellectual property related to the DosePro delivery system prior to the closing of the asset purchase. Aradigm retained a 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. Endo Ventures pays royalties to Aradigm Corporation on sales of Sumavel DosePro subsequent to the sale of the business to Endo in May 2014. The Company pays royalties for any additional revenue generated from differences between actual and estimated returns of Sumavel DosePro prior to the sale of the business.

The Company made an initial payment to Aradigm at the closing of the asset purchase and made an additional milestone payment upon the U.S. commercialization of Sumavel DosePro 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 in other assets in the consolidated balance sheet and was amortizing the prepaid royalties over the estimated useful life of the technology to royalty expense. As a result of Endo's intention to discontinue Sumavel DosePro (see Note 6), the Company recorded an impairment charge of $2.0 million to write off the remaining carrying amount of the prepaid royalties.

Other Asset Acquisitions

In October 2016, the Company paid $1.5 million to acquire the global rights to a preclinical development program for orphan CNS disorders in an asset acquisition. At the date of acquisition, the project had not yet reached technological feasibility, was deemed to have no alternative use, and was immediately charged to operating expense. The asset purchase agreement provides for potential additional payments if certain development and sales milestones are achieved. Due to the preclinical stage of development and the nature of this arrangement, any future potential payments related to the attainment of the specified milestones over a period of several years are inherently uncertain.

4. Consolidated Balance Sheet Details

Inventory (in thousands)

	December 31,	
	2016	2015

Raw materials	$4,397	$3,775
Work in process	2,650	8,255
	$7,047	$12,030

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Property and Equipment, Net (in thousands)

	December 31,	
	2016	2015
Machinery, equipment and tooling	$11,011	$12,859
Construction in progress	104	4,647
Computer equipment and software	78	579
Leasehold improvements	1,372	1,271
Furniture and fixtures	659	667
Property and equipment, at cost	13,224	20,023
Less accumulated depreciation	(11,514)	(10,769)
	$1,710	$9,254

Depreciation expense for 2016, 2015 and 2014 was $1.4 million, $1.6 million and $1.6 million, respectively.
The Company and Endo have recently entered into a letter agreement acknowledging Endo's decision to have the Company discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. As a result, the Company performed an analysis to estimate cash flows from property and equipment used in the production of Sumavel DosePro. Based on this analysis, the Company determined its fair value exceeded the carrying value by $6.4 million and recognized an impairment charge for long-lived assets in the fourth quarter of 2016. See Note 6 for additional information.
The Company had net long-lived assets consisting of property and equipment in the following regions as of December 31, 2016 and 2015 (in thousands):

	December 31,	
	2016	2015
United States	$629	$796
Europe	1,081	8,458
	$1,710	$9,254

Other Assets (in thousands)

	December 31,	
	2016	2015
Prepaid royalty expense	$—	$2,000
Deposits	376	556
Prepaid clinical trial costs	771	775
	$1,147	$3,331

Accrued Expenses (in thousands)

	December 31,	
	2016	2015
Accrued product returns	$99	$1,985
Accrued interest payable, current	121	178
Accrued clinical trial costs	3,657	1,162
Other accrued expenses	2,497	1,292
	$6,374	$4,617

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Other Long-Term Liabilities (in thousands)

	December 31,	
	2016	2015
Deferred rent	$661	$767
Accretion of terminal fee due at maturity on term loan	729	407
Asset retirement obligation	—	371
Other long-term liabilities	—	43
	$1,390	$1,588

5. Sale of Zohydro ER business

On March 10, 2015, the Company entered into an asset purchase agreement with Pernix Ireland Limited and Pernix Therapeutics (collectively, Pernix) whereby the Company agreed to sell its Zohydro ER business to Pernix, and on April 24, 2015, the Company completed the sale to Ferrimill Limited, a subsidiary of Pernix, as a substitute purchaser. The Zohydro ER business divestiture included the registered patents and trademarks, certain contracts, the new drug application and other regulatory approvals, documentation and authorizations, the books and records, marketing materials and product data relating to Zohydro ER.

The Company received consideration of $80.0 million in cash, subject to an escrow holdback of $10.0 million, and $10.6 million in Pernix Therapeutics common stock. The escrow period expired in March 2016. The Company may receive additional cash payments, not to exceed $283.5 million based on the achievement of certain regulatory and sales milestones. As of December 31, 2016, the Company had not received and does not expect to receive any additional cash payments. The Company recognized an after-tax gain of $75.4 million in discontinued operations in 2015.

As a result of the Company’s strategic decision to sell the Zohydro ER business and focus on clinical development of ZX008 and Relday, the consolidated statements of operations for the year ended December 31, 2014 was retrospectively revised to reflect the financial results from the Zohydro ER business as discontinued operations. The results of operations for discontinued operations presented below include certain allocations that management believes fairly reflect the utilization of services provided to the Zohydro ER business. The allocations do not include amounts related to general corporate administrative expenses or interest expense. Therefore, the results of operations from the Zohydro ER business do not necessarily reflect what the results of operations would have been had the business operated as a stand-alone entity.

The following table summarizes the results of discontinued operations presented in the consolidated statements of operations for the periods indicated (in thousands):

	Year Ended December 31,		
Discontinued operations	2016	2015	2014
Net product revenue	$532	$11,299	$11,584
Operating expense (income):			
Cost of product sold	15	2,205	10,554
Royalty expense	32	835	1,127
Research and development	—	5,504	7,043
Selling, general and administrative	1,594	14,820	54,260
Restructuring expense	—	588	—
Gain on sale of business	—	(89,484)	—
Total operating expense (income)	1,641	(65,532)	72,984
Other income	—	5,077	8,500
Net (loss) income from discontinued operations before tax	(1,109)	81,908	(52,900)

Tax benefit (expense)	88	(14,060)	—
Net loss (income) from discontinued operations	$(1,021)	$67,848	$(52,900)

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Other income of $5.0 million in 2015 was attributed to payment received for the Company's waiver of its regulatory exclusivity rights. Other income in 2014 was comprised of $3.5 million for the sale of right of reference to certain carcinogenicity data generated by the Company and a $5.0 million payment received for the Company's waiver of its regulatory exclusivity rights.

The following table summarizes the assets and liabilities of discontinued operations as of December 31, 2016 and 2015 related to the Zohydro ER business (in thousands):

	December 31, 2016	2015
Assets		
Current assets		
Trade accounts receivable	$—	$4
Inventory	—	15
Prepaid expenses and other current assets	—	189
Total current assets of discontinued operations	$—	$208
Liabilities		
Current liabilities		
Accrued expenses	414	2,796
Deferred revenue	—	110
Total current liabilities of discontinued operations	$414	$2,906

Stock-based compensation included in discontinued operations was $0.7 million in 2015 and $2.0 million in 2014. Amortization expense included in discontinued operations was $0.2 million in 2015 and $0.6 million in 2014. These noncash expenses included in discontinued operations were not material in 2016.

6. Sale of Sumavel DosePro Business

On May 16, 2014, the Company completed the sale of its Sumavel DosePro business to Endo, which included registered trademarks, regulatory and all rights to market, sell and distribute Sumavel DosePro under the trademark and commercialization rights under a specified subset of the Company's technology patents. The Company retained all rights to the DosePro technology patents and know-how for use with other products. The Company received $85.0 million in cash, subject to an escrow holdback of $8.5 million, and $4.6 million in cash for the purchase of Sumavel DosePro finished goods inventory on hand at the Company's standard cost. The escrow period expired in May 2015. As part of the transaction, the Company entered into a supply agreement with Endo for the exclusive right, and contractual obligation, to manufacture and supply Sumavel DosePro to Endo. Endo will purchase all Sumavel DosePro from the Company at cost plus a 2.5% mark-up and reimburse the Company for its royalty obligations due Aradigm Corporation on sales of Sumavel DosePro. The agreement provides for an initial term of 8 years. To support the Company's Sumavel DosePro manufacturing operations, Endo provided the Company with an interest-free working capital advance of $7.0 million under a promissory note (see Note 10). The working capital advance is collateralized by liens on materials and unreleased finished Sumavel DosePro inventory and matures upon termination of the supply agreement.

The Company accounted for this transaction as a multiple-element arrangement and applied the applicable accounting guidance to separate the discrete deliverables into different units of accounting, and to determine the arrangement consideration for those separate units of accounting. The Company identified two primary deliverables consisting of the asset sale of the Company's Sumavel DosePro business and the long-term contract manufacturing supply agreement, which includes the interest-free working capital advance. Other deliverables include a transition services agreement and participation in a joint supply committee with Endo which were determined to have minimal value relative to the total sales consideration. The Company determined that the asset sale and supply agreement each had standalone value and represented separate units of accounting. Cash consideration received of $89.6 million was

allocated to the asset sale and supply agreement based on the relative selling price method (see Note 2). Approximately $85.3 million was allocated to the asset sale and the remaining $4.4 million was allocated to the supply agreement, which includes the interest-free working capital advance. This resulted in a gain of $80.0 million, net of $0.7 million in transaction costs, on the sale of Sumavel DosePro business. The cash consideration allocated to the supply agreement consists of imputed interest of $4.7 million on the interest-free working capital advance, based on the Company's incremental borrowing rate for a debt instrument with similar terms, and $9.1 million for Sumavel

DosePro products to be delivered over the term of the supply agreement. The Company recorded the imputed interest as debt discount against the working capital advance proceeds and will amortize the debt discount using the effective interest method over the term of the supply agreement. The $9.1 million was recorded as deferred revenue and is to be recognized as contract manufacturing revenue as services are performed using the proportional performance method. The sale of the Sumavel DosePro business did not qualify as discontinued operations due to continuing involvement based on the applicable accounting guidance in effect in 2014.

The Company and Endo have recently entered into a letter agreement acknowledging Endo's decision to have the Company discontinue the manufacturing and supply of the Sumavel DosePro product under the supply agreement while the parties finalize termination of the supply agreement. The Company expects to fulfill current open orders during the first half of 2017 and not to supply Endo with additional Sumavel DosePro following such time.

The Company recorded impairment charges of $8.4 million consisting of $6.4 million for long-lived assets associated with the production of Sumavel DosePro in the fourth quarter of 2016 and $2.0 million in prepaid royalties. In addition, the performance period under the supply agreement was adjusted to conclude by mid-2017, which was accounted for prospectively as a change in accounting estimate (see Note 2). The Company recognized revenue for the inception-to-date effect of this change in estimate in the fourth quarter of 2016. As of December 31, 2016, deferred revenue of $1.2 million is expected to be recognized upon fulfillment of the remaining open orders.

7. Acquisition of Zogenix International Limited

On October 24, 2014, Zogenix Europe Limited (Zogenix Europe), a wholly-owned subsidiary of the Company, acquired all the capital stock of Zogenix International Limited, a privately-held company organized under the laws of England and Wales. Zogenix International Limited owned worldwide development and commercialization rights to ZX008, low-dose fenfluramine, for the treatment of Dravet syndrome. The Company paid cash consideration of $20.0 million, net of cash acquired, issued 11,995,202 shares of the Company's common stock valued at $15.2 million and contingent consideration with an estimated acquisition date fair value of $53.0 million for an aggregate purchase price of $88.2 million. Under the contingent consideration arrangement, the Company agreed to pay up to $95.0 million if certain milestones are achieved, including regulatory approvals and sales targets. Transaction costs associated with this acquisition of $0.3 million were expensed as incurred in selling, general and administrative expense in 2014.

The fair value of contingent consideration liability on the acquisition date of $53.0 million was estimated based on the probability of achieving the specified objectives using a probability-weighted discounted cash flow model. This fair value measurement is based on significant inputs not observed in the market and thus represents a Level 3 measurement as defined in connection with the fair value hierarchy (see Note 2). Any future change in the estimated fair value of the contingent consideration will be recognized in operating expenses within the consolidated statements of operations.

The Company accounted for this acquisition as a business combination and recorded the assets acquired and liabilities assumed at their respective fair values as of the acquisition date. The following summarizes the aggregate purchase price allocation (in thousands):

Cash and cash equivalents	$74
Prepaid expenses and other current assets	34
Property and equipment	4
Intangible assets	102,500
Goodwill	6,234
Accounts payable	(112)
Deferred tax liability	(20,500)
Total purchase price	$88,234

Intangible assets acquired represent in-process research and development (IPR&D) related to ZX008. The in-process research and development currently has an indefinite life and is tested for potential impairment at least annually or whenever indicators of potential impairment are present. Upon completion and development of the related project, the IPR&D will be assigned a useful life and amortized over the estimated period of its future economic benefit, or impaired if the technology is abandoned and is not able to be used for another purpose. The fair value of the developed technology and trade name was

estimated using an income approach. Under the income approach, an intangible asset's fair value is equal to the present value of future economic benefits to be derived from ownership of the asset. The estimated fair value was developed by discounting future net cash flows to their present value at market-based rates of return.

The excess of the fair value of the total consideration over the estimated fair value of the net assets acquired was recorded as goodwill, which was primarily attributable to expected benefit derived from utilizing the Company's established research and development infrastructure. The goodwill recognized is not deductible for income tax purposes.

8. Commitments and Contingencies

The Company is not currently involved in any material legal proceedings. The Company may become involved in various legal proceedings and claims that arise in the ordinary course of business. Such matters are subject to uncertainty and there can be no assurance that such legal proceedings will not have a material adverse effect on its business, results of operations, financial position or cash flows.

Operating Leases

The Company leases office space for its general and administrative, supply chain and inventory management and research and product development operations in Emeryville, California under a noncancelable operating lease that expires in November 2022. The base rent is subject to a 3% 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 under certain conditions, as well as a renewal option for an additional five year term upon the expiration date. The Company will also pay a portion of common area and pass-through expenses in excess of base year amounts.

The Company's noncancelable lease for its former headquarters in San Diego, California runs through March 2020. The facility has been substantially vacated as of December 31, 2016, and the Company intends to sublease this space. The base rent will increase approximately 3.25% on an annual basis throughout the term. The Company is also required to pay a portion of common area and pass-through expenses in excess of base year amounts. The Company received incentives of abated rent for approximately 4.5 months of the lease term totaling $0.3 million and a tenant improvement allowance of up to $0.4 million.

The Company recognizes rent expense on a straight-line basis over the noncancelable term of its operating leases. Rent expense for 2016, 2015 and 2014 was $1.9 million, $1.5 million and $0.9 million, respectively.

Future minimum lease payments required under operating leases that have initial or remaining noncancelable lease terms in excess of one year at December 31, 2016 were as follows (in thousands):

2017	$1,838
2018	1,896
2019	1,955
2020	1,234
2021	1,004
Thereafter	945
Total	$8,872

Manufacturing and Supply Agreements

The Company has a manufacturing services agreement with Patheon UK Limited (Patheon) related to Sumavel DosePro, which is scheduled to expire at the end of April 2017. As the Company will have no further obligation to supply Endo with Sumavel DosePro after fulfillment of the remaining open orders (see Note 6), the manufacturing services agreement with Patheon will not be renewed. As of December 31, 2016, purchase commitments under this agreement totaled approximately $2.7 million. In addition, the Company is obligated to pay Patheon up to $0.3 million (based on year-end exchange rates) for the removal of manufacturing equipment related to Sumavel DosePro from Pantheon's facility upon the expiration of the agreement. The asset retirement obligation was included in current

liabilities in the Company's consolidated balance sheet as of December 31, 2016.

The Company has manufacturing and supply agreements with several third-party suppliers for the production of key components of Sumavel DosePro in addition to Patheon. As of December 31, 2016, aggregate noncancelable purchase orders under these arrangements totaled $0.3 million. The Company is currently engaged in discussions with these third-party suppliers related to discontinuing Sumavel DosePro and may incur additional costs associated with the wind down activities.

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9. Debt Obligations

Term Debt

Scheduled maturities of the term debt are as follows (in thousands):

2017	$—
2018	8,000
2019	8,000
2020	4,000
Principal balance outstanding	20,000
Less: unamortized debt discount and issuance costs	(1,176)
Net carrying value of debt	18,824
Less: current portion	—
Long-term debt	$18,824

In December 2014, the Company entered into a Loan and Security Agreement (the Loan Agreement) with Oxford Finance LLC ("Oxford") and Silicon Valley Bank ("SVB") (collectively, the "Lenders"), under which the Company borrowed a $20.0 million term loan. In addition, the Loan Agreement provided for a revolving credit facility of up to $4.0 million. The obligations under the Loan Agreement are secured by liens on the Company's personal property and the Company has agreed to not encumber any of its intellectual property. The Loan Agreement includes a material adverse change clause, which enables the Lenders to require immediate repayment of the outstanding debt if certain subjective acceleration provisions are triggered. The material adverse change clause covers provisions including a material impairment of underlying collateral, change in business operations or condition or material impairment of the Company's prospects for repayment of any portion of the remaining debt obligation.

In connection with the Loan Agreement, the Lenders were issued warrants to purchase an aggregate of up to 63,559 shares of the Company's common stock at a per share exercise price of $9.44. The warrants are exercisable for 10 years. The fair value of the warrants was estimated to be $0.6 million using the Black-Scholes valuation model and was recorded at issuance as debt discount to the term loan with a corresponding increase to additional paid in capital in the consolidated balance sheet.

The term loan bore interest at an annual rate equal to the greater of (i) 8.75% or (ii) the sum of the prevailing prime rate (as report by the Wall Street Journal) plus 5.25%. Payments under the loan were interest-only until January 1, 2016, followed by equal monthly payments of principal and interest through the scheduled maturity date of December 1, 2018.

On April 23, 2015, in connection with the sale of the Zohydro ER business, the Company and the Lenders entered into an amendment to the Loan Agreement, which terminated all encumbrances on the Company's personal property related to its Zohydro ER business.

On June 17, 2016, the Company entered into a second amendment (the Second Amendment) to the Loan Agreement with the Lenders. The Second Amendment modified the loan repayment terms to be interest-only from July 1, 2016 to February 1, 2018, followed by equal monthly payments of principal and interest through the new maturity date of July 1, 2020. Under the terms of the Second Amendment, the interest rate applicable to the term loan bears interest at an annual rate equal to the greater of (i) 7.00% or (ii) the sum of the prevailing prime rate (as report by the Wall Street Journal) plus 3.25%. In addition, the Second Amendment terminated the revolving credit facility previously available under the Loan Agreement. In connection with the Second Amendment, the Company paid (i) the end of term fee of $1.0 million due under the Loan Agreement as a result of this refinancing transaction and (ii) the end of term fee of $0.1 million with respect to the termination of the revolving credit facility. The Second Amendment also includes an end of term fee of $1.4 million payable on July 1, 2020, or upon early repayment of the term loan. An early repayment will be subject to a prepayment penalty of $0.2 million.

The Loan Agreement required the Company to establish a controlled deposit account with SVB containing at least 85% of the Company's account balances at all financial institutions which can be utilized by the Lenders to satisfy the obligations in the event of default. The Second Amendment permitted the Company to maintain collateral account balances exceeding the greater of (i) $50.0 million, or (ii) 50% of the Company's total collateral account balances (other than specifically excluded accounts), with financial institutions other than the Lenders; provided that, if the Company's total collateral account balances are below $50.0 million, all such balances will be maintained with the Lenders. Other affirmative covenants include, among others, requiring the Company to maintain legal existence and governmental approvals, deliver certain financial reports, maintain

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

insurance coverage and satisfy certain requirements regarding accounts receivable. Negative covenants include, among others, restrictions on transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, selling assets and suffering a change in control, in each case subject to certain exceptions. The Company was in compliance with these covenants at December 31, 2016 and 2015.

Working Capital Advance Note Payable

In connection with the sale of the Sumavel DosePro business, Endo provided the Company with an interest-free working capital advance of $7.0 million, which is evidenced by a promissory note. The note payable is secured by a lien on the Company's Sumavel DosePro raw materials and unreleased finished inventory. The note payable was initially recorded on the consolidated balance sheet net of a $4.7 million debt discount. The debt discount is being amortized as interest expense using the effective interest method over the supply agreement's initial term of eight years, as the note payable matures upon termination of the related supply agreement.

In the fourth quarter of 2016, the Company changed its classification of the note payable from long-term to current as a result of the impending termination of the supply agreement (see Note 6) because the extinguishment of the liability is reasonably expected to require the use of existing current assets, including cash and the underlying collateral of Sumavel DosePro materials and unreleased finished inventory. The carrying value of the note payable was $3.3 million and $2.8 million at December 31, 2016 and 2015, respectively.

10. Stockholders' Equity

Common Stock

The number of authorized shares of the Company's common stock is 50.0 million shares with a par value of $0.001 par value. Holders of the Company's common stock are entitled to one vote per share.

At December 31, 2016, common stock reserved for future issuance is as follows (in thousands):

	December 31,	
	2016	2015
Stock options and restricted stock units outstanding	3,388	2,714
Warrants to purchase common stock	1,975	1,975
Shares authorized for future issuance under equity and purchase plans	952	678
	6,315	5,367

Common Stock Warrants

In December 2014, in connection with a financing transaction, the Company issued warrants to Oxford and SVB exercisable into an aggregate of 63,559 shares of common stock. The warrants are exercisable at $9.44 per share of common stock and have a term of 10 years. In 2015, warrants to purchase 31,779 shares of common stock were exercised in a cashless exercise whereby 16,719 shares were issued and 15,060 shares withheld to satisfy the exercise price of the warrants. The value of the warrants of approximately $0.6 million was recorded as debt discount and additional paid in capital upon issuance.

In July 2012, in connection with a public offering of common stock and warrants, the Company sold warrants to purchase 1,973,025 shares of common stock. The warrants are exercisable at an exercise price of $20.00 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). There were no exercises for these warrants in 2016 and 2015. In 2014, warrants to purchase 58,156 shares of common stock were exercised. The fair value of outstanding warrants issued in connection with the 2012 public offering was approximately $0.7 million and $6.1 million as of December 31, 2016 and 2015, respectively.

In July 2011, in connection with a financing agreement, the Company issued a warrant to Healthcare Royalty Partners, exercisable immediately upon issuance, to purchase up to 28,125 shares of common stock. The warrant has an exercise price of $72.00 per share of common stock with a term of 10 years. As the warrant included covenants where compliance under certain circumstances were not within the Company's control, the warrant was recorded as a liability and is being marked to market at

each reporting date (see Note 2) while outstanding. The fair value of the warrant was approximately $0.1 million and $0.1 million as of December 31, 2016 and 2015, respectively.

In June 2011, and in connection with entering into an amendment to the second amended and restated loan and security agreement with Oxford and Silicon Valley Bank (the Oxford Agreement), the Company issued warrants to Oxford and Silicon Valley Bank exercisable into an aggregate of 3,306 shares of common stock. The warrants are exercisable at $30.24 per share of common stock and have a term of 7 years. The value of the warrants of approximately $0.1 million was recorded as debt discount and additional paid in capital in the consolidated balance sheet as of December 31, 2011.

11. Stock-Based Compensation

Description of Equity Incentive Plans

In 2006, the Company adopted the 2006 Equity Incentive Award Plan, as amended, (the 2006 Plan) under which 141,750 shares of common stock were reserved for issuance to employees, directors and consultants of the Company. 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 with 25% vesting on the first anniversary of the vesting commencement date and 1/48th each month thereafter.

In 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 280,459 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 canceled 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.

Service-based options granted pursuant to the 2010 Plan generally vest over four years and vest with 25% vesting on the first anniversary of the vesting commencement date and 1/48th each month thereafter. Performance-based options are subject to the employee's continued service and become vested and exercisable based on the completion of a specified regulatory milestone. Service-based restricted stock units granted pursuant to the 2010 Plan generally cliff vest one year from the date of grant.

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 1,162,500, 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, 2016 and 2015, 571,778 and 324,713 shares of common stock were available for future issuance under the Restated 2010 Plan, respectively.

On December 4, 2013, the Company adopted the Employment Inducement Equity Incentive Award Plan (the Inducement Plan). The terms of the Inducement Plan are substantially similar to the terms of the Company's 2010 Equity Incentive Award Plan with two principal exceptions: (1) incentive stock options may not be granted under the Inducement Plan; and (2) the annual compensation paid by the Company to specified executives will be deductible only to the extent that it does not exceed $1.0 million, as the conditions of Section 162(m) of the Internal Revenue Code will not be met. The Inducement Plan was adopted by the board of directors without stockholder approval pursuant to Rule 5635(c)(4) of the NASDAQ Listing Rules.

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

The Company has initially reserved 337,500 shares of the Company's common stock for issuance pursuant to awards granted under the Inducement Plan. In accordance with Rule 5635(c)(4) of the NASDAQ Listing Rules, awards under the Inducement Plan may only be made to an employee who has not previously been an employee or member of the board of directors of the Company or any parent or subsidiary, or following a bona fide period of non-employment by the Company or a parent or subsidiary, if he or she is granted such award in connection with his or her commencement of employment with the Company or a subsidiary and such grant is an inducement material to his or her entering into employment with the Company or such subsidiary. As of December 31, 2016 and 2015, there were 236,625 and 202,230 shares of common stock available for future issuance under the Inducement Plan, respectively.

The 2006 Plan, Restated 2010 Plan and Inducement Plan are intended to encourage ownership of stock by employees, consultants and non-employee directors of the Company, as applicable, and with respect to the 2006 Plan and Restated 2010 Plan, 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 the issuance of new shares.

The following sections summarize activity under the Company's stock plans.

Stock Options

The following table summarizes the Company's stock option activity for 2016:

	Shares (in thousands)	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2015	2,714	$ 17.18		
Granted	902	$ 10.02		
Exercised	(6)	$ 7.27		
Canceled	(325)	$ 19.88		
Outstanding at December 31, 2016	3,285	$ 15.46	7.5	$ 2,458
Exercisable at December 31, 2016	1,887	$ 17.76	6.5	$ 651
Vested and expected to vest at December 31, 2016	3,196	$ 15.56	7.5	$ 2,340

As of December 31, 2016, options outstanding include 137,000 shares that become vested and exercisable upon the achievement of a certain regulatory milestone for the Company's ZX008 product candidate. The total intrinsic value of options exercised in 2016, 2015 and 2014 was $24,000, $0.3 million and $0.3 million, respectively.

Restricted Stock Units

The following table summarizes the Company's restricted stock unit activity for 2016:

	Shares (in thousands)	Weighted Average Fair Value per Share at Grant Date
Nonvested at December 31, 2015	—	$ —
Granted	112	10.31
Vested	—	—
Canceled	(9)	10.35
Nonvested at December 31, 2016	103	10.31

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The restricted stock units granted in 2016 cliff vests on the earlier of two years from the date of grant or the achievement of a certain regulatory milestone for the Company's ZX008 product candidate.

The intrinsic value of restricted stock units vested during 2014 was $3.0 million. There were no vestings of restricted stock units in 2016 and 2015. As of December 31, 2016, nonvested restricted stock units had a weighted average remaining contractual term of 1.2 years with an intrinsic value of $1.3 million.

Employee Stock Purchase Plan (ESPP)

In 2010, the Company adopted the 2010 Employee Stock Purchase Plan (Purchase Plan), which allows employees to purchase shares of the Company's common stock during specified offering periods at a discount to the fair market value at the time of purchase. The Purchase Plan is implemented by overlapping, twelve-month offering periods and each offering period may contain up to two purchase periods of six months each. At any one time, there may be up to two offering periods under the Purchase Plan. In general, a new twelve-month offering period commences on each June 1 and December 1 of a calendar year.

Stock may be purchased under the Purchase Plan at a price equal to 85% of the fair market value of the Company's stock on either the date of purchase or the first day of an offering period, whichever is lower. Eligible employees may elect to withhold up to 20% of their compensation through payroll deductions during an offering period for the purchase of stock. The Purchase Plan contains a reset provision whereby if the price of the Company's common stock on the first day of a new offering period is less than the price on the first day of any preceding offering period, all participants in the preceding offering period with higher first day price will be automatically withdrawn from such offering periods and re-enrolled in the new offering period. The reset feature, when triggered, will be accounted for as a modification to the original offering period, resulting in incremental expense to be recognized over the twelve-month period of the new offering.

The Purchase Plan limits the maximum number of shares that may be purchased by any one participant in an offering period to 2,500 shares. In addition, the Internal Revenue Code limits purchases under an ESPP to $25,000 worth of stock in any one calendar year, valued as of the first day of the offering period.

At December 31, 2016 and 2015, a total of 147,576 and 151,490 shares of common stock were reserved for issuance under the Purchase Plan, respectively. A total of 35,164, 25,204, and 62,987 shares were issued under the Purchase Plan in 2016, 2015 and 2014, respectively.

Stock-Based Compensation

Valuation of Equity Awards

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,		
	2016	2015	2014
Stock Options			
Risk free interest rate	1.1% to 2.1%	1.5% to 1.9%	1.6% to 2.0%
Expected term	5.1 to 6.1 years	5.1 to 6.1 years	5.1 to 6.1 years
Expected volatility	76.5 to 78.1%	76.7 to 79.2%	79.7 to 84.9%
Expected dividend yield	—%	—%	—%
Weighted-average fair value of option on grant date	$6.69	$8.37	$18.58
Employee Stock Purchase Plan			
Risk free interest rate	0.5% to 0.8%	0.1% to 0.5%	0.1%

Expected term	0.5 to 1.0 years	0.5 to 1.0 years	0.5 to 1.0 years
Expected volatility	59.5% to 71.3%	67.4% to 77.8%	65.0% to 83.2%
Expected dividend yield	—%	—%	—%

The risk-free interest rate assumption was based on the rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the stock option or purchase right being valued. The assumed dividend yield was zero as the Company currently does not intend to pay 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

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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, when necessary, 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.

Restricted Stock Units

The fair value of restricted stock units granted is determined based on the price of the Company's common stock on the date of grant.

Stock-Based Compensation Expense

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

	Year Ended December 31,		
	2016	2015	2014
Cost of revenue	$386	$390	$467
Research and development	1,924	1,266	1,236
Selling, general and administrative	5,043	5,285	5,833
Total	$7,353	$6,941	$7,536

As of December 31, 2016, there was approximately $9.4 million of total unrecognized compensation costs related to outstanding equity awards, which is expected to be recognized over a weighted average period of 2.3 years.

At December 31, 2016, there were 32,000 unvested options and RSUs outstanding to consultants, with approximately $0.3 million of related unrecognized compensation expense based on a December 31, 2016 measurement date. These unvested stock options outstanding to consultants are expected to vest over approximately 2.5 years. In accordance with accounting guidance for stock-based compensation, the Company remeasures 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 (income) recognized for equity awards to consultants was $0.1 million, $0.2 million and $(0.2) million for 2016, 2015 and 2014, respectively, and was included in the consolidated statement of operations within selling, general and administrative expense.

12. Employee Benefit Plan

Effective February 1, 2007, the Company 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 Plan also provides the Company to make discretionary matching contributions. In 2016, the Company made discretionary matching contributions of $0.1 million. There were zero discretionary contributions made in 2015 and 2014.

13. 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 balance of unrecognized tax benefits at December 31, 2016 of $1.2 million are tax benefits that, if the Company recognizes them, would not impact the Company's effective tax rate as long as they remain subject to a full valuation allowance.

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Notes to Consolidated Financial Statements (continued)

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

	December 31,		
	2016	2015	2014
Beginning balance of unrecognized tax benefits	$1,132	$1,019	$899
Gross increases based on tax positions related to current year	116	113	120
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	$1,248	$1,132	$1,019

The Company's accounting policy for interest and penalties related to income tax matters are classified as income tax expense and was zero for all periods presented.

The Company is subject to taxation in the U.S. and various state and foreign jurisdictions. The Company's tax years for 2008 and forward can be subject to examination by the U.S. and various state and foreign tax authorities due to the carryforward of net operating losses.

For financial reporting purposes, (loss) income from continuing operations before income taxes includes the following components (in thousands):

	December 31,		
	2016	2015	2014
United States	(24,285)	(40,845)	62,479
Foreign	(45,349)	(16,760)	(908)
Total	$(69,634)	$(57,605)	$61,571

At December 31, 2016, the Company's U.S. federal, state, and foreign income tax net operating loss carryforwards were approximately $208.9 million, $191.3 million and $63.5 million, respectively, which may be subject to limitations as described below. If not utilized, the federal tax loss carryforwards will begin to expire in 2026 and the state tax loss carryforwards will begin to expire in 2016. In addition, the Company has federal and California research and development income tax credit carryforwards of $3.0 million and $3.6 million, respectively. If not utilized, the federal research and development income tax credit carryforwards will begin to expire in 2026. The California research and development income tax credit carryforwards do not expire and can be carried forward indefinitely.

The Company has elected the "with and without method – direct effects only", under the applicable accounting guidance for income taxes, with respect to recognition of stock option windfall tax benefits within additional paid-in capital and will utilize general net operating losses to offset taxable income before utilizing net operating losses attributable to windfall tax benefits.

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, 2016 the Company had three 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 $1.9 million 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, 2011 by $121.1 million and research and development income tax credits as of December 31, 2011 by $3.0 million. The Company also reduced its California net operating loss carryforwards as of December 31, 2011 by $53.3 million as a result of the second ownership change. The Company had a third ownership change as defined by IRC Sections 382 and 383, which occurred in January 2014. There was no forfeiture in federal and California net operating loss carryforwards or research and development income tax credits as a result of the third

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.

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

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

	December 31,		
	2016	2015	2014
Tax at statutory rate	$(23,675)	$(19,586)	$20,934
State taxes, net of federal benefit	(65)	(691)	1,499
Change in valuation allowance	16,024	(14,042)	(12,968)
Valuation allowance adjustment for continuing operations	—	15,498	—
Permanent interest disallowed	(1,832)	375	(8,608)
Foreign rate change - Impact on Deferred Taxes	521	(1,993)	—
Other permanent differences	1,307	114	1,226
Research and development tax credits	(145)	(1,060)	(1,387)
State tax rate benefit	578	2,181	(503)
Foreign rate differential	6,122	2,550	—
Credits and other	217	753	(109)
Tax (benefit) expense	$(948)	$(15,901)	$84

ASC 740-20 requires total income tax expense or benefit to be allocated among continuing operations, discontinued operations, extraordinary items, other comprehensive income and items charged directly to shareholders' equity. This allocation is referred to as intra-period tax allocation. As a result of the gain recognized in discontinued operations from the sale of the Company's Zohydro ER business to Pernix in 2015, ASC 740-20-45-7 required us to allocate a tax expense to discontinued operations and a tax benefit to continuing operations. The amount of income tax expense recorded as part of discontinued operations is limited to the tax benefit from income from continuing operations. Accordingly, the Company has recorded a tax expense of $14.1 million in 2015 in discontinued operations and a corresponding income tax benefit from continuing operations. The remaining tax benefit to continuing operations primarily relates to tax rate reductions enacted in the U.K. in November 2015 which resulted in a decrease to deferred tax liability.

Significant components of the Company's deferred tax assets are presented below. A valuation allowance of $112.3 million and $96.3 million as of December 31, 2016 and 2015, respectively, has been established against the deferred tax assets for which it is more likely than not that the tax benefit will not be realized.

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Notes to Consolidated Financial Statements (continued)

	December 31,	
	2016	2015
Deferred tax assets:		
Net operating losses	$90,543	$72,402
Capitalized research and development	4,504	5,768
Accrued expenses	1,240	1,266
Research and development credits	4,596	4,451
Accrued product returns	34	324
Inventory reserve and UNICAP	175	1,063
Amortization	1,680	1,998
Depreciation	1,533	—
Deferred revenue	475	3,494
Other, net	7,542	6,432
Total deferred tax assets	112,322	97,198
Less valuation allowance	(112,322)	(96,298)
Net deferred tax assets	—	900
Deferred tax liabilities:		
Depreciation	—	(900)
IPR&D	(17,425)	(18,450)
Total deferred tax liabilities	(17,425)	(19,350)
Net deferred tax liability	$(17,425)	$(18,450)

On December 31, 2015, the California Supreme Court overturned the California Appellate court decision on The Gillette Company et al. v. California Franchise Tax Board. The court held that the taxpayers couldn't elect an evenly weighted, three-factor apportionment formula pursuant to the Multistate Tax Compact, or MTC. The Company had previously elected the three-factor apportionment formula pursuant to the MTC for 2013 and 2014. As a result of the California Supreme Court decision, the Company has reduced its deferred tax assets and offsetting valuation allowance related to the California NOL calculated in 2013 and 2014 pursuant to the MTC election.

The Company recorded income tax expense of $52,000, $45,000 and $84,000 in 2016, 2015 and 2014, respectively, related to the taxable income generated by its wholly-owned subsidiary, Zogenix Europe Limited. In addition, the Company recorded income tax benefit of $1.0 million, $2.1 million and zero in 2016, 2015 and 2014, respectively, related to the operations of its other wholly-owned subsidiary, Zogenix International Limited. The tax benefits were due to income tax rate reductions enacted in the United Kingdom in 2016 and 2015, which resulted in a decrease in the Company's deferred tax liabilities.

14. Summarized Quarterly Data (Unaudited)

The following financial information reflects all adjustments, which includes all normal recurring adjustments and the items described in (1) to (4) below, 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 2016 and 2015 is as follows:

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Notes to Consolidated Financial Statements (continued)

	2016 Quarter Ended			
	March 31	June 30	September 30	December 31[4]
	(in thousands, except per share amounts)			
Revenue	$9,206	$2,088	$ 6,570	$ 10,986
Gross profit	$1,402	$27	$ 179	$ 5,069
Loss from continuing operations	$(10,220)	$(18,246)	$ (16,618)	$ (23,602)
Loss (income) from discontinued operations	$(169)	$(582)	$ (379)	$ 109
Net loss	$(10,389)	$(18,828)	$ (16,997)	$ (23,493)
Net loss per share, basic and diluted	$(0.42)	$(0.76)	$ (0.69)	$ (0.95)

	2015 Quarter Ended			
	March 31	June 30 [1]	September 30 [2]	December 31[3]
	(in thousands, except per share amounts)			
Revenue	$4,614	$7,367	$ 9,120	$ 6,081
Gross profit	$691	$1,564	$ 1,340	$ 1,231
Loss from continuing operations	$(10,165)	$(6,696)	$ (12,981)	$ (11,862)
(Loss) income from discontinued operations	$(12,696)	$79,160	$ (1,635)	$ 3,019
Net (loss) income	$(22,861)	$72,464	$ (14,616)	$ (8,843)
Net (loss) income per share, basic and diluted	$(1.19)	$3.78	$ (0.65)	$ (0.36)

(1) Net income from discontinued operations included an after-tax gain on sale of the Zohydro ER business of $75.6 million. Net loss from continuing operations included a tax benefit of $6.9 million for this divestiture.

(2) Net loss from continuing operations included an impairment charge for investments acquired in connection with the sale of the Zohydro ER business of $5.5 million, offset by a $5.5 million tax benefit for this divestiture. Net loss from discontinued operations included an adjustment of $2.5 million to the gain on sale of the Zohydro ER business for incremental income tax expense.

(3) Net loss from continuing operations included a tax benefit related to the sale of Zohydro ER of $3.5 million. Net income from discontinued operations included an adjustment to increase the gain on sale of Zohydro ER business of $2.3 million, which primarily consisted of derecognition of income tax liability due to a reduction in the applicable tax rate, offset by an accrual of $0.4 million related to contingent consideration.

(4) Net loss from continuing operations included impairment charges of $8.4 million for long-lived assets associated with the production of Sumavel DosePro and prepaid royalties (See Note 6).

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SIGNATURES

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

ZOGENIX, INC.

Date: March 9, 2017 By: /s/ Stephen J. Farr
President and Chief Executive Officer

Date: March 9, 2017 By: /s/ Michael P. Smith
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/ STEPHEN J. FARR, PH.D. Stephen J. Farr, Ph.D.	Chief Executive Officer and Director (Principal Executive Officer)	March 9, 2017
/S/ MICHAEL P. SMITH Michael P. Smith	Executive Vice President, Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer)	March 9, 2017
/S/ CAM L. GARNER Cam L. Garner	Chairman of the Board	March 9, 2017
/S/ LOUIS C. BOCK Louis C. Bock	Director	March 9, 2017
/S/ JAMES B. BREITMEYER, M.D., Ph.D. James B. Breitmeyer, M.D., Ph.D	Director	March 9, 2017
/S/ ROGER L. HAWLEY Roger L. Hawley	Director	March 9, 2017
/S/ ERLE T. MAST Erle T. Mast	Director	March 9, 2017
/S/ RENEE TANNENBAUM, Pharm.D. Renee Tannenbaum, Pharm.D.	Director	March 9, 2017

/S/ MARK WIGGINS Mark Wiggins	Director	March 9, 2017

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EXHIBIT INDEX

Exhibit Number	Description
2.1†(18)	Asset Purchase Agreement dated April 23, 2014 by and among the Registrant, Endo Ventures Bermuda Limited and Endo Ventures Limited
2.2†(21)	Sale and Purchase Agreement dated October 24, 2014 by and among the Registrant, Zogenix Europe Limited, Brabant Pharma Limited and Anthony Clarke, Richard Stewart, Ann Soenen-Darcis, Jennifer Watson, Rekyer Securities plc and Aquarius Life Science Limited, as sellers
2.3†(27)	Asset Purchase Agreement, dated March 10, 2015, by and among the Registrant, Pernix Ireland Limited and Pernix Therapeutics Holdings, Inc.
2.4(24)	Amendment to Asset Purchase Agreement, dated April 23, 2015, by and among the Registrant, Pernix Ireland Limited and Pernix Therapeutics Holdings, Inc.
3.1(2)	Fifth Amended and Restated Certificate of Incorporation of the Registrant
3.2(6)	Certificate of Amendment of Fifth Amended and Restated Certificate of Incorporation of the Registrant
3.3(26)	Certificate of Amendment of Fifth Amended and Restated Certificate of Incorporation of the Registrant
3.3(2)	Amended and Restated Bylaws of the Registrant
4.1(3)	Form of the Registrant's Common Stock Certificate
4.2(4)	Second Amendment to Third Amended and Restated Investors' Rights Agreement dated June 30, 2011
4.3(1)	Warrant dated June 30, 2008 issued by the Registrant to CIT Healthcare LLC (subsequently transferred to The CIT Group/Equity Investments, Inc.)
4.4(1)	Transfer of Warrant dated March 24, 2009 from CIT Healthcare LLC to The CIT Group/Equity Investments, Inc.
4.5(4)	Warrant dated July 18, 2011 issued by the Registrant to Cowen Healthcare Royalty Partners II, L.P.
4.6(22)	Warrant dated December 30, 2014 issued to Oxford Finance LLC
4.7(22)	Warrant dated December 30, 2014 issued to Silicon Valley Bank
10.1(2)	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#(2)	2010 Equity Incentive Award Plan and forms of option and restricted stock agreements thereunder
10.5#(2)	2010 Employee Stock Purchase Plan and form of Offering document thereunder

10.6#(1)	Executive Officer Employment Agreement dated March 1, 2010 by and between the Registrant and Ann D. Rhoads
10.7†(1)	Supply Agreement dated September 29, 2004 by and between the Registrant and Dr. Reddy's Laboratories, Inc.
10.8†(1)	Asset Purchase Agreement dated August 25, 2006 by and between the Registrant and Aradigm Corporation
10.9(1)	Lease dated October 31, 2006 by and between the Registrant and Emery Station Joint Venture, LLC
10.10(1)	First Amendment to Lease dated July 10, 2007 by and between the Registrant and Emery Station Joint Venture, LLC
10.11(1)	Second Amendment to Lease dated October 20, 2009 by and between the Registrant and Emery Station Joint Venture, LLC
10.12†(2)	Manufacturing Services Agreement dated November 1, 2008 by and between the Registrant and Patheon U.K. Ltd.

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10.13†(1)	Commercial Manufacturing and Supply Agreement dated April 1, 2009 by and between the Registrant and MGlas AG
10.14†(4)	Development and License Agreement dated July 11, 2011 by and between the Registrant and Durect Corporation
10.15#(4)	2011 Annual Incentive Plan
10.16†(8)	Co-Marketing and Option Agreement dated March 29, 2012 by and between the Registrant and Battelle Memorial Institute
10.17†(11)	Manufacturing Services Agreement dated February 28, 2013 by and between the Registrant and Patheon UK Limited
10.18(11)	Independent Director Compensation Policy as amended and restated effective March 15, 2013
10.19(11)	Annual Incentive Plan as amended and restated effective March 15, 2013
10.20†(11)	Amendment No. 1 to the Development and License Agreement dated March 18, 2013 and made retroactive to January 1, 2013 by and between the Registrant and Durect Corporation
10.21†(11)	First Amendment to the Co-marketing and Option Agreement dated March 29, 2012 entered into as of March 21, 2013 by and between the Registrant and Battelle Memorial Institute
10.22(12)	Form of Restricted Stock Unit Award Agreement under the 2010 Equity Incentive Award Plan
10.23†(13)	Co-promotion Agreement dated June 27, 2013, by and between the Registrant and Valeant Pharmaceuticals North America LLC
10.24†(15)	Amendment #1 to the Manufacturing Services Agreement, dated February 28, 2013 with an effective date of November 1, 2013, by and between the Registrant and Patheon UK Limited
10.25†(15)	Co-Marketing and Development Services Agreement dated November 26, 2013, by and between the Registrant and Battelle Memorial Institute
10.26#(14)	Employment Inducement Equity Incentive Award Plan and form of stock option agreement thereunder
10.27#(15)	Annual Incentive Plan as amended and restated effective, December 4, 2013
10.28(15)	Employment Agreement dated December 17, 2013 by and between the Registrant and Bradley S. Galer, M.D.
10.29†(15)	Development and Option Agreement dated November 1, 2013 by and between the Registrant and Altus Formulation, Inc.
10.30†(16)	Amendment No. 1 - Development and Option Agreement dated March 10, 2014 by and between the Registrant and Altus Formulation Inc.
10.31(16)	Independent Director Compensation Policy as amended and restated effective March 21, 2014

10.32#(17)	Annual Incentive Plan as amended and restated effective July 22, 2014
10.33†(18)	Manufacturing and Supply Agreement dated May 16, 2014 by and between the Registrant and Endo Ventures Limited
10.34†(19)	License Agreement dated May 16, 2014 by and between the Registrant and Endo Ventures Bermuda Limited
10.35†(19)	Third Amendment to License Agreement dated September 12, 2014 by and between the Registrant and Daravita Limited
10.36†(19)	First Amendment to Commercial Manufacturing and Supply Agreement dated September 12, 2014 by and between the Registrant and Daravita Limited
10.37†(19)	Amendment No. 2 - Development & Option Agreement dated September 15, 2014 by and between the Registrant and Altus Formulation, Inc.
10.38†(19)	Collaboration and License Agreement dated as of October 23, 2014 by and among The Katholieke Universiteit Leuven, University Hospital Antwerp and Brabant Pharma Limited
10.39(19)	Office Lease dated August 5, 2014 by and between the Registrant and Kilroy Realty, L.P.

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10.40(20)	Controlled Equity OfferingSM Sales Agreement between the Registrant and Cantor Fitzgerald & Co.
10.41(22)	Loan and Security Agreement dated December 30, 2014 by and among the Registrant, Oxford Finance LLC, as collateral agent, and the lenders party thereto from time to time, including Oxford Finance LLC and Silicon Valley Bank
10.42†(23)	Amendment No. 3 - Development & Option Agreement dated October 30, 2014 by and between the Registrant and Altus Formulation, Inc.
10.43(24)	First Amendment to Loan and Security Agreement, dated April 23, 2015, by and among the Registrant, Oxford Finance LLC, as collateral agent for the Lenders (as defined therein) and Silicon Valley Bank
10.44#(25)	General Release of Claims, dated April 23, 2015, by and between the Registrant and Roger L. Hawley
10.45#(25)	Annual Incentive Plan as amended and restated effective April 27, 2015
10.46#(26)	Amended and Restated Employment Agreement, dated April 27, 2015, by and between the Registrant and Stephen J. Farr, Ph.D.
10.47#(26)	Employment Agreement, dated June 29, 2015, by and between the Registrant and Gail M. Farfel, Ph.D.
10.48#(26)	Employment Agreement, dated June 29, 2015, by and between the Registrant and Thierry Darcis
10.49#(26)	Independent Director Compensation Policy as amended and restated effective April 23, 2015
10.50(26)	Third Amendment to Office Lease, dated July 20, 2015, by and between the Registrant and Emery Station Joint Venture, LLC
10.50(26)	Third Amendment to Office Lease, dated July 20, 2015, by and between the Registrant and Emery Station Joint Venture, LLC
10.51(28)	Independent Director Compensation Policy as amended and restated effective March 8, 2016
10.52(28)	Amendment #2 to the Manufacturing Services Agreement, dated April 28, 2016, by and between the Registrant and Patheon UK Limited
10.53(29)	Controlled Equity OfferingSM Sales Agreement, dated May 10, 2016, by and between the Registrant and Cantor Fitzgerald & Co.
10.54(30)	Second Amendment to Loan and Security Agreement, dated June 17, 2016, by and among the Registrant, Oxford Finance LLC, as collateral agent for the Lenders (as defined therein) and Silicon Valley Bank
10.55(31)	Amendment #3 to the Manufacturing Services Agreement, dated July 31, 2016, by and between the Registrant and Patheon UK Limited
10.56†(5)	Amendment #4 to the Manufacturing Services Agreement, dated October 31, 2016, by and between the Registrant and Patheon UK Limited
21.1(5)	Subsidiaries of the Registrant.

23.1	Consent of Independent Registered Public Accounting Firm
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
32.1	Certification of Chief Executive Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
32.2	Certification of Chief Financial Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)
101	The following financial statements from Zogenix, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2016, filed on March 9, 2017, formatted in XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations; (iii) Consolidated Statements of Comprehensive (Loss) Income, (iv) Consolidated Statements of Cash Flows, and (v) the Notes to Consolidated Financial Statements.

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(1) Filed with the Registrant's Registration Statement on Form S-1 on September 3, 2010 (Registration No. 333-169210).
(2) Filed with Amendment No. 2 to Registrant's Registration Statement on Form S-1 on October 27, 2010 (Registration No. 333-169210).
(3) Filed with Amendment No. 3 to the Registrant's Registration Statement on Form S-1 on November 4, 2010 (Registration No. 333-169210).
(4) Filed with the Registrant's Quarterly Report on Form 10-Q on August 11, 2011.
(5) Filed herewith.
(6) Filed with the Registrant's Quarterly Report on Form 10-Q on November 8, 2012.
(7) Filed with the Registrant's Quarterly Report on Form 10-K on March 12, 2012.
(8) Filed with the Registrant's Quarterly Report on Form 10-Q on May 15, 2012.
(9) Filed with the Registrant's Quarterly Report on Form 10-Q on August 9, 2012.
(10) Filed with the Registrant's Annual Report on Form 10-K on March 15, 2013.
(11) Filed with the Registrant's Quarterly Report on Form 10-Q on May 9, 2013.
(12) Filed with the Registrant's Quarterly Report on Form 10-Q on August 8, 2013.
(13) Filed with the Registrant's amendment to its Quarterly Report on Form 10-Q on January 14, 2014.
(14) Filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K on December 5, 2013.
(15) Filed with the Registrant's Annual Report on Form 10-K on March 7, 2014.
(16) Filed with the Registrant's Quarterly Report on Form 10-Q on May 8, 2014.
(17) Filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K on July 24, 2014.
(18) Filed with the Registrant's Quarterly Report on Form 10-Q on August 6, 2014.
(19) Filed with the Registrant's Quarterly Report on Form 10-Q on November 6, 2014.
(20) Filed with the Registrant's Registration Statement on Form S-3 on November 6, 2014 (Registration No. 333-199957).
(21) Filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K/A on December 23, 2014.
(22) Filed with the Registrant's Current Report on Form 8-K on December 31, 2014.
(23) Filed with the Registrant's Annual report on Form 10-K on March 11, 2015.
(24) Filed with the Registrant's Current Report on Form 8-K on April 28, 2015.
(25) Filed with the Registrant's Quarterly Report on Form 10-Q on May 11, 2015.
(26) Filed with the Registrant's Quarterly Report on Form 10-Q on August 10, 2015.
(27) Filed with Amendment No. 1 to the Registrant's Current Report on Form 8-K on August 18, 2015.

† Confidential treatment has been granted or requested, as applicable, 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.