ZOGENIX, INC.
Form 10-K
February 28, 2019
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# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**WASHINGTON, DC 20549**

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# Form 10-K

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| x | **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934** |

**For the fiscal year ended December 31, 2018**

**or**

| | |
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| ¨ | **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**

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# Zogenix, Inc.

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| **Delaware** **(State of Incorporation)** | **20-5300780** **(I.R.S. Employer Identification No.)** |
| **5858 Horton Street, Suite 455 Emeryville, California** | **94608** |

**(510) 550-8300**

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

| | |
|---|---|
| **Common Stock, par** | **The Nasdaq** |

| | |
|---|---|
| **value $0.001 per share** | **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 x No ¨

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Exchange 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 every Interactive Data File required to be submitted 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 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, a smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

| | | |
|---|---|---|
| Large accelerated filer x | Accelerated filer o | |
| Non-accelerated filer o | | Smaller reporting company o |
| | Emerging growth company o | |

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ¨

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

As of June 30, 2018, the aggregate market value of common stock held by non-affiliates of the Registrant, computed by reference to the closing price and shares outstanding, was approximately $1.4 billion.

As of February 15, 2019, there were 42,218,424 shares of the Registrant's common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the Registrant's definitive Proxy Statement to be filed for its 2019 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the Registrant's fiscal year ended December 31, 2018.

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**For the Year Ended December 31, 2018**
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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 of our lead product candidate Fintepla/ZX008;
•the safety and efficacy of our product candidates;
•the timing of submissions to, and decisions made by the U.S. Food and Drug Administration (FDA) and other regulatory agencies, including foreign regulatory agencies, with regards to the demonstration of the safety and efficacy of our product candidates and adequacy of the manufacturing processes related to our product candidates to the satisfaction of the FDA and such other regulatory agencies;
•our ability to obtain, maintain and successfully enforce adequate patent and other intellectual property or regulatory exclusivity protection of our product candidates and the ability to operate our business without infringing the intellectual property rights of others;
•the goals of our development activities and estimates of the potential markets for our product candidates, and our ability to compete within those markets;
•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 Fintepla 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 other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

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Fintepla®, Zogenix™ and DosePro® 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., a Delaware corporation, and its consolidated subsidiaries.

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**Item 1. Business**

**Company Overview**

Zogenix, Inc. (Zogenix, We or the Company) is a pharmaceutical company developing and commercializing transformative central nervous system (CNS) therapies for people living with serious and life-threatening rare CNS disorders and medical conditions. We are currently focused on developing and commercializing CNS therapies to address rare, or "orphan" childhood-onset epilepsy disorders.

We currently own and control worldwide development and commercialization rights to Fintepla/ZX008, our lead product candidate. Fintepla is low-dose fenfluramine under development for the treatment of seizures associated with two rare and catastrophic forms of childhood-onset epilepsy: Dravet syndrome and Lennox-Gastaut syndrome (LGS).

Dravet syndrome is a rare form of pediatric-onset epilepsy with life threatening consequences for patients and for which current treatment options are very limited. Fintepla has received orphan drug designation in the United States and the European Union (EU) for the treatment of Dravet syndrome. In addition, Fintepla for the treatment of Dravet syndrome received Fast Track designation from the U.S. Food and Drug Administration (FDA) in January 2016. In February 2019, we completed our rolling submission of a New Drug Application (NDA) with the FDA and submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for Fintepla for the treatment of seizures associated with Dravet syndrome. The EMA has accepted the MAA and initiated its review.

We initiated our Phase 3 clinical trials for Fintepla for the treatment of seizures associated with Dravet syndrome in North America (Study 1501) in January 2016 and in Europe and Australia in June 2016 (Study 1502). Study 1501 and Study 1502 are each identical randomized, double-blind placebo-controlled studies of Fintepla as adjunctive therapy for patients with uncontrolled seizures who have Dravet syndrome. In January 2017, we announced our plan to report top-line results from Study 1501 and Study 1502 via a prospective merged study analysis approach whereby top-line results from the first approximately 120 subjects randomized into either Study 1501 or 1502 would have their study results analyzed and be reported initially as "Study 1". In April 2017, we completed enrollment of Study 1 and, in September 2017, we announced positive top-line results for the 119 patients included in the Study 1 Phase 3 trial. The Study 1 trial met its primary objective of demonstrating that Fintepla, at a dose of 0.8 mg/kg/day (30mg/day maximum), is superior to placebo as adjunctive therapy in the treatment of Dravet syndrome in children and young adults based on change in the frequency of convulsive seizures between the 6-week baseline observation period and the 14-week treatment period ($p<0.001$). In the trial, Fintepla at a dose of 0.8 mg/kg/day also demonstrated statistically significant improvements versus placebo in all key secondary measures, including the proportion of patients with clinically meaningful reductions in seizure frequency (50% or greater) and longest seizure-free interval. The same analyses comparing a 0.2 mg/kg/day Fintepla dose versus placebo also demonstrated statistically significant improvement compared with placebo. Fintepla was generally well tolerated without any signs or symptoms of valvulopathy or pulmonary hypertension.

In September 2016, we initiated Cohort 1 of Study 1504 that investigated the pharmacokinetic profile and safety of Fintepla when co-administered with the stiripentol regimen (stiripentol, valproate and/or clobazam). Based on the results of the Cohort 1 pharmacokinetic and safety portion of the trial, in February 2017 we initiated the Cohort 2 safety and efficacy portion of Study 1504 utilizing a dose of Fintepla 0.5mg/kg/day (20mg/day maximum). Study 1504 Cohort 2, a two-arm study, compared Fintepla versus placebo across the titration and 12-week maintenance periods at multiple sites located in France, the Netherlands, United States, Canada, Germany, the United Kingdom and Spain. In January 2018, we announced patient enrollment was complete at 87 patients, with 43 patients randomized into the Fintepla-arm and 44 patients randomized to the placebo arm. In July 2018, we reported positive top-line results from Cohort 2 of Study 1504. The study results, which are consistent with those reported in Study 1, successfully met the primary objective of demonstrating that Fintepla, at a dose of 0.5 mg/kg/day, when co-administered with stiripentol regimen (stiripentol, valproate and/or clobazam), was superior to placebo as adjunctive therapy in the treatment of Dravet syndrome in children and young adults based on change in the frequency of convulsive seizures between the 6-week baseline observation period and the 15-week treatment period ($p<0.001$). In the trial, Fintepla at a dose of 0.5 mg/kg/day also demonstrated statistically significant improvements versus placebo in all key secondary measures, the proportion of patients with clinically meaningful reductions in seizure frequency (50% or greater) and longest seizure-free interval. Fintepla was generally well-tolerated in this study, with

the adverse events consistent with those observed in Study 1 and the known safety profile of fenfluramine without any signs or symptoms of valvular heart disease (valvulopathy) or pulmonary hypertension.

Upon completion of our Fintepla Phase 3 trials, eligible patients were permitted to enroll in an ongoing open-label extension (OLE) trial to study the long-term safety and effectiveness of Fintepla (Study 1503). In December 2018, we presented interim data from Study 1503 regarding the effectiveness and overall safety of Fintepla observed in the study, including the long-term cardiovascular assessments and findings at the 72nd Annual Meeting of the American Epilepsy Society (AES). A total of 232 patients from Study 1503 were included in the interim analysis of the OLE trial. As of March 13, 2018, the interim

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cutoff date, the median duration of treatment with Fintepla was 256 days and the range was 58-634 days (equivalent to 161 patient-years of exposure to Fintepla). In this interim analysis population of 232 patients, a total of 22 (9.5%) patients had discontinued treatment for the following reasons: lack of efficacy (16), subject withdrawal (2), adverse event (1), Sudden Unexpected Death in Epilepsy (SUDEP) (1), physician decision (1), and withdrawal by caregiver (1). Approximately 90% of patients remained in the study at the time of the interim analysis. The median percent reduction in monthly convulsive seizure frequency over the entire OLE treatment period was 66.8% (compared with baseline frequency established in the core Phase 3 studies). Over the same period, 64.4% of children and young adults showed a >50% reduction in convulsive seizure frequency and 41.2% showed a >75% reduction. The occurrence of adverse events was consistent with the Phase 3 placebo-controlled studies. The most common adverse events occurring in more than 10% of children and young adults were pyrexia (22%), nasopharyngitis (20%), decreased appetite (16%), influenza (12%), diarrhea (11%), and upper respiratory tract infection (10%). A total of 13.4% of children lost >7% body weight at some point during the trial; in 42% of those children weight loss abated during the period covered by the interim analysis. Over the course of the OLE treatment period, one patient died from SUDEP that was deemed unrelated to Fintepla. A total of 703 color doppler echocardiograms were performed to assess cardiovascular health at baseline, week 4 or 6, and then every 3 months during the OLE trial. No patient developed valvular heart disease (valvulopathy) or pulmonary arterial hypertension at any time after daily treatment with Fintepla.

In February 2019, we completed our rolling submission of a NDA with the FDA and submitted a MAA to the EMA for Fintepla for the treatment of seizures associated with Dravet syndrome. Both applications were based on data from Study 1 and Study 1504 in Dravet syndrome and the interim analysis from Study 1503. The EMA has accepted the MAA and initiated its review.

LGS is another rare, refractory, debilitating pediatric-onset epilepsy with life threatening consequences for patients and for which current treatment options are limited and suboptimal. Beginning in first quarter of 2016, we funded an open-label, dose-finding, investigator-initiated study of the effectiveness and tolerability of Fintepla as an adjunctive therapy 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 clinical trial at the 70th Annual Meeting of the AES. In this interim analysis, Fintepla was observed to provide clinically meaningful improvement in major motor seizure frequency in patients with severe refractory LGS, with 7 out of 13 patients (54%) achieving at least a 50% reduction in the number of major motor seizures, at doses below the 0.8 mg/kg/day maximum allowed dose. In addition, Fintepla was generally well tolerated without any observed signs or symptoms of valvulopathy or pulmonary hypertension. We believe these data indicate that Fintepla has the potential to be a safe and effective adjunctive treatment of major motor seizures for patients with LGS. Based on the strength of the LGS data generated, in the first quarter of 2017, we submitted an Investigational New Drug Application (IND) to the FDA to initiate a Phase 3 program of Fintepla in LGS. Our IND for Fintepla as a potential treatment for LGS became effective in April 2017. In the first half of 2017, Fintepla received orphan drug designation for the treatment of LGS from the FDA in the United States and the EMA in the EU. In November 2017, we announced the initiation of our multicenter global Phase 3 clinical trial of Fintepla as an adjunctive treatment for seizures in patients with LGS (Study 1601) and are currently enrolling patients into the study. In December 2018, we announced that we expect to complete enrollment for Study 1601 in the second half of 2019 and be able to announce top-line results from the study in the first quarter of 2020.

**Our Strategy**

We are committed to developing and commercializing therapeutic solutions for people living with serious and life-threatening rare CNS disorders and medical conditions. Our strategy centers on developing and advancing our lead therapeutic product candidate, Fintepla, low-dose fenfluramine for the treatment of Dravet syndrome, LGS, and potentially other rare and catastrophic epilepsy disorders. In addition to Fintepla, we aim to identify, develop, and advance other transformative therapeutic product candidates with the potential to treat patients living with serious and life-threating rare CNS disorders. The key elements of our strategy are:

•**Seek regulatory approval and commence commercialization of Fintepla for the treatment of patients with Dravet syndrome.** In February 2019, we completed our rolling submission of a NDA with the FDA and submitted a MAA to the EMA for Fintepla for the treatment of seizures associated with Dravet syndrome. Also in February 2019, we entered into a master supply agreement with Aptuit (Oxford) Limited, an Evotec company, or Aptuit, pursuant to

which Aptuit will be our commercial manufacturer and supplier of the fenfluramine active pharmaceutical ingredient (API) used in our product candidate Fintepla. We are continuing to build our internal commercial capabilities for potential commercialization.

•**DevelopingFintepla for the treatment of Lennox-Gastaut syndrome.** In November 2017, we announced the initiation of Study 1601 for Fintepla as an adjunctive treatment of seizures associated with LGS with the enrollment of the first patient into the study. In December 2018, we announced that we expect to complete enrollment for Study 1601 in the second half of 2019 and be able to announce top-line results from the study in the first quarter of 2020. Fintepla received orphan drug designation for the treatment of LGS from the FDA and the EMA in the first half of 2017.

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•**EvaluatingFintepla 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 Fintepla 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 orphan pediatric-onset epilepsy indications where there is a significant unmet medical need. For example, we are evaluating whether Fintepla has the potential to treat patients with Doose Syndrome, another rare pediatric epileptic encephalopathy that is often refractory to currently available anticonvulsant medication. There is currently no FDA approved medication for the treatment of seizures associated with Doose Syndrome. We plan to initiate a Phase 3 placebo-controlled trial in Doose Syndrome in the second half of 2019.

•**Identifyingtransformative, differentiated, promising product development candidates in the therapeutic area of rare CNS disorders for acquisition and further development**. Our business development team focuses on identifying and evaluating 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.

**Our Clinical Product Candidate**

We currently have one product candidate in clinical development being studied as a potential treatment for rare CNS disorders.

***Fintepla (ZX008; Low-Dose Fenfluramine) for Patients with Dravet Syndrome***

Dravet syndrome is a rare childhood-onset 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 most often treatment resistant, meaning that currently available medications and therapies are not able to achieve complete or clinically meaningful seizure control and, in some cases, worsen the condition. Individuals with Dravet syndrome face a higher incidence of Status Epilepticus and SUDEP. These patients suffer from severe cognitive and other developmental impairment throughout life, as well as neurobehavioral disorders such as autistic-like behavior and attention deficit hyperactivity disorder, and motor abnormalities. The prognosis for patients with Dravet syndrome to become seizure free is poor. A recent study by Wu et. al. published by the American Academy of Pediatrics in 2015 reported an incidence rate for Dravet syndrome of approximately 1 per 16,000 live births.

Prior to 2018, there were no FDA-approved treatments indicated for the treatment of seizures associated with Dravet syndrome. In June 2018, the FDA approved the first treatment of seizures associated with Dravet syndrome, Epidiolex® (cannabidiol or CBD) liquid oral solution and in August 2018, the FDA approved a second treatment, Diacomit® (stiripentol), for the treatment of seizures associated with Dravet syndrome in patients who are also taking clobazam. Prior to 2018, the standard of care for the treatment of seizures in patients with Dravet syndrome usually involved a combination of the following anticonvulsant drugs: clobazam, clonazepam, levetiracetam, topiramate, valproic acid, ethosuximide and zonisamide. In addition to the United States, stiripentol is approved in Europe, Canada, Australia and Japan for the treatment of seizures associated with Dravet syndrome in conjunction with valproate and/or clobazam. In Europe, stiripentol was granted an orphan drug designation for the treatment of Dravet syndrome in 2001. 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. Pre-clinical and clinical evidence of the drug's ability to treat refractory pediatric epileptic seizures was first described in the 1980s. Fenfluramine was withdrawn from the market in 1997 because the risk outweighed the benefit in this adult obese population, after cases of heart valve defects and pulmonary hypertension were reported in adults who had taken fenfluramine, most often with phentermine. However, at this time, academic pediatric neurologists in Belgium continued to evaluate low doses of fenfluramine in a small number of refractory patients under a government approved compassionate use 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 the original Dravet syndrome patients being treated in Belgium under this government approved protocol at the 70th AES Annual Meeting. At that time ten original patients who started treatment with fenfluramine prior to 2010 had been treated with low-dose fenfluramine for a mean of 17.5 years (range: 7-28 years) From the analysis, low-dose fenfluramine, as an adjunctive therapy to standard antiepileptic

drugs, was providing these difficult to treat patients with long-term, durable seizure control. As reported at the meeting, for the most immediate past six years of treatment leading up to the analysis, 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 developed any clinically meaningful signs or symptoms of cardiac valvulopathy or pulmonary hypertension, while two patients had mild and stable cardiac valve thickening

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on the most recent cardiac echocardiogram that was deemed to be clinically unimportant. After 2010, an additional 11 Dravet syndrome patients started adjuvant treatment with low-dose fenfluramine under the Belgium government approved protocol and data on this cohort was presented at the 71st AES Annual Meeting. The mean age at start of fenfluramine in this cohort was 12.5 years (range, 1- 30 years) and treatment with fenfluramine was for a median duration of 3.0 years (range, 1- 7 years). Ninety-one percent of these patients had a clinically meaningful reduction (≥50%) and 73% had substantial reductions (≥75%) in major motor seizure frequency at the prior visit. Fenfluramine was generally well tolerated with no clinical and/or echocardiographic signs of cardiac valvulopathy or pulmonary hypertension. In this ongoing Belgian study of low dose fenfluramine treating refractory Dravet syndrome patients, no patient has stopped treatment for any adverse event.

Because of the known cardiac side effects of fenfluramine reported when prescribed in higher doses for the treatment of adult obesity (without baseline cardiac data), the ongoing Belgian study requires ongoing periodic evaluations of the heart and, in particular, the heart valves and measures assessing for the presence of pulmonary hypertension 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 29-year study period. There have been no clinically significant findings related to cardiac valvulopathy and no reports of pulmonary hypertension in any Fintepla or low-dose fenfluramine studies to date.

We have participated in formal meetings with regulatory agencies in the United States and the EU to obtain concurrence on remaining pre-clinical and clinical requirements for regulatory approval. Based upon this information, we believe our two pivotal placebo-controlled Phase 3 studies in Dravet syndrome will be sufficient to support an application for regulatory approval of Fintepla in the United States and in Europe. The FDA accepted our IND for Fintepla for the treatment of Dravet syndrome in December 2015. We initiated our Phase 3 clinical trials in North America (Study 1501) in January 2016 and in Europe and Australia in June 2016 (Study 1502). Study 1501 and Study 1502 are each identical randomized, double-blind, placebo-controlled studies of Fintepla as adjunctive therapy for patients with uncontrolled seizures who have Dravet syndrome. In January 2017, we announced our plan to report top-line results from Study 1501 and Study 1502 via a prospective merged study analysis approach whereby top-line results from the first approximately 120 subjects randomized into either Study 1501 or 1502 would have their study results analyzed and be reported initially as “Study 1.” In April 2017, we completed enrollment of Study 1 and, in September 2017, we announced positive top-line results for the 119 patients included in the Study 1 Phase 3 trial. The Study 1 trial met its primary objective of demonstrating that Fintepla, at a dose of 0.8 mg/kg/day, was superior to placebo as adjunctive therapy in the treatment of Dravet syndrome in children and young adults based on change in the frequency of convulsive seizures between the 6-week baseline observation period and the 14-week treatment period ($p<0.001$). In the trial Fintepla 0.8 mg/kg/day also demonstrated statistically significant improvements versus placebo in all key secondary measures, including the proportion of patients with clinically meaningful reductions (50% or greater) in convulsive seizure frequency and longest seizure-free interval. The same analyses comparing a 0.2 mg/kg/day Fintepla dose versus placebo also resulted in statistically significant improvement compared with placebo. Patients completing the Phase 3 trials are given the opportunity to enroll in an open label long-term extension safety study (Study 1503).

In September 2016, we initiated Part 1 of Study 1504, a two-part, double blind, randomized, two arm pivotal Phase 3 clinical trial of Fintepla in Dravet syndrome patients who are taking stiripentol, valproate and/or clobazam as part of their baseline standard care. Part 1 investigated the pharmacokinetic profile and safety of Fintepla when co-administered with the stiripentol regimen (stiripentol, valproate and/or clobazam). Based on the results of the pharmacokinetic and safety portion of the trial, in February 2017 we initiated the safety and efficacy portion of Study 1504 utilizing a dose of Fintepla 0.5mg/kg/day (20mg/day maximum). Study 1504, a two-arm study, compared Fintepla versus placebo across the titration and 12-week maintenance periods at multiple sites located the Netherlands, United States, Canada, Germany, the United Kingdom and Spain. In January 2018, we announced patient enrollment was complete at 87 patients, with 43 patients randomized into the Fintepla-arm and 44 patients randomized to the placebo arm.

In July 2018, we reported positive top-line results from Cohort 2 of Study 1504. The study results, which are consistent with those reported in Study 1, successfully met the primary objective of demonstrating that Fintepla, at a dose of 0.5 mg/kg/day, when co-administered with stiripentol regimen (stiripentol, valproate and/or clobazam), was

superior to placebo as adjunctive therapy in the treatment of Dravet syndrome in children and young adults based on change in the frequency of convulsive seizures between the 6-week baseline observation period and the 15-week treatment period ($p<0.001$). In the trial, Fintepla at a dose of 0.5 mg/kg/day also demonstrated statistically significant improvements versus placebo in all key secondary measures, the proportion of patients with clinically meaningful reductions in seizure frequency (50% or greater) and longest seizure-free interval. Fintepla was generally well-tolerated in this study, with the adverse events consistent with those observed in Study 1 and the known safety profile of fenfluramine without any signs or symptoms of valvular heart disease (valvulopathy) or pulmonary hypertension.

Upon completion of our Fintepla Phase 3 trials, eligible patients were permitted to enroll in an ongoing OLE trial to study the long-term safety and effectiveness of Fintepla (Study 1503). In December 2018, we presented interim data from Study 1503 regarding the effectiveness and overall safety of Fintepla observed in the study, including the long-term cardiovascular

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assessments and findings at the 72nd Annual Meeting of the AES. A total of 232 patients from Study 1503 were included in the interim analysis of the OLE trial. As of March 13, 2018, the interim cutoff date, the median duration of treatment with Fintepla was 256 days and the range was 58-634 days (equivalent to 161 patient-years of exposure to Fintepla). In this interim analysis population of 232 patients, a total of 22 (9.5%) patients had discontinued treatment for the following reasons: lack of efficacy (16), subject withdrawal (2), adverse event (1), SUDEP (1), physician decision (1), and withdrawal by caregiver (1). Approximately 90% of patients remained in the study at the time of the interim analysis. The median percent reduction in monthly convulsive seizure frequency over the entire OLE treatment period was 66.8% (compared with baseline frequency established in the core Phase 3 studies). Over the same period, 64.4% of children and young adults showed a >50% reduction in convulsive seizure frequency and 41.2% showed a >75% reduction.

The occurrence of adverse events was consistent with the Phase 3 placebo-controlled studies. The most common adverse events occurring in more than 10% of children and young adults were pyrexia (22%), nasopharyngitis (20%), decreased appetite (16%), influenza (12%), diarrhea (11%), and upper respiratory tract infection (10%). A total of 13.4% of children lost >7% body weight at some point during the trial; in 42% of those children weight loss abated during the period covered by the interim analysis. Over the course of the OLE treatment period included in the interim analysis, one patient died from SUDEP that was deemed unrelated to Fintepla. A total of 703 color doppler echocardiograms were performed to assess cardiovascular health at baseline, week 4 or 6, and then every 3 months during the OLE trial. No patient developed valvular heart disease (valvulopathy) or pulmonary arterial hypertension at any time after daily treatment with Fintepla.

In February 2019, we completed our rolling submission of a NDA with the FDA and submitted a MAA to the EMA for Fintepla for the treatment of seizures associated with Dravet syndrome. The EMA has accepted the MAA and initiated its review. In the event that the FDA requires a risk management plan (RMP) as a condition of approval to manage potential risks through education, labeling, and monitoring where appropriate, we are currently developing the appropriate elements of an RMP for Fintepla in the United States, as well as a similar RMP for Europe. This is consistent with other drugs with known safety issues that are approved for serious diseases with high unmet need.

***Fintepla for Patients with LGS***

LGS is a severe, refractory and debilitating form of epilepsy that typically becomes apparent during early childhood. Affected children experience generalized tonic-clonic seizures, tonic seizures, atonic seizures, and tonic/atonic seizures, all of which can result in “drop attacks.” Other seizure types that occur in some LGS patients include non-convulsive seizures, such as atypical absences, focal seizures, and myoclonic seizures. Children with LGS most often 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 makes up 1% to 4% of all pediatric epilepsies. There is no specific therapy for LGS that is effective in all cases and the disorder has proven particularly resistant to most currently available 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 prescribed 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 polypharmacotherapy with multiple AEDs, and yet still most continue to have refractory seizures. Although a variety of specific drugs have been approved by the FDA and/or EMA for the treatment of LGS including Epidiolex (cannabidiol), topiramate, lamotrigine, clobazam, rufinamide, felbamate and clonazepam, these medications typically have limited success and in addition, are often associated with intolerable side effects, especially in individuals who receive multidrug, high-dose regimens. Furthermore, all current AEDs can also become less effective over time.

Beginning in first quarter of 2016, we funded an open-label, dose-finding, investigator-initiated study of the effectiveness and tolerability of Fintepla as an adjunctive therapy 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 clinical trial at the 70th Annual Meeting of the AES. In this interim analysis, Fintepla was observed to provide clinically meaningful improvement in major motor seizure frequency in patients with severe refractory LGS, with 7 out of 13 patients (54%) achieving at least a 50% reduction in the number of major motor seizures, at doses below the 0.8 mg/kg/day maximum allowed dose. In addition, Fintepla was generally well tolerated without any observed signs

or symptoms of valvulopathy or pulmonary hypertension. We believe these data indicate that Fintepla has the potential to be a safe and effective adjunctive treatment of major motor seizures for patients with LGS. Based on the strength of the LGS data generated, in the first quarter of 2017, we submitted an Investigational New Drug Application (IND) to the FDA to initiate a Phase 3 program of Fintepla in LGS. Our IND for Fintepla as a potential treatment for LGS became effective in April 2017. In the first half of 2017, Fintepla received orphan drug designation for the treatment of LGS from the FDA in the United States and the EMA in the EU. In November 2017, we announced the initiation of our multicenter global Phase 3 clinical trial of Fintepla as an adjunctive treatment for seizures in patients with LGS (Study 1601) and are currently enrolling patients into the study. In December 2018, we announced that we

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expect to complete enrollment for Study 1601 in the second half of 2019 and be able to announce top-line results from the study in the first quarter of 2020.

Beyond Dravet syndrome and LGS, we also intend to evaluate Fintepla's potential to treat additional indications in other rare pediatric-onset epileptic encephalopathies such as Doose Syndrome and related medical conditions in the future.

**Competition**

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and differentiated 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 biopharmaceutical companies, biotechnology companies, academic institutions, government agencies and private and public research institutions, many of which have greater financial resources, research and development capabilities, sales and marketing capabilities, manufacturing capabilities, experience in obtaining regulatory approvals for product candidates and/or 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.

***Fintepla***

Prior to 2018, there were no FDA-approved treatments indicated for the treatment of seizures associated with Dravet syndrome. The standard of care for the treatment of seizures in patients with Dravet syndrome usually involved a combination of the following anticonvulsant drugs: clobazam, clonazepam, levetiracetam, topiramate, valproic acid, ethosuximide and zonisamide. In June 2018, the FDA approved the first treatment of seizures associated with Dravet syndrome, as well as LGS, GW Pharmaceuticals' Epidiolex® (cannabidiol or CBD). Epidiolex is a liquid drug formulation of plant-derived purified CBD, which is a chemical component of the Cannabis sativa plant, more commonly known as marijuana. In August 2018, the FDA approved a second treatment, Biocodex's Diacomit® (stiripentol), for the treatment of seizures associated with Dravet syndrome in patients who are also taking clobazam. Stiripentol is approved in Europe, Canada and Japan for the treatment of Dravet syndrome when used in conjunction with valproate and/or clobazam. GW Pharmaceuticals plc has filed a MAA in Europe for CBD in Dravet syndrome and LGS.

Fintepla has a novel 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 the EU for the treatment of epileptic encephalopathies like Dravet syndrome, including cannabidiol or stiripentol. Currently approved drugs have a different and distinct mechanism of action from Fintepla. As such, we do not expect the recent approvals of cannabidiol or stiripentol in the United States or Europe will block the FDA or EMA from granting approval of Fintepla.

Insys Therapeutics (Insys) is developing a synthetic CBD for the treatment of pediatric epilepsies, including Dravet syndrome. Insys previously 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 initiated Phase 2 development of its CBD product candidate for childhood absence epilepsy in December of 2017 and initiated a Phase 3 trial in infantile spasms, a pediatric epilepsy syndrome in the first quarter of 2018.

Ovid Therapeutics, Inc. is currently evaluating its product candidate OV935, a first-in-class inhibitor of the enzyme cholesterol 24-hydroxylase (CH24H), for the potential treatment of adult and pediatric patients with Dravet syndrome and LGS in Phase 2 clinical trials.

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

**Manufacturing and Supply**

We do not own or operate, and currently have no plans to establish or own any manufacturing facilities with respect to the manufacture of Fintepla or any future product candidates. In February 2019, we entered into a master supply agreement with Aptuit pursuant to which Aptuit will be our commercial manufacturer and supplier of the fenfluramine API used in Fintepla. The term of the master supply agreement is five years, which term shall be automatically extended for successive two year periods thereafter, unless terminated earlier. Aptuit has been providing the API to us for our clinical trial material supply needs and registration batches for the past several years.

We 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

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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 formulate, fill, label, package and distribute investigational drug products and eventually our products, if and when our product candidates receive approval. This approach allows us to maintain a more efficient infrastructure while enabling us to focus our expertise on developing and commercializing our product candidates. Although we believe we have multiple potential sources for the manufacture of our product candidates and their related raw materials, we currently rely on single manufacturers for different aspects of manufacturing Fintepla.

**Strategic and License Agreements**

In October 2014,we acquired Brabant Pharma Limited (Brabant) and obtained worldwide development and commercialization rights to Fintepla (ZX008; low-dose fenfluramine), its lead product candidate. Under the terms of the sale and purchase agreement, we agreed to make future milestone payments to the former owners of Brabant for up to $95.0 million in the event we achieve certain milestones with respect to Fintepla, consisting of $50.0 million in regulatory-related milestones and $45.0 million in sales-related milestones. In February 2019, we completed our rolling submission of a NDA with the FDA and submitted a MAA to the EMA for Fintepla for the treatment of seizures associated with Dravet syndrome. The EMA has accepted the MAA, which triggered a $10.0 million development milestone payment. An additional $10.0 million milestone payment shall become due and payable if our NDA is accepted by the FDA.

In addition, we have a collaboration and license agreement with the Universities of Antwerp and Leuven in Belgium (the Universities) that runs through September 2045. Under the terms of the agreement, the Universities granted us an exclusive worldwide license to use the data obtained from a study related to fenfluramine for the treatment of Dravet syndrome, as well as certain other intellectual property. We are required to pay a mid-single-digit percentage royalty on net sales of Fintepla for the treatment of Dravet syndrome or, in the case of a sublicense of Fintepla for the treatment of Dravet syndrome, a percentage in the mid-twenties of the sub-licensing revenues. The agreement may be terminated by the Universities if we: (a) do not use commercially reasonable efforts to (i) develop and commercialize Fintepla for the treatment of Dravet syndrome or related conditions stemming from infantile epilepsy, or (ii) seek approval of Fintepla for the treatment of Dravet syndrome in the United States; or (b) if we become insolvent or make an assignment for the benefit of creditors or should any petition in bankruptcy, or similar relief, be filed by or against us. We can terminate the agreement upon specified prior written notice to the Universities.

**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.

As of December 31, 2018, we have rights to four issued U.S. patents and two issued foreign patents, one of which is involved in an Opposition Proceeding in the European Patent Office. These patents, entitled “Method for the Treatment of Dravet Syndrome,” cover claims related to methods for treatment of seizures associated with Dravet syndrome with Fintepla and are expected to provide protection of the associated claims in the U.S. and other countries through 2033 and 2034, respectively. In addition, we also have 36 currently pending U.S. patent applications (which includes six provisional applications) and 74 pending foreign applications (which includes two allowed South Africa applications and seven Patent Cooperation Treaty applications) in the Fintepla series of patent cases. Our pending patent applications may not result in the issuance of any additional patents.

**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 (FFDCA) and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, record keeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable FDA or other requirements may subject a company to a variety of administrative or judicial sanctions, such as the FDA’s refusal to approve pending applications, a clinical hold, warning letters, recall or seizure of products, partial or total suspension of production, withdrawal of the product from the market, injunctions, fines, civil penalties or criminal prosecution.

FDA approval is required before any new 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:

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•completion of pre-clinical laboratory and animal testing and formulation studies in compliance with the FDA's current good laboratory practice (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 (GCP) regulations, to establish the safety and efficacy of the proposed drug product for each intended use;
•submission, review and approval to the FDA of an NDA; and
•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 (cGMP) requirements.

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 by the FDA on a timely basis, if at all. Pre-clinical tests include laboratory evaluation of product chemistry, potency, biological activity, 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 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, pre-clinical information or cGMP requirements 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 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 pre-clinical and clinical studies to further assess the drug's safety and effectiveness after NDA approval. Such post-approval studies are typically referred to as Post-Marketing or Phase 4 studies.

The results of product development, pre-clinical studies and clinical trials are submitted to the FDA as part of an NDA. NDAs must also contain extensive information relating to the product's pharmacology, chemistry, manufacturing, and controls (CMC) and proposed labeling, among other things. In February 2019, we submitted a NDA to the FDA for Fintepla for the treatment of seizures associated with Dravet syndrome.

For some drugs, the FDA may determine that a Risk Evaluation and Mitigation Strategies (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. In determining whether a REMS is necessary, the FDA considers the seriousness of known or potential adverse events, the expected benefit of the drug, the seriousness of the disease or condition to be treated, the size of the population likely to use the drug, , the duration of treatment, , and whether the drug is a new molecular entity. 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. The submission of an NDA is additionally subject to a substantial application user fee, and the

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manufacturer and/or sponsor under an approved NDA are also subject to annual program user fees. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. 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, quality system regulation ("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 (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.

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 is 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.

***Expedited Development and Review Programs***

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Unique to a fast track product, 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. Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current Prescription Drug User Fee Act (PDUFA) review goals.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on

irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

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The Food and Drug Administration Safety and Innovation Act established a category of drugs referred to as "breakthrough therapies" that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a product candidate as a "breakthrough therapy" if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug. In February 2018, granted breakthrough therapy designation for Fintepla in the United States for the treatment of Dravet syndrome.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. For example, the FDA may rescind breakthrough therapy designation for Fintepla based on an assessment of whether Fintepla continues to meet the criteria for breakthrough therapy designation in light of the FDA's approval in June 2018 of Epidiolex for the treatment of seizures associated with Dravet syndrome and the FDA's approval in August 2018 of Diacomit for the treatment of seizures associated with Dravet syndrome in patients who are also taking clobazam and neither Epidiolex nor Diacomit was approved as an existing therapy at the time the FDA granted breakthrough therapy designation for Fintepla.

***Post-Approval Requirements***

Once an NDA is approved, a product will be subject to 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 (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.

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.

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 (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

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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 requirements for identifying and tracking prescription drugs as they are distributed in the United States. The requirements of this 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 available 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.

The FDA may require post-approval studies and clinical trials if the FDA finds they are appropriate based on available 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. The FDA may 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.

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.

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 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

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an indication broader than the rare disease or condition for which it received orphan drug designation, it may not be entitled to exclusivity.

Fintepla has received orphan drug designation in the United States and the EU for the treatment of Dravet syndrome and LGS. We may seek orphan drug designation for Fintepla 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.

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.

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***DEA Regulation***

The Controlled Substances Act of 1970 (CSA) 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 Fintepla, 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 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 February 2019, we submitted a MAA for Fintepla for the treatment of seizures associated with Dravet syndrome under a centralized procedure to the EMA, which has accepted the MAA and initiated its review.

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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 and criminal false claims laws, including 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 $11,463 to $22,927 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 federal Civil Monetary Penalties Law prohibits, among other things, the offering or transferring of remuneration to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of Medicare or Medicaid payable items or services. Noncompliance with such beneficiary inducement provision of the federal Civil Monetary Penalties Law can result in civil money penalties for each wrongful act, assessment of three times the amount claimed for each item or service and exclusion from the federal healthcare programs.

The Health Insurance Portability and Accountability Act of 1996 (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.

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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 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 $165,786 per year (and up to an aggregate of $1.105 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 (OIG Guidance) and the Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals (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.

Federal and state government price reporting laws require manufacturers to calculate and report complex pricing metrics to government programs. Such reported prices may be used in the calculation of reimbursement and/or discounts on marketed products. Participation in these programs and compliance with the applicable requirements subject manufacturers to potentially significant discounts on products, increased infrastructure costs, and potentially limit the ability to offer certain marketplace discounts.

***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 (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. In addition to HIPAA and HITECH, there are state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act and CCPA), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators.

We are also subject to foreign privacy laws in the foreign jurisdictions in which we sell our testing products. The interpretation, application and interplay of consumer and health-related data protection laws in the U.S., Europe and elsewhere are often uncertain, contradictory and in flux. For example, the European Union enacted Regulation (EU) 2016/679 (General Data Protection Regulation, or GDPR), has been enacted in the European Union and went into full effect in May 2018. These texts introduce many changes to privacy and security in the European Union, including stricter rules on consent and security duties for critical industries, including for the health sector. The interpretation of some rules is still unclear, and some requirements will be completed by national legislation. More generally, foreign laws and interpretations governing data privacy and security are constantly evolving and it is possible that laws may

be interpreted and applied in a manner that is inconsistent with current practices, subjecting entities to government-imposed fines or orders. These fines can be very high. For instance, the GDPR introduces fines of up to EUR 20 million or 4% of a group's worldwide annual turnover for certain infringements. In addition, privacy regulations differ widely from country to country.

***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

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-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. The Bipartisan Budget Act of 2018 increased the point-of-sale discount manufacturers must agree to offer under the Medicare part D coverage gap discount program from 50% to 70%, starting in 2019. Additionally, on December 14, 2018, a U.S. District Court Judge in the Northern District of Texas (“Texas District Court Judge”), ruled that the entire PPACA is invalid based primarily on the fact that the Tax Cuts and Jobs Act of 2017 repealed the tax-based shared responsibility payment imposed by the PPACA, on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the “individual mandate”. While the Texas District Court Judge, as well as the current presidential administration and CMS, have stated that this ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the PPACA will impact the PPACA. PPACA and other healthcare reform measures continue to put pressure on pharmaceutical pricing, as well as increase our regulatory burdens and operating costs.

Other legislative changes have also been proposed and adopted in the United States since the PPACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things included 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 2027 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012, 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 and enacted legislation 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. Individual states have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and to encourage importation from other countries and bulk purchasing. 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.

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.

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***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, 2018, we employed 90 full-time employees. Of the full-time employees, 60 were engaged in product development, quality assurance and clinical development and regulatory activities, 7 were engaged in sales and marketing and 23 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.

**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 (510) 550-8300. We conduct our research and development activities and general and administrative functions primarily from our Emeryville, California location.

**Available Information**

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports, are available for free at www.zogenix.com as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission (SEC). They are also available for free on the SEC's website at 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.

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## Item 1A. Risk Factors

*We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. Certain factors may have a material adverse effect on our business prospects, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this Annual Report on Form 10-K and our other public filings with the Securities and Exchange Commission (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 only product candidate in development, Fintepla. We cannot be certain that Fintepla or our product candidates will receive regulatory approval or be successfully commercialized.***

We have only one product candidate in clinical development, Fintepla, and our business depends substantially on its successful development and commercialization. We currently have no drug products approved for sale, and we may not be able to develop marketable drug products in the future. Fintepla and 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 U.S. Food and Drug Administration (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 a New Drug Application (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. In February 2019, we completed our rolling submission of a NDA with the FDA and submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for Fintepla for the treatment of seizures associated with Dravet syndrome. The EMA has accepted the MAA and initiated its review. However, 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 Fintepla or 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 Fintepla and would have a material and adverse impact on our business.

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 Fintepla or our product candidates, which could prevent or significantly delay their regulatory approval.***

Fintepla and our product candidates are prone to the risks of failure inherent in drug development. Before obtaining U.S. regulatory approval for the commercial sale of Fintepla or our product candidates, we must gather substantial evidence from well-controlled clinical trials that demonstrate to the satisfaction of the FDA that the product candidate in question 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 Fintepla is 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.

***The results of previous clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or non-U.S. regulatory authorities.***

The results from the prior clinical trials of Fintepla discussed elsewhere in this report may not necessarily be predictive of the results of future clinical trials or preclinical studies. Even if we are able to complete our planned

clinical trials of Fintepla according to our current development timeline, the results from our prior clinical trials of Fintepla may not be replicated in these future trials. Clinical data are often susceptible to varying interpretations and analyses, and many companies that believed

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their product candidates performed satisfactorily in prior clinical trials nonetheless have failed to obtain FDA approval. If we fail to produce positive results in our clinical trials of Fintepla, the development timeline and regulatory approval and commercialization prospects for Fintepla and our business and financial prospects, would be adversely affected.

Further, Fintepla may not be approved even though recent, positive top-line results showed that Fintepla met its primary and all key secondary endpoints in our ongoing Phase 3 clinical trials. The FDA or non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. In addition, any of these regulatory authorities may change its requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal clinical trial that, if successful, would potentially form the basis for an application for approval by the FDA or another regulatory authority. Furthermore, any of these regulatory authorities may also approve our product candidates for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials.

***Top-line data may not accurately reflect the complete results of a particular study or trial.***

We may publicly disclose top-line or interim data from time to time, which is based on a preliminary analysis of then-available efficacy and safety data such as the top-line results we reported from Study 1504, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimations, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or drug and our company in general. In addition, the information we may publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the top-line data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

***Delays in the commencement or completion of clinical testing for Fintepla or pre-clinical or clinical testing for our 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 Fintepla or pre-clinical or clinical testing for our product candidates could significantly affect our product development costs and business plan.

Our Phase 3 program for Fintepla includes three randomized, double-blind placebo-controlled clinical trials of Fintepla as adjunctive therapy for patients with uncontrolled seizures who have Dravet syndrome and one randomized, double-blind placebo-controlled clinical trial of Fintepla for patients with Lennox-Gastaut Syndrome (LGS). In September 2017, we announced positive top line data from two identical clinical trials, Study 1501 in the U.S. and Canada and Study 1502 in Europe and Australia, which we collectively refer to as Study 1. Study 1 evaluated two dose levels of Fintepla (0.2 mg/kg/day and 0.8 mg/kg/day, up to a maximum daily dose of 30 mg) and met its primary efficacy endpoint of reducing convulsive seizures experienced by patients after treatment of Fintepla compared to treatment with a placebo. In December 2017, we reported additional data from Study 1. Study 1504 is evaluating a single dose a Fintepla (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, valproate and/or clobazam. Study

1504 is a multi-national study commenced in the third quarter 2016 and is being conducted in western Europe and North America. We reported top-line results from the trial in July 2018. 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 ongoing Phase 3 clinical trials may be delayed.

In November 2017, we enrolled our first patient in our Phase 3 clinical trial of Fintepla as an adjunctive treatment of seizures associated with LGS, Study 1601. Study 1601 is divided in two parts. Part 1 is a double-blind, placebo-controlled investigation to assess the safety, tolerability and efficacy of Fintepla, low-dose fenfluramine, when added to a patient's current

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anti-epileptic therapy. The trial will include two dose levels of Fintepla (0.2 mg/kg/day and 0.8 mg/kg/day, up to a maximum daily dose of 30 mg), as well as placebo. After establishing baseline seizure frequency for 4 weeks, randomized patients will be titrated to their dose over a 2-week titration period, followed by a 12-week fixed dose maintenance period. We are targeting a total of 225 patients (75 per treatment arm) in the trial. The primary endpoint of the clinical trial is change in the number of seizures that result in drops between baseline and the combined titration and maintenance periods at the 0.8 mg/kg/day dose. Part 2 of Study 1601 will be a 12-month open-label extension to evaluate the long-term safety, tolerability and effectiveness of Fintepla.

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

•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 (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.

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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 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 Fintepla and our 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 Fintepla may not lead to a faster development or review process.***

We have been granted a Fast Track designation for Fintepla in the United States for the treatment of Dravet syndrome. 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 Fintepla, it may not actually result in faster clinical development or regulatory review or approval. Furthermore, such a designation does not increase the likelihood that Fintepla will receive marketing approval in the United States.

***Any breakthrough therapy designation that we may receive from the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.***

In February 2018, the FDA granted breakthrough therapy designation for Fintepla in the United States for the treatment of Dravet syndrome. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. We cannot be sure that any evaluation we may make of our product candidates as qualifying for breakthrough therapy designation will meet the FDA's expectations. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. For example, the FDA may rescind breakthrough therapy designation for Fintepla based on an assessment of whether Fintepla continues to meet the criteria for breakthrough therapy designation in light of the FDA's approval in June 2018 of Epidiolex for the treatment of seizures associated with Dravet syndrome and the FDA's approval in August 2018 of Diacomit for the treatment of seizures associated with Dravet syndrome in patients who are also taking clobazam and neither Epidiolex nor Diacomit was approved as an existing therapy at the time the FDA granted breakthrough therapy designation for Fintepla.

***If the FDA does not conclude that certain of our product candidates satisfy the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements for such product candidates under Section 505(b)(2) are not as we expect, the approval pathway for those product candidates will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may***

***not be successful.***

We are developing proprietary product candidates, including Fintepla, for which we may seek FDA approval through the Section 505(b)(2) regulatory pathway. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, added Section 505(b)(2) to the Federal Food, Drug and Cosmetic Act (FDCA). Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from trials that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505(b)(2), if applicable to us under the FDCA, would allow an NDA we submit to the FDA to rely in part on data in the public domain or the FDA's prior

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conclusions regarding the safety and effectiveness of approved compounds, which could expedite the development program for our product candidates by potentially decreasing the amount of clinical data that we would need to generate in order to obtain FDA approval. If the FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as we anticipated, we may need to conduct additional clinical trials, provide additional data and information and meet additional standards for regulatory approval.

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. In addition, the pharmaceutical industry is highly competitive, and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of our NDAs for up to 30 months or longer depending on the outcome of any litigation. It is not uncommon for a manufacturer of an approved product to file a citizen petition with the FDA seeking to delay approval of, or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay, or even prevent, the approval of the new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if we are able to utilize the Section 505(b)(2) regulatory pathway, there is no there is no guarantee this would ultimately lead to accelerated product development or earlier approval.

Moreover, even if our product candidates are approved under Section 505(b)(2), the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

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

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.

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 other CNS 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, Fintepla may compete against other products and product candidates. In June 2018, the FDA approved the first treatment of seizures associated with Dravet syndrome, as well as LGS, GW Pharmaceuticals' Epidiolex® (cannabidiol or CBD). Epidiolex is a liquid drug formulation of plant-derived purified cannabidiol, or CBD, which is a chemical component of the Cannabis sativa plant, more commonly known as marijuana. In August 2018, the FDA approved a second treatment, Biocodex's Diacomit® (stiripentol), for the treatment of seizures associated with Dravet syndrome in patients who are also taking clobazam. Stiripentol is approved in Europe, Canada, Australia and Japan for the treatment of Dravet syndrome when used in conjunction with valproate and/or clobazam. GW

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Pharmaceuticals plc has filed a MAA in Europe for CBD in Dravet syndrome and LGS. Insys Therapeutics (Insys) is developing a synthetic cannabidiod (CBD) for the treatment of pediatric epilepsies, including Dravet syndrome. Insys previously 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 initiated Phase 2 development of its CBD product candidate for childhood absence epilepsy in December of 2017 and initiated a Phase 3 trial in infantile spasms, a pediatric epilepsy syndrome, in the first quarter of 2018. Ovid Therapeutics, Inc. is currently evaluating its product candidate OV935, a first-in-class inhibitor of the enzyme cholesterol 24-hydroxylase (CH24H), for the potential treatment of adult and pediatric patients with Dravet syndrome and LGS in Phase 2 clinical trials.

We expect Fintepla, 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 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 Fintepla 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 Fintepla, 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;

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•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 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 Fintepla or any of our product candidates for which we obtain marketing approval from the FDA or other regulatory authorities and gain broad market acceptance may require significant resources and may never be successful. If our products do not achieve an adequate level of acceptance by physicians, third-party payors, 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 at least the 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 our operations since the inception and have an accumulated deficit of $696.0 million as of December 31, 2018. In 2018, we used $111.7 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 costs incurred related to the development and commercialization of Fintepla. Additionally, in the event that Fintepla is approved in the United States or the EU, we will owe milestone payments related to our 2014 acquisition of worldwide development and commercialization rights to Fintepla. Our ability to generate revenues from Fintepla 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, if at all. If we do not generate significant sales from Fintepla our product candidate 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 Fintepla. 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

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and regulatory requirements. We and our CROs are required to comply with good clinical practice (GCP) requirements for clinical studies of our product candidates, and good laboratory practice (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 (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.

***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 Fintepla, 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.

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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 manufacturing supply chain, all of which are currently single source suppliers, for the clinical supply of Fintepla, and if we experience problems with any of these suppliers, the development of Fintepla could be delayed.***

We outsource all manufacturing and packaging of the clinical trial materials for Fintepla to third parties. For example, in February 2019, we entered into a master supply agreement with Aptuit (Oxford) Limited, an Evotec company ("Aptuit"), pursuant to which Aptuit will be our commercial manufacturer and supplier of the fenfluramine active pharmaceutical ingredient (API) used in our product candidate Fintepla, 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 Fintepla.

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

Reliance on suppliers entails risks to which we would not be subject if we manufactured our product candidate 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 candidate 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.

***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, 2018, we employed 90 full-time employees. Of the full-time employees, 60 were engaged in product development, quality assurance and clinical and regulatory activities, 7 were engaged in sales and marketing and 23 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, especially in the San Francisco Bay Area where we operate. 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

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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 Fintepla and our product candidates. 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.

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 our partners, contractors and consultants are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. For example, we have in the past experienced failures in our information systems and computer servers, which may have been the result of a cyber-attack. These failures resulted in an interruption of our normal business operations and required substantial expenditure of financial and administrative resources to remedy. We cannot be sure that similar failures will not occur in the future. System failures, accidents or security breaches can cause interruptions in our operations, and can result in a material disruption of our commercialization activities, drug development programs and our business operations. The loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval and post-market study compliance efforts and significantly increase our costs to recover or reproduce the data. Similarly, we rely on a large number of third parties to supply components for and manufacture our 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 our product candidates could be delayed or otherwise adversely affected.

***Cyber-attacks or other failures in telecommunications or information technology systems could result in information theft, data corruption and significant disruption of our business operations.***

We use information technology, computer systems and networks to process, transmit and store electronic information in connection with our business activities. Cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency, scope and sophistication in every industry. These threats pose a risk to the security of our systems and networks and the confidentiality, availability and integrity of our data, and may cause a disruption in our operations, harm our reputation and increase our stock trading risk. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our third-party collaborators, distributors and other contractors and consultants will be successful in protecting our data that is stored on their systems. A cyberattack or destruction or loss of data could have a material adverse effect on our business and prospects. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

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

We conduct research and development activities in the UK and other European countries and some of the payments for these activities are denominated in Euros and UK 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 UK pound sterling, such as the decline in value of the UK pound sterling following the results of the UK's referendum on withdrawal from the EU. A significant appreciation in the Euro or UK pound sterling relative to the U.S. dollar will result in higher expenses and cause increases in our net losses. Likewise, to the extent that we

generate any revenues denominated in foreign currencies, or become required to make payments in other foreign currencies, fluctuations in the exchange rate between the U.S. dollar and those foreign currencies could also negatively impact our results of operations. We currently have not entered into any foreign currency hedging contracts to reduce the effect of changes in foreign currency exchange rates, and foreign currency hedging is inherently risky and may result in unanticipated losses.

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***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.

***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;
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•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 Fintepla, 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 candidate outside of the United States.***

We intend to market Fintepla outside of the United States, if approved. For example, Fintepla has received orphan drug designation in the EU, and we completed a Phase 3 clinical trial, which included sites in Europe and Australia, in 2017, and submitted a MAA to the EMA for Fintepla for the treatment of seizures associated with Dravet syndrome in February 2019. The EMA has accepted the MAA and initiated its review. 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 (EEA), which comprised of 28 EU member states plus Iceland, Liechtenstein, and Norway, medicinal products can only be commercialized after obtaining a Marketing Authorization (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 (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 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

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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 have taken 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.***

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 (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 UK's referendum on withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business.***

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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 UK elected to withdraw from the EU in a national referendum. The referendum was advisory, and in March 2017, the government of the UK served notice under Article 50 of the Treaty of the European Union to formally initiate a withdrawal process. The UK and EU have had a two-year period under Article 50 to negotiate the terms of the UK's withdrawal from the EU. The withdrawal agreement and political declaration that were endorsed at a special meeting of the European Council in November 2018 did not receive the approval of the UK Parliament in January 2019. Further discussions are ongoing, although the European Commission has stated that the EU will not reopen the withdrawal agreement. Any extension of the negotiation period for withdrawal will require the consent of all remaining 27 member states of the EU. The referendum has created significant uncertainty about the future relationship between the UK and the EU, and has given rise to calls for certain regions within the UK to preserve their place in the EU by separating from the UK 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 UK laws and regulations as the UK 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 UK, increase costs, depress economic activity and restrict our access to capital. If the UK and the EU are unable to negotiate acceptable withdrawal terms or if other EU member states pursue withdrawal, barrier-free access between the UK and other EU member states or among the European economic area overall could be diminished or eliminated.

Since a significant proportion of the regulatory framework in the UK is derived from EU directives and regulations, the UK's withdrawal from the EU could materially impact the regulatory regime with respect to the approval of product candidates, disrupt the importation and export of active substances and other components of drug formulations, and disrupt the supply chain for clinical trial product and final authorized formulations. Any delay in obtaining, or an inability to obtain, any marketing approvals or otherwise, would prevent us from commercializing our product candidates in the UK and/or the EU. In view of the uncertainty surrounding the UK's future relationship with the EU, we are unable to predict the effects of such disruption to the regulatory framework and supply chain in Europe. Any of these factors, and/or those stated above, 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. In September 2017, our remaining revenue-generating agreement to manufacture and supply Sumavel DosePro to Endo International plc (Endo) was terminated. 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, 2018, 2017 and 2016, we incurred net losses of $123.9 million, $126.8 million and $69.7 million, respectively, and our cash used in operating activities was $111.7 million, $75.9 million and $72.9 million, respectively. As of December 31, 2018, we had an accumulated deficit of $696.0 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 in the future 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. We will require additional capital in the future to fund our operations, including:

•further development of our 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 our product candidates and any future product candidates that we may develop, in-license or acquire;

•the timing of regulatory approval for any of our 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 our 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; and

•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 Fintepla.

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 funds when needed, 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.

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***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, we currently have an at-the-market sales agreement with Cantor Fitzgerald & Co (Cantor) for the offer and sale of up to $75.0 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.

***We may be unable to benefit from favorable UK tax legislation.***

As a company that carries out extensive research and development activities, we benefit from the UK's small and medium-sized enterprises (SMEs) R&D tax relief scheme. For each discrete tax year, we have an option to receive an enhanced UK tax deduction on our eligible R&D activities or, when we are in a net operating loss position for that year, we can elect to surrender net operating losses that arose from our eligible R&D activities in exchange for a cash payment from the UK tax authorities for amounts up to 33.35% of qualifying expenditures. Qualifying expenditures largely comprise employment costs for research staff, consumables and certain internal overhead costs incurred as part of research projects. The majority of our R&D activities consist of qualifying expenditures under the UK's SME R&D tax relief scheme. To date, aggregate cash payments received under this tax relief scheme were approximately $10.1 million. We may not be able to continue to benefit from the UK's SME R&D tax relief scheme in the future as we increase our personnel and expand our business as this means we may no longer qualify as an SME. In addition, changes in UK tax legislation may reduce or limit any future claims. For example, on October 29, 2018, the UK Government proposed that from April 1, 2020, the amount of cash claims that a qualifying loss-making SME may receive through the SME R&D tax relief scheme in any one year will be capped at three times that SME's total Pay As You Earn and National Insurance Contributions liability for that year.

***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 (IRC), substantial changes in our ownership may limit the amount of net operating loss and research and development income tax credit carryforwards, and certain other attributes (such as any future carryovers resulting from any business interest deductions that are disallowed under the recently-enacted U.S. tax legislation) (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 Code, 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. Based on the Company's most recent assessment through December 31, 2018, no reduction was made to the federal and state net operating loss carryforwards or federal and state tax income tax credit carryforwards under these rules. 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. Furthermore, under recently enacted U.S. tax legislation, although the treatment of tax losses generated before December 31, 2017 has generally not changed, tax losses generated in calendar year 2018 and beyond may only offset 80% of our taxable income. This change may require us to pay federal income taxes in future years despite generating a loss for federal income tax purposes in prior years.

***Recent U.S. tax legislation may materially adversely affect our financial condition, results of operations and cash flows.***

The Tax Cut and Jobs Act of 2017 (Tax Act) has significantly changed the U.S. federal income taxation of U.S. corporations, including by reducing the U.S. corporate income tax rate, limiting interest deductions, adopting elements of a

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territorial tax system, imposing a one-time transition tax (repatriation tax) on all undistributed earnings and profits of certain U.S.-owned foreign corporations, revising the rules governing net operating losses and the rules governing foreign tax credits, and introducing new anti-base erosion provisions. Many of these changes are effective immediately, without any transition periods or grandfathering for existing transactions. While we have completed the accounting for the income tax effects of the Tax Act on our financial statements as of December 31, 2018, the Tax Act is unclear in many respects and could be subject to potential amendments and technical corrections, as well as interpretations and implementing regulations by the Treasury and Internal Revenue Service (IRS), any of which could lessen or increase certain adverse impacts of the legislation. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation, which often uses federal taxable income as a starting point for computing state and local tax liabilities. If clarifying guidance is provided in the future, it may have a material adverse effect on our financial results.

***We are exposed to fluctuations in the market values of our investments.***

As of December 31, 2018, our cash, cash equivalents and marketable securities totaled $514.2 million. Our cash equivalents and marketable securities include money market funds and certificate of deposits, securities issued by the U.S. government and its agencies, corporate debt securities and commercial paper meeting the criteria of our investment policy, which prioritizes the preservation of capital. These investments are subject to general credit, liquidity, market and interest rate risks, instability in the global financial markets, or other factors. As a result, the value or liquidity of our investments could decline and result in a material impairment, which could have a material adverse effect on our financial results and the availability of cash to fund our operations.

**Risks Related to Government Regulation**

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

We currently are developing Fintepla for the treatment of seizures associated with Dravet syndrome and LGS, and we completed our rolling submission of a NDA with the FDA for the treatment of seizures associated with Dravet syndrome in February 2019. 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 Fintepla or any of our 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 (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 Fintepla, 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;

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•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.

Our lead product candidate Fintepla and any of our other product candidates may not achieve their specified endpoints in clinical trials. Further, Fintepla and 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 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 (REMS) program, which can limit the labeling and distribution of a drug product.

The safety and effectiveness of Fintepla has been evaluated in a single, continuing, long-term, open-label, study in patients with Dravet syndrome in Belgium. We initiated a Phase 3 clinical trial for Fintepla as an adjunctive treatment of seizures in children with Dravet syndrome in North America in January 2016 (Study 1501) and in Europe and Australia in June 2016 (Study 1502). In September 2017, we announced positive top-line results from Study 1501 and Study 1502 via a prospective merged study analysis approach whereby top-line results from the first approximately 120 subjects randomized into either Study 1501 or 1502 would have their study results analyzed and be reported initially as "Study 1". In September 2016, we initiated Cohort 1 of Study 1504 that investigated the pharmacokinetic profile and safety of Fintepla when co-administered with the stiripentol regimen (stiripentol, valproate and/or clobazam). Based on the results of the Cohort 1 pharmacokinetic and safety portion of the trial, in February 2017 we initiated the Cohort 2 safety and efficacy portion of Study 1504 at multiple sites located in France, the Netherlands, United States, Canada, Germany, the United Kingdom and Spain. In July 2018, we reported positive top-line results from Study 1504, which are consistent with those reported in Study 1.

If we are unable to obtain regulatory approval for Fintepla or any of our 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 Fintepla.***

We have obtained orphan drug designation for Fintepla in the United States and Europe for both the treatment of Dravet syndrome and LGS. 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 Fintepla has incremental benefit over any other approved product for that orphan disorder. In July 2018, we reported positive top-line results from Study 1504 and in February 2019, we submitted a MAA to the EMA for Fintepla for the treatment of seizures associated with Dravet syndrome. The EMA has accepted the MAA and initiated its review. Currently in Europe, only stiripentol has orphan drug status, which has been approved 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

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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, quality system regulation 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.

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

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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, 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. 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.

In addition, 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. For example, certain policies of the current presidential administration may impact our business and industry. Namely, the current presidential administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

***Changes in funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.***

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

***Fintepla 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 Fintepla or any of our other 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;

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•we could be sued and held liable for harm caused to patients; and
•our reputation may suffer.

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.

***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. 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, which, through subsequent legislative amendments, was be increased to 70%, starting in 2019, 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;
•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 90$^{th}$ 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; 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 current presidential administration and U.S. Congress. In addition, Congress could consider subsequent legislation to replace repealed elements of the PPACA. Recently, the Tax Act was enacted, which, among other things, removes penalties for not complying with the PPACA's

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individual mandate to carry health insurance. Further, on December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the PPACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the PPACA are invalid as well. While the Trump Administration and the Centers for Medicare & Medicaid Services have both stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, if any, will impact the law. 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. For example, in August 2011, the Budget Control Act of 2011, among other things included 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 2027 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012, 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 and enacted legislation 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. For example, in an effort to lower prescription drug prices, on January 31, 2019, the Department of Health and Human Services issued a proposed rule that removes from existing anti-kickback statute safe harbor protection certain reductions in price paid by pharmaceutical manufacturers to Medicare Part D plan sponsors, Medicaid managed care organizations, and those entities' pharmacy benefit managers (PBMs) and instead, adds two new safe harbors that protect certain point-of-sale price reductions offered directly to patients by pharmaceutical manufacturers as well as certain fixed fee service payments from pharmaceutical manufacturer to PBMs. Individual states have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and to encourage importation from other countries and bulk purchasing. 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.

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.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

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

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

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***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. A person or entity no longer needs 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 False Claims Act;

•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;

•federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;

•federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

•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. Similar to the federal Anti-Kickback Statute, a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

•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;

•federal price reporting laws, which require us to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on our commercial products;

•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; and

•similar healthcare laws and regulations in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and requirements regarding the collection, distribution, use, security, and storage of personally identifiable information and other data relating to individuals (including the European Union enacted Regulation (EU) 2016/679 (General Data Protection Regulation)).

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.

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

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

We are subject to risks associated with the regulations relating to the import and export of products and materials. We cannot predict whether the import and/or export of our products will be adversely affected by changes in, or enactment of, new quotas, duties, taxes or other charges or restrictions imposed by 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 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 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 receiving rights to 4 U.S. patents in 2017, we did not own or control any issued patents covering Fintepla or its use. There is no guarantee that any of our pending applications will issue as patents. The patents covering the API in Fintepla have expired and therefore it is not subject to patent protection. The initial applications covering methods of treatment using Fintepla were licensed 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 Fintepla 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 additional 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

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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 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 Fintepla 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 patents or 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 are not Orange-Book eligible;
•it is possible that there are dominating patents to Fintepla of which we are not aware;
•it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
•it is possible that others may circumvent our owned or in-licensed patents;
•it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
•the 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 of 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

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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.

***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 license with 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 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.

***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 candidate 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 Fintepla. 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 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,

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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 candidate, 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 or our licensors. 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.

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, 2018, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price of $33.42 to a high sale price of $62.75. 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 Fintepla;

•the development status of Fintepla, including the results from our clinical trials;

•variations in the level of expenses related to Fintepla clinical development programs, including relating to the timing of invoices from, and other billing practices of, our CROs and clinical trial sites;
•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;

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•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 Fintepla 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 Fintepla development programs;
•results of clinical trials for Fintepla;
•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

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determination in any such litigation or any amounts paid to settle any such actual or threatened litigation could require that we make significant payments.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. As of December 31, 2018, we had research coverage by only 10 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, 2018, we had 42,078,164 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.

Certain of our directors and executive officers have established, or 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

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

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

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

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

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

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses. 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 LLC 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

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reports on a timely basis, could increase our operating costs and could materially impair our ability to operate our business. Moreover, effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent fraud. If we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal controls that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would entail expenditure of additional financial and management resources.

**Item 1B. Unresolved Staff Comments**

None.

**Item 2. Properties**

As of December 31, 2018, our corporate headquarters, which includes executive offices and research and development and business operations, consist of approximately 22,000 square feet of leased office and laboratory space in Emeryville, California. In October 2018, we entered into a new lease agreement with our current landlord for our new headquarters, which is also located in Emeryville, California, that includes approximately 37,307 square feet of office and laboratory space under a noncancellable lease that expires on June 30, 2027 and has a renewal option for an additional five years. Upon completion of our relocation to our new headquarters, which is expected to be by the end of the second quarter of 2019, the lease agreement for our existing headquarters will be terminated. We also lease limited office space in Maidenhead, United Kingdom under a month-to-month arrangement.

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**

Zogenix common stock is listed on the Nasdaq Global Market under the symbol "ZGNX".

**Holders of Common Stock**

According to the records of our transfer agent, there were 10 holders of record of our common stock on February 15, 2019. 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.

**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, 2018 to the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes an initial investment of $100 on December 31, 2013, and that all dividends were reinvested. The comparisons in the graph are required by the SEC 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.

**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.

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**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, 2018, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017 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, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016, 2015 and 2014 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, | | | | |
|---|---|---|---|---|---|
| | 2018 | 2017 | 2016 | 2015 | 2014 |
| | (In Thousands, Except Per Share Amounts) | | | | |
| **Statement of Operations Data** | | | | | |
| **Revenue:** | | | | | |
| Contract manufacturing revenue [1] | $ — | $ 9,821 | $ 28,525 | $ 24,369 | $ 15,392 |
| Net product revenue | — | — | — | — | 9,840 |
| Service and other product revenue | — | — | 325 | 2,813 | 3,715 |
| Total revenue | — | 9,821 | 28,850 | 27,182 | 28,947 |
| **Operating expenses:** | | | | | |
| Cost of contract manufacturing [1] | — | 10,729 | 22,173 | 22,356 | 14,342 |
| Cost of goods sold | — | — | — | — | 5,263 |
| Royalty expense | — | — | 295 | 345 | 591 |
| Research and development | 100,925 | 67,449 | 41,840 | 27,860 | 11,893 |
| Selling, general and administrative | 38,950 | 25,885 | 26,996 | 26,347 | 34,639 |
| Loss on contract termination | — | 478 | — | — | — |
| Change in fair value of contingent consideration [2] | 1,300 | 24,100 | 1,800 | (2,000) | — |
| Restructuring costs | — | — | — | — | — |
| Asset impairment charges [3] | — | 1,116 | 8,431 | — | 838 |
| Net gain on sale of business | — | — | — | — | (79,980) |
| Total operating expenses (income) | 141,175 | 129,757 | 101,535 | 74,908 | (12,414) |

| | | | | | |
|---|---|---|---|---|---|
| **(Loss) income from operations** | (141,175) | (119,936) | (72,685) | (47,726) | 41,361 |
| Other income (expense): | | | | | |
| Interest income (expense), net | 7,164 | (1,554) | (2,382) | (2,959) | (3,070) |
| Loss on sale of marketable securities [4] | — | — | — | (5,746) | — |
| Loss on extinguishment of debt[5] | — | (4,876) | — | — | (1,254) |
| Change in fair value of common stock warrant liabilities | 169 | 297 | 5,387 | (1,103) | 25,332 |
| Change in fair value of embedded derivatives | — | — | — | — | (14) |
| Other income (expense)[6] | 10,126 | 47 | 46 | (71) | (784) |
| Total other (expense) income | 17,459 | (6,086) | 3,051 | (9,879) | 20,210 |
| **(Loss) income from continuing operations before income taxes** | (123,716) | (126,022) | (69,634) | (57,605) | 61,571 |
| Income tax benefit (expense) [7] | — | — | 948 | 15,901 | (84) |
| **Net (loss) income from continuing operations** | $ (123,716) | (126,022) | (68,686) | (41,704) | 61,487 |
| **Net (loss) income from discontinued operations** | (198) | (795) | (1,021) | 67,848 | (52,900) |
| **Net (loss) income** | $ (123,914) | (126,817) | (69,707) | 26,144 | 8,587 |
| Net (loss) income per share, continuing operations, basic | $ (3.27) | $ (4.62) | $ (2.77) | $ (1.94) | $ 3.45 |
| Net (loss) income per share, continuing operations, diluted | $ (3.27) | $ (4.62) | $ (2.77) | $ (1.94) | $ 3.44 |

(1) Amounts relate to supplying Sumavel DosePro to Endo under a long-term supply agreement (Supply Agreement), which was terminated in 2017. See Note 3 to our consolidated financial statements included in this Form 10-K.

(2) Reflects changes in the estimated fair value of the contingent consideration liability related to potential regulatory and sales-based milestone payments. See Notes 2 and 5 to our consolidated financial statements included in this Form 10-K.

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(3) Includes the impairment of long-lived assets used in the production of Sumavel DosePro in 2016 and 2017. See Note 3 to our consolidated financial statements included in this Form 10-K.
(4) Represents loss on sale of marketable securities, which was included as part of the sales consideration received from the divestiture of our Zohydro ER business.
(5) Reflects loss on extinguishment of our term loan and a working capital advance note payable in 2017 and the early termination of a financing agreement with Healthcare Royalty Partners in 2014.
(6) Includes income recognized for qualifying research and development expenditures under UK's SME R&D tax relief scheme. See Notes 2 and 13 to our consolidated financial statements included in this Form 10-K.
(7) Tax benefit in 2015 resulted from the sale of Zohydro ER.

| | As of December 31, 2018 | 2017 | 2016 | 2015 | 2014 |
|---|---|---|---|---|---|
| | (In Thousands) | | | | |
| **Balance Sheet Data:** | | | | | |
| Cash, cash equivalents and marketable securities | $ 514,187 | $ 293,503 | $ 155,349 | $ 155,349 | $ 42,205 |
| Working capital | 474,355 | 283,720 | 154,517 | 154,517 | 33,741 |
| Total assets | 648,331 | 417,613 | 305,822 | 305,822 | 202,835 |
| Long-term debt, less current portion | — | 18,824 | 15,899 | 15,899 | 21,703 |
| Accumulated deficit | (695,954) | (572,040) | (375,516) | (375,516) | (401,660) |
| Total stockholders' equity | 522,801 | 301,521 | 182,760 | 182,760 | 55,279 |

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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 developing and commercializing transformative central nervous system (CNS) therapies for people living with serious and life-threatening rare CNS disorders and medical conditions. Our current primary area of therapeutic focus is rare, or "orphan" childhood-onset epilepsy disorders.

We currently own and control worldwide development and commercialization rights to Fintepla/ZX008, our lead product candidate. Fintepla is low-dose fenfluramine under development for the treatment of seizures associated with two rare and catastrophic forms of childhood-onset epilepsy: Dravet syndrome and Lennox-Gastaut syndrome (LGS).

**Fintepla for Patients with Dravet Syndrome**

Dravet syndrome is a rare form of pediatric-onset epilepsy with life threatening consequences for patients and for which current treatment options are very limited. Fintepla has received orphan drug designation in the United States and the European Union (EU) for the treatment of Dravet syndrome. In addition, Fintepla for the treatment of Dravet syndrome received Fast Track designation from the U.S. Food and Drug Administration (FDA) in January 2016. We have completed multiple clinical trials of Fintepla for the treatment of Dravet syndrome, including Study 1, a double-blind placebo-controlled studies of Fintepla as adjunctive therapy for patients with uncontrolled seizures who have Dravet syndrome, Study 1504, which investigated the pharmacokinetic profile and safety of Fintepla when co-administered with the stiripentol regimen and Study 1503, our ongoing open-label extension (OLE) trial to study the long-term safety and effectiveness of Fintepla, which is available to eligible patients who have completed our Phase 3 trials. In February 2019, we completed our rolling submission of a New Drug Application (NDA) with the FDA and submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for Fintepla for the treatment of seizures associated with Dravet syndrome. The EMA has accepted the MAA and initiated its review. Both applications were based on data from Study 1 and Study 1504 in Dravet syndrome and the interim analysis from the ongoing OLE trial Study 1503.

**Fintepla for Patients with LGS**

LGS is another rare, refractory, debilitating pediatric-onset epilepsy with life threatening consequences for patients and for which current treatment options are limited and suboptimal. Beginning in first quarter of 2016, we funded an open-label, dose-finding, investigator-initiated study of the effectiveness and tolerability of Fintepla as an adjunctive therapy 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 clinical trial at the 70th Annual Meeting of the AES. In this interim analysis, Fintepla was observed to provide clinically meaningful improvement in major motor seizure frequency in patients with severe refractory LGS, with 7 out of 13 patients (54%) achieving at least a 50% reduction in the number of major motor seizures, at doses below the 0.8 mg/kg/day maximum allowed dose. In addition, Fintepla was generally well tolerated without any observed signs or symptoms of valvulopathy or pulmonary hypertension. We believe these data indicate that Fintepla has the potential to be a safe and effective adjunctive treatment of major motor seizures for patients with LGS. Based on the strength of the LGS data generated, in the first quarter of 2017, we submitted an Investigational New Drug Application (IND) to the FDA to initiate a Phase 3 program of Fintepla in LGS. Our IND for Fintepla as a potential treatment for LGS became effective in April 2017. In the first half of 2017, Fintepla received orphan drug designation for the treatment of LGS from the FDA in the United States and the EMA in the EU.

*Study 1601*

In November 2017, we announced the initiation of our multicenter global Phase 3 clinical trial of Fintepla as an adjunctive treatment for seizures in patients with LGS (Study 1601). Study 1601 is planned for up to 85 sites in North America, Europe, Asia-Pacific, South America, South Africa and Australia and is divided in two parts. Part 1 is a double-blind, placebo-controlled investigation to assess the safety, tolerability and efficacy of Fintepla, low-dose fenfluramine, when added to a

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patient's current anti-epileptic therapy. The trial will include two dose levels of Fintepla (0.2 mg/kg/day and 0.8 mg/kg/day, up to a maximum daily dose of 30 mg), as well as placebo. After establishing baseline seizure frequency for 4 weeks, randomized patients will be titrated to their dose over a 2-week titration period, followed by a 12-week fixed dose maintenance period. We are targeting a total of 225 randomized patients (75 per treatment arm) in the trial. The primary endpoint of the clinical trial is change in the number of seizures that result in drops between baseline and the combined titration and maintenance periods at the 0.8 mg/kg/day dose. The key secondary endpoints include change in the number of seizures that result in drops between baseline and the combined titration and maintenance periods at the 0.2 mg/kg/day dose, and the proportion of patients achieving a 50 percent reduction in drop seizures. Part 2 of the clinical trial will be a 12-month open-label extension to evaluate the long-term safety, tolerability and effectiveness of Fintepla. In December 2018, we announced that we expect to complete enrollment for Study 1601 in the second half of 2019 and be able to announce top-line results from the study in the first quarter of 2020.

**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 (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.

***Contingent Consideration Liabilities Resulting from a Business Combination***

In conjunction with our business combination we have recorded contingent consideration liabilities payable upon the achievement of specified development, regulatory approval or sales-based milestone events. The contingent consideration liabilities are measured at their respective fair values as of the acquisition date. The models used in valuing the contingent consideration liabilities are based on significant unobservable inputs, including but not limited to:

- estimates of revenues related to the products or product candidates;
- the probability of success for unapproved product candidates considering their stages of development;
- the time to complete the development and approval of product candidates;
- the life of the potential commercialized products and associated risks, including the inherent difficulties and uncertainties in developing a product candidate such as obtaining FDA and other regulatory approvals;
- risks related to the viability of and potential alternative treatments in any future target markets; and
- risk adjusted discount rates.

We revalue contingent consideration obligations each quarter following the acquisition and record increases or decreases in fair value within the change in fair value of contingent consideration line item in our consolidated statements of operations.

Increases or decreases in the fair value of our contingent consideration liabilities can result from updates to assumptions such as the expected timing or probability of achieving the specified milestones, changes in projected revenues, changes in time periods to attain events or revenue targets, or changes in discount rates. Significant judgment is employed in determining these assumptions as of the acquisition date and for each subsequent period. Updates to assumptions could have a significant impact on our results of operations in any given period. Actual results may differ from estimates.

We believe the fair values used to record contingent consideration liabilities incurred in connection with the business combination are based upon reasonable estimates and assumptions given the facts and circumstances as of the related valuation dates.

***Goodwill and Indefinite-Lived Intangible Assets***
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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. Accordingly, our review of goodwill impairment indicators is performed at the entity-wide level. In performing each annual impairment assessment and any interim impairment assessment, we determine if we should qualitatively assess whether it is more likely than not that the fair value goodwill is less than its carrying amount (the qualitative impairment test). Some of the factors considered in the assessment include general macro-economic conditions, conditions specific to the industry and market, cost factors, the overall financial performance and whether there have been sustained declines in the Company's share price. If we conclude it is more likely than not that the fair value of the reporting unit is less than its carrying amount, or elect not to use the qualitative impairment test, a quantitative impairment test is performed using a two-step process. The first step of the goodwill qualitative impairment assessment 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. In 2018, we elected to bypass the qualitative goodwill impairment assessment. As of October 1, 2018, we determined through step one of our quantitative impairment test that the fair value of our single reporting unit significantly exceeded its carrying value and concluded that goodwill was not impaired. We did not recognize any goodwill impairment in any of the years presented.

*Indefinite-Lived Intangible Asset*

Our indefinite-lived intangible asset consists of in-process research and development (IPR&D) acquired in a business combination 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 perform a final test for impairment and 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.

In performing each annual impairment assessment and any interim impairment assessment, we determine if we should qualitatively assess whether it is more likely than not that the fair value of our IPR&D asset is less than its carrying amount (the qualitative impairment test). If we conclude that is the case, or elect not to use qualitative impairment test, we would proceed with quantitatively determining the fair value of the IPR&D asset and comparing its fair value to its carrying value to determine the amount of impairment, if any (the quantitative impairment test).

In performing the qualitative impairment test, we consider the results of the most recent quantitative impairment test and identify the most relevant divers of the fair value for the IPR&D asset. The most relevant drivers of fair value we have identified are consistent with the assumptions used in the quantitative estimate of the IPR&D asset discussed below. Using these

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drivers, we identify events and circumstances that may have an effect on the fair value of the IPR&D asset since the last time the IPR&D's fair value was quantitatively determined. We then weigh these factors to determine and conclude if it is not more likely than not that the IPR&D asset is impaired. If it is more likely than not that the IPR&D asset is impaired we proceed with quantitatively determining the fair value of the IPR&D asset.

We use the income approach to determine the fair value of our IPR&D asset. 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. This estimate includes significant assumptions regarding the estimates that market participants would make in evaluating the IPR&D asset, including the probability of successfully completing clinical trials and obtaining regulatory approval to market the IPR&D asset, the timing of and the expected costs to complete IPR&D projects, future net cash flows from potential drug sales, which are based on estimates of the sales price of the drug, the number of patients who will be diagnosed and treated and our competitive position in the marketplace, and appropriate discount and tax rates. Any impairment to be recorded is calculated as the difference between the fair value of the IPR&D asset as of the date of the assessment with the carrying value of the IPR&D asset on our consolidated balance sheet.

For 2018, we performed a qualitative test and concluded that it is more-likely-than-not that the fair value of our IPR&D asset exceeded the carrying value and no further testing was required. We did not recognize any IPR&D impairment in any of the years presented.

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 periodically for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset (group) may not be recoverable. An impairment loss would be recognized when the carrying amount of the assets (asset group) exceeds the estimated undiscounted net cash flows. The amount of the impairment loss to be recorded is calculated as the excess of the carrying value of the assets (asset group) over their fair value.

In the fourth quarter of 2016, Endo informed us of their decision to discontinue Sumavel DosePro and we commenced the wind down of our manufacturing operations related to the supply of Sumavel DosePro to Endo (see Note 6 to our consolidated financial statements included in this Form 10-K). As a result, we performed an analysis to estimate cash flows from property and equipment used in the production of Sumavel DosePro in the fourth quarter of 2016. Based on this analysis, we recognized an impairment charge for long-lived assets of $6.4 million. In the first quarter of 2017, we recorded an additional asset impairment charge of $0.8 million for long-lived manufacturing assets associated with the production of Sumavel DosePro. There was no impairment to our long-lived assets in 2018.

***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 (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. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received. Such payments are evaluated for current or long term classification based on when they will be realized.

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***Stock-Based Compensation***

For equity awards that vest subject to the satisfaction of service requirements, compensation expense is measured based on the fair value of the award on the date of grant and is recognized as expense on a straight-line basis over the requisite service period. For stock awards which have a performance component, compensation cost is measured based on the fair value on the grant date (the date performance targets are established) and is expensed over the requisite service period for each separately vesting tranche when achievement of the performance objective becomes probable. We assess the probability of the performance objectives being met on a continuous basis.

We use a Black-Scholes option-pricing model to determine the fair value of our stock options. This fair value determined using this model is affected by our stock price, as well as assumptions regarding a number of subjective variables. These variables include the expected stock price volatility over the expected term of the option, the expected term of the option and the risk-free interest rate associated with the expected term of the option. The expected term of employee options granted is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term).We estimate expected volatility based on our historical stock prices over the expected term. If any of the assumptions used in the Black-Scholes option pricing model change significantly, stock-based compensation expense may differ materially in the future from that recorded in the current period. We recognize forfeitures as they occur.

We expect to continue to grant stock options and awards in the future, and to the extent that we do, our actual stock-based compensation expense recognized in future periods will likely increase.

***Income Taxes***

We account for income taxes under the asset and liability method of accounting. We recognize deferred tax assets and liabilities for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, as well as for operating loss and tax credit carryforwards. We measure deferred tax assets and liabilities using enacted tax rates expected to apply to taxable income in the years in which we expect to recover or settle those temporary differences. We recognize the effect of a change in tax rates on deferred tax assets and liabilities in the results of operations in the period that includes the enactment date. We reduce the measurement of a deferred tax asset, if necessary, by a valuation allowance if it is more likely than not that we will not realize some or all of the deferred tax asset.

We account for uncertain tax positions by recognizing the financial statement effects of a tax position only when, based upon technical merits, it is more likely than not that the position will be sustained upon examination. Significant judgment is required in determining the accounting for income taxes. In the ordinary course of business, many transactions and calculations arise where the ultimate tax outcome is uncertain. Our judgments, assumptions and estimates relative to the accounting for income taxes take into account current tax laws, our interpretation of current tax laws, and possible outcomes of future audits conducted by foreign and domestic tax authorities. Although we believe that our estimates are reasonable, the final tax outcome of matters could be different from our assumptions and estimates used when determining the accounting for income taxes. Such differences, if identified in future periods, could have a material effect on the amounts recorded in our consolidated financial statements.

**Results of Operations**

***Comparison of Years Ended December 31, 2018, 2017 and 2016***

***Revenue***

| | Year Ended December 31, | | | 2017 to 2018 | | 2016 to 2017 | |
|---|---|---|---|---|---|---|---|
| (Dollars in thousands) | 2018 | 2017 | 2016 | $ change | % change | $ change | % change |
| Contract manufacturing revenue | $ — | $ 9,821 | $ 28,525 | $ (9,821) | (100)% | $ (18,704) | (66)% |
| Other | — | — | 325 | — | —% | (325) | (100)% |
| Total revenue | $ — | $ 9,821 | $ 28,850 | $ (9,821) | (100)% | $ (19,029) | (66)% |

We did not generate any revenue in 2018 as we currently do not have any products approved for sale. Revenue

generated in 2017 and 2016 resulted from supplying Sumavel DosePro to Endo under the Supply Agreement, which terminated in September 2017.

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***Cost of Contract Manufacturing***

| | Year Ended December 31, | | | 2017 to 2018 | | 2016 to 2017 | |
|---|---|---|---|---|---|---|---|
| (Dollars in thousands) | 2018 | 2017 | 2016 | $ change | % change | $ change | % change |
| Cost of contract manufacturing | $ — | $ 10,729 | $ 22,173 | $ (10,729) | (100)% | $ (11,444) | (52)% |

The decrease in cost of manufacturing in 2017 as compared to 2016 corresponded to the decrease in revenue in 2017 as compared to 2016. Cost of contract manufacturing in 2017 included a $2.2 million write-down of inventory to its net realizable value.

***Research and Development Expenses***

| | Year Ended December 31, | | | 2017 to 2018 | | 2016 to 2017 | |
|---|---|---|---|---|---|---|---|
| (Dollars in thousands) | 2018 | 2017 | 2016 | $ change | % change | $ change | % change |
| Research and development | $ 100,925 | $ 67,449 | $ 41,840 | $ 33,476 | 50% | $ 25,609 | 61% |

Research and development expenses consist of expenses incurred in developing, testing and seeking marketing approval of our product candidates, including: license and milestone payments; payments made to third-party clinical research organizations, or CROs, and investigational sites, which conduct our clinical 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 utilize contract manufacturing organizations, CROs, contract laboratories and independent contractors to produce product candidate material and for the conduct of our 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 estimated progress toward completion at the end of each reporting period. We coordinate clinical trials through a number of contracted investigational sites and recognize the associated expense based on a number of factors, including actual and estimated subject enrollment and visits, direct pass-through costs and other clinical site fees. The table below sets forth information regarding our research and development costs for our major development programs.

The table below sets forth information regarding our research and development costs for our major development programs.

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | (In Thousands) | | |
| **Research and development expenses:** | | | |
| Fintepla for Dravet syndrome | $ 52,765 | $ 44,181 | $ 29,133 |
| Fintepla for LGS | 15,295 | 3,638 | — |
| Relday [1] | — | 40 | 439 |
| Other [2] | 32,865 | 19,590 | 12,268 |
| Total | $ 100,925 | $ 67,449 | $ 41,840 |

(1) In August 2017, the development and license agreement with respect to Relday was terminated and all product rights reverted back to its owner.
(2) Other research and development expenses include employee and infrastructure resources that are not tracked on a program-by-program basis.
The increases in Fintepla for Dravet syndrome expense in 2018 as compared to 2017, and in 2017 as compared to 2016 were attributable to the progression and expansion of our clinical trial activities related to our Phase 3 development program of Fintepla in Dravet syndrome including Study 1, Study 1504 and Study 1503.
The increase in Fintepla for LGS expense in 2018 as compared to 2017 was primarily attributable to the initiation of (Study 1601) in November 2017.
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
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development activities on a program-by-program basis. The increases in research and development expense, other in 2018 as compared to 2017, and in 2017 as compared to 2016 were primarily attributable to increased headcount to support our increased clinical trial activities.

***Selling, General and Administrative Expenses***

| | Year Ended December 31, | | | 2017 to 2018 | | 2016 to 2017 | |
|---|---|---|---|---|---|---|---|
| (Dollars in thousands) | 2018 | 2017 | 2016 | $ change | % change | $ change | % change |
| Selling | $ 15,734 | $ 4,762 | $ 6,002 | $ 10,972 | 230% | $ (1,240) | (21)% |
| General and administrative | 23,216 | 21,123 | 20,994 | 2,093 | 10% | 129 | 1% |
| Total | $ 38,950 | $ 25,885 | $ 26,996 | $ 13,065 | 50% | $ (1,111) | (4)% |

Selling expense consists primarily of salaries and benefits of marketing and commercial personnel, marketing and advertising costs, service fees under our co-promotion agreement and product sample costs.

Selling expense increased significantly in 2018 as compared to 2017 due primarily to an increase in marketing and commercial headcount and commercial expenses including marketing and pricing studies to prepare for a potential commercial launch of Fintepla. The decrease in selling expense in 2017 as compared to 2016 reflected lower spend on market research activities related to Fintepla.

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, tax and accounting services.

General and administrative expense increased by $2.1 million in 2018 as compared to 2017 due primarily to increased general and administrative headcount as we build our infrastructure to support the expansion of our operations.

General and administrative expenses remained flat in 2017 as compared to 2016.

***Change in Fair Value of Contingent Consideration and Asset Impairment Charges***

| | Year Ended December 31, | | | 2017 to 2018 | | 2016 to 2017 | |
|---|---|---|---|---|---|---|---|
| (Dollars in thousands) | 2018 | 2017 | 2016 | $ change | % change | $ change | % change |
| Change in fair value of contingent consideration | $ 1,300 | $ 24,100 | $ 1,800 | $ (22,800) | (95)% | $ 22,300 | 1,239% |
| Asset impairment charges | $ — | $ 1,116 | $ 8,431 | $ (1,116) | (100)% | $ (7,315) | (87)% |

The contingent consideration liability resulted from our October 2014 acquisition of worldwide development and commercialization rights to Fintepla, where we agreed to pay additional consideration upon the achievement of certain regulatory-related and commercial-related milestones.

In 2018, we recorded a charge of $1.3 million to reflect an increase in the estimated fair value of contingent consideration liability primarily to reflect a reduction in the discount periods due to the passage of time, partially offset by a change in discount rate.

In 2017, we revised the fair value estimates for contingent consideration liability to incorporate increased probabilities of success as a result of positive top-line data from Study 1 in September 2017, and the initiation of Study 1601 in November 2017. Accordingly, we recorded a charge associated with the resulting change in the estimated fair value of $24.1 million.

In 2016, we recorded a charge of $1.8 million to reflect an increase in the estimated fair value of contingent consideration liability resulting from adjustments to the estimated time frame necessary to achieve the developmental milestones, changes in market interest rates as well as the passage of time.

Asset impairment charges incurred in 2017 and 2016 were primarily associated with long-lived assets used in the contract manufacturing of Sumavel DosePro to our single customer Endo under the Supply Agreement, which terminated in 2017.

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***Other income (expense)***

| | Year Ended December 31, | | | 2017 to 2018 | | 2016 to 2017 | |
|---|---|---|---|---|---|---|---|
| (Dollars in thousands) | 2018 | 2017 | 2016 | $ change | % change | $ change | % change |
| Interest income | $ 7,170 | $ 1,090 | $ 443 | $ 6,080 | 558% | $ 647 | 146% |
| Interest expense | (6) | (2,644) | (2,825) | 2,638 | (100)% | 181 | (6)% |
| Loss on extinguishment of debt | — | (4,876) | — | 4,876 | (100)% | (4,876) | —% |
| Change in fair value of common stock warrant liabilities | 169 | 297 | 5,387 | (128) | (43)% | (5,090) | 94% |
| Other income (expense), net | 10,126 | 47 | 46 | 10,079 | 21,445% | 1 | 2% |
| Total other income (expense) | $ 17,459 | $ (6,086) | $ 3,051 | $ 23,545 | (135)% | $ (9,137) | 299% |

***Interest Income***

In 2018, we invested our excess cash from net proceeds received from our August 2018 follow-on offering in marketable securities. Interest income increased in 2018 as compared to 2017 and was attributable to interest earned from purchases of and investments in marketable securities. Interest income increased in 2017 as compared to 2016 and was attributable to interest earned from higher average cash and cash equivalents balances.

***Interest Expense***

In 2018, we had no debt. Interest expense incurred in 2017 and 2016 were primarily attributable to our term loan which was repaid in 2017 and amortization of imputed interest on an interest-free working capital advance related to the Supply Agreement, which was settled in 2017. See Note 8 to our consolidated financial statements for additional information.

***Loss on Extinguishment of Debt***

Loss on extinguishment of debt in 2017 consisted of a $1.5 million loss resulting from the early prepayment of our term loan and a $3.4 million noncash charge for the extinguishment of the working capital advance note payable related to the Supply Agreement resulting in the write-off of unamortized debt discount. See Note 8 to our consolidated financial statements for additional information.

***Change in Fair Value of Common Stock Warrant Liabilities***

The change in fair value of common stock warrant liabilities resulted from the periodic remeasurement of the estimated fair value (see Note 5 to our consolidated financial statements for additional discussion). The decrease in fair value of common stock warrant liabilities in 2017 as compared to 2016 was due to the expiration of outstanding warrants in July 2017, which were exercisable for 1.9 million shares of common stock with an exercise price of $20.00 per share. The warrants were issued in connection with a 2012 common stock public offering. As of December 31, 2018, we had outstanding warrants to purchase up to 28,125 shares of common stock at an exercise price of $72.00 per share that are measured at fair value at each reporting date. These warrants will expire in July 2021

if not exercised.

***Other Income (Expense), Net***

Other income (expense), net increased by $10.1 million in 2018 as compared to 2017 and was attributable to income related to claims submitted under UK's small and medium sized enterprises (SME) research and development (R&D) tax relief scheme for qualifying expenditures incurred in the 2015 and 2016 tax years. See Notes 2 and 13 in Part IV, Item 15, Notes to Consolidated Financial Statements for additional details. Other income (expense), net in 2017 and 2016 consisted of foreign currency transaction gains and losses.

***Income Taxes***

| | Year Ended December 31, | | | | | 2017 to 2018 | | 2016 to 2017 |
|---|---|---|---|---|---|---|---|---|
| **(Dollars in thousands)** | **2018** | **2017** | **2016** | **$ change** | **% change** | **$ change** | **% change** | |
| Income tax benefit | $ — | $ — | $ 948 | $ — | (100)% | $ (948) | (100)% | |

In 2017 and 2018, no tax provision has been recognized because of our operating losses and the full valuation allowance provided on all deferred tax assets, including net operating losses. In 2016, we recognized a tax benefit of $0.9 million primarily due to the impact of changes in tax laws (tax rate reductions) enacted in the UK, which decreased our deferred tax liability.

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**LIQUIDITY AND CAPITAL RESOURCES**

Since we commenced operations in 2006, our operations have been financed primarily through equity and debt financings and proceeds from two business divestitures—Sumavel DosePro and Zohydro ER. Excluding gains from business divestitures, we have incurred significant net losses from operations and negative cash flows from operating activities since inception. As of December 31, 2018, we have an accumulated deficit of $696.0 million. We currently do not have an approved product for sale and we have no source of revenue. We expect to continue to incur significant operating losses and negative cash flows from operations to advance our product candidates through development and commercialization. Additionally, upon acceptance of our regulatory submissions or approval by the FDA or the EMA for Fintepla, if at all, we will owe milestone payments related to our acquisition of worldwide development and commercialization rights to Fintepla. For example, the EMA's acceptance of our MAA in February 2019 triggered a $10.0 million development milestone payment due to the former owners of Brabant and an additional $10.0 million milestone payment shall become due and payable if our NDA, filed in February 2019, is accepted by the FDA. We do not know when, or if, we will generate any revenue from product sales and do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of, and commercialize Fintepla. To date, we have relied primarily on the proceeds from equity offerings to finance our operations. Our recent equity offerings include the following transactions.

In the third quarter of 2017, we sold a total of 1,550,880 shares of our common stock pursuant to an at-the-market sale agreement with Cantor Fitzgerald & Co. (ATM Agreement) resulting in net proceeds of approximately $19.4 million.

In October 2017, we completed an underwritten public offering for the sale of 7,700,000 shares of our common stock. Net proceeds raised from the offering amounted to approximately $271.3 million.

In the second quarter of 2018, we sold a total of 740,417 shares of our common stock pursuant to the ATM Agreement and received net proceeds of approximately $30.3 million.

In August 2018, we completed an underwritten public offering for the sale of 6,000,000 shares of our common stock. Net proceeds raised from the offering were approximately $292.9 million.

The following table summarizes our cash and cash equivalents and marketable securities as of December 31, 2018 and 2017:

| | 2018 | 2017 | $ Change |
|---|---|---|---|
| | (In Thousands) | | |
| Cash and cash equivalents | $ 68,454 | $ 293,503 | $ (225,049) |
| Marketable securities | 445,733 | — | 445,733 |
| Total | $ 514,187 | $ 293,503 | $ 220,684 |

A summary of our cash flows for the periods presented was as follows:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | (In Thousands) | | |
| Operating activities | $ (111,658) | $ (75,874) | $ (72,880) |
| Investing activities | (444,750) | (76) | (103) |
| Financing activities | 331,359 | 277,902 | (817) |

*Operating Activities*

Net cash used in operating activities of $111.7 million in 2018 was primarily attributable to a net loss of $123.9 million, offset by noncash charges of $14.8 million including $15.5 million of stock-based compensation, and a net cash inflow from changes in operating assets and liabilities of $2.5 million. The change in our net operating assets and

liabilities was primarily due to increases in accrued expenses related to an increase in our research and development activities and timing of prepayments for CRO clinical costs.

Net cash used in operating activities of $75.9 million in 2017 was primarily attributable to a net loss of $126.8 million, offset by aggregate noncash charges of $39.5 million including $24.1 million from the fair value remeasurement of our contingent consideration liability, and a net cash inflow from changes in operating assets and liabilities of $11.4 million. The increase in cash provided by the net change in operating assets and liabilities was primarily attributable to cash received under the Supply Agreement for previously delivered product. Certain working capital balances which were net settled by the

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extinguishment of the working capital advance note payable pursuant to the termination of the Supply Agreement were accounted for as a noncash activity.

Net cash used in operating activities of $72.9 million in 2016 was primarily attributable to a net loss of $69.7 million and a net cash outflow from changes in operating assets and liabilities of $17.8 million, offset by aggregate noncash charges of $14.6 million. 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 Fintepla, 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 contract manufacturing operations related to the supply of Sumavel DosePro to our single customer.

*Investing Activities*

Net cash used in investing activities in 2018 included cash outflows of $569.5 million from the purchase of available-for-sale securities and $1.0 million for construction of tenant improvements at our new corporate headquarters. Cash outflows were partially offset by cash inflows of $125.8 million from maturities of available-for-sale securities.

Net cash used in investing activities in 2017 and 2016 was primarily related to purchases of computers and other office equipment.

*Financing Activities*

Net cash provided by financing activities of $331.4 million in 2018 consisted of net proceeds of $292.9 million from a follow-on offering of common stock, $30.2 million from the sale of common stock pursuant to the ATM Agreement and $9.7 million from issuance of common stock under equity incentive plans, offset by $1.4 million for payment of employee withholding taxes related to net share settlement of equity awards.

Net cash provided by financing activities of $277.9 million in 2017 consisted of net proceeds of $271.3 million from a follow-on offering of common stock, $19.4 million from sale of common stock pursuant to the ATM Agreement and $9.2 million from issuance of common stock under equity incentive plans, offset by $21.9 million to repay all outstanding indebtedness.

Net cash used in financing activities of $0.8 million in 2016 consisted of $1.2 million for net debt repayment, offset by cash receipts of $0.4 million from issuance of common stock under equity incentive plans.

**Future Funding Requirements**

Our principal uses of cash are research and development expenses, selling, general and administrative expenses and other working capital requirements. 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 our product candidates and any future product candidates that we may develop, in-license or acquire;

•the timing of regulatory approval for any of our 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 our 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; and

•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 Fintepla.

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

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terms, or at all. If we are unsuccessful in raising additional funds when needed, 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.

**Contractual Obligations and Commitments**

The following table describes our contractual cash obligations and commitments as of December 31, 2018:

| | Payments due by period | | | | |
|---|---|---|---|---|---|
| | Total | Less than 1 year | 1-3 years | 4-5 years | More than 5 years |
| | (In Thousands) | | | | |
| Operating lease obligations (1) | $ 15,821 | $ 1,201 | $ 3,479 | $ 3,845 | $ 7,296 |

(1) Represents the minimum rental payments, net of sublease income.

In connection with our acquisition of Fintepla, we may be required to make certain regulatory and sales-based milestone payments. 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 were not included in the table above. See Notes 2 and 5 to our consolidated financial statements in this Form 10-K for additional details of our potential 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 arrangements, as defined in Item 303(a)(4)(ii) of Regulation S-K.

**Item 7A. Quantitative and Qualitative Disclosures About Market Risk**

As part of our investment portfolio, we own financial instruments that are sensitive to market risks. The primary objective of our investment activities is to preserve our capital until it is required to fund operations, including our research and development activities.

***Interest Rate Risk***

As of December 31, 2018, we had cash, cash equivalents and marketable securities of $514.2 million. We invest our excess cash primarily in money market funds and certificates of deposit, securities issued by the U.S. government and its agencies, corporate debt securities and commercial paper. These investments are denominated in U.S. Dollars. We place our investments with high quality credit issuers and, by policy, limit the amount of credit exposure to any one issuer. A portion of our investments consisting of interest-bearing securities are subject to interest rate risk and could decline in value if interest rates fluctuate. The portfolio includes cash equivalents and investments in marketable securities with active secondary or resale markets to ensure portfolio liquidity. Due to the conservative nature of these instruments, we do not believe that we have a material exposure to interest rate risk. A 100 basis points change in interest rates would not have a significant impact on the total value of our portfolio. We had no debt outstanding as of December 31, 2018.

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***Foreign Exchange Risk***

As a result of our UK operations, we face exposure to movements in foreign currency exchange rates, primarily the British Pound Sterling and the Euro against the U.S. Dollar. The current exposures arise primarily from cash and payables and accruals denominated in the British Pound Sterling and the Euro. We have not hedged our foreign currency since the exposure has not been material to our historical operating results. Based on our foreign currency exchange rate exposures at September 30, 2018, a hypothetical 10% adverse fluctuation in the average exchange rate of the Euro or the British Pound Sterling would not have had a material impact on our consolidated financial statements. We will continue to monitor and evaluate our exposure to 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**

The financial statements and supplementary data required by Item 8 are included herein, commencing on page F-1 of this report.

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

None.

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**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 SEC'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 SEC 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, 2018 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**

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, 2018, 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, 2018, which is included below.

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**Report of Independent Registered Public Accounting Firm**

To the Stockholders and the Board of Directors of Zogenix, Inc.

**Opinion on Internal Control over Financial Reporting**

We have audited Zogenix, Inc.'s internal control over financial reporting as of December 31, 2018, 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"). In our opinion, Zogenix, Inc. ("the Company") maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of the Company as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes and our report dated February 28, 2019 expressed an unqualified opinion thereon.

**Basis for Opinion**

The Company'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 are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. 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.

**Definition and Limitations of Internal Control Over Financial Reporting**

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.

/s/ Ernst & Young LLP

Redwood City, California

February 28, 2019

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**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 2019 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, 2018, 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 the signature page to this Annual Report on Form 10-K 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**

To the Stockholders and the Board of Directors of Zogenix, Inc.

**Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of Zogenix, Inc. (the "Company") as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2018, 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 February 28, 2019 expressed an unqualified opinion thereon.

**Basis for Opinion**

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2007.

Redwood City, California

February 28, 2019

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**Zogenix, Inc.**
**Consolidated Balance Sheets**
**(In thousands, except per share amounts)**

| | December 31, 2018 | 2017 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 68,454 | $ 293,503 |
| Marketable securities | 445,733 | — |
| Prepaid expenses | 6,718 | 5,994 |
| Other current assets | 11,825 | 5,206 |
| Total current assets | 532,730 | 304,703 |
| Property and equipment, net | 2,870 | 245 |
| Indefinite-lived intangible asset | 102,500 | 102,500 |
| Goodwill | 6,234 | 6,234 |
| Other assets | 3,997 | 3,931 |
| Total assets | $ 648,331 | $ 417,613 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 7,989 | $ 3,356 |
| Accrued clinical trial expenses | 10,621 | 8,657 |
| Accrued compensation | 5,277 | 6,616 |
| Other accrued liabilities | 1,845 | 1,842 |
| Current portion of contingent consideration | 32,300 | — |
| Common stock warrant liabilities | 343 | 512 |
| Total current | 58,375 | 20,983 |

| | | |
|---|---|---|
| liabilities | | |
| Contingent consideration, net of current portion | 45,900 | 76,900 |
| Deferred tax liability | 17,425 | 17,425 |
| Other long-term liabilities | 3,830 | 784 |
| Commitments and contingencies | | |
| Stockholders' equity: | | |
| Preferred stock, $0.001 par value, 10,000 shares authorized, none issued and outstanding | — | — |
| Common stock, $0.001 par value; 50,000 shares authorized; 42,078 and 34,808 shares issued and outstanding at December 31, 2018 and 2017, respectively. | 42 | 35 |
| Additional paid-in capital | 1,218,710 | 873,526 |
| Accumulated deficit | (695,954) | (572,040) |
| Accumulated other comprehensive income | 3 | — |
| Total stockholders' equity | 522,801 | 301,521 |
| Total liabilities and stockholders' equity | $ 648,331 | $ 417,613 |

See accompanying notes to the consolidated financial statements.

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**Zogenix, Inc.**
**Consolidated Statements of Operations**
**(In thousands, except per share amounts)**

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2018** | **2017** | **2016** |
| Revenue: | | | |
| Contract manufacturing revenue | $ — | $ 9,821 | $ 28,525 |
| Other | — | — | 325 |
| Total revenue | — | 9,821 | 28,850 |
| Operating expenses (income): | | | |
| Cost of contract manufacturing | — | 10,729 | 22,173 |
| Royalty expense | — | — | 295 |
| Research and development | 100,925 | 67,449 | 41,840 |
| Selling, general and administrative | 38,950 | 25,885 | 26,996 |
| Loss on contract termination | — | 478 | — |
| Change in fair value of contingent consideration | 1,300 | 24,100 | 1,800 |
| Asset impairment charges | — | 1,116 | 8,431 |
| Total operating expenses | 141,175 | 129,757 | 101,535 |
| Loss from operations | (141,175) | (119,936) | (72,685) |
| Other income (expense): | | | |
| Interest income | 7,170 | 1,090 | 443 |
| Interest expense | (6) | (2,644) | (2,825) |
| Loss on extinguishment of debt | — | (4,876) | — |
| Change in fair value of common stock warrant liabilities | 169 | 297 | 5,387 |
| Other income (expense), net | 10,126 | 47 | 46 |
| Total other income (expense) | 17,459 | (6,086) | 3,051 |
| Loss from continuing operations before | (123,716) | (126,022) | (69,634) |

| | | | |
|---|---|---|---|
| income taxes | | | |
| Income tax benefit | — | — | 948 |
| Loss from continuing operations | (123,716) | (126,022) | (68,686) |
| Loss from discontinued operations, net of tax | (198) | (795) | (1,021) |
| Net loss | $ (123,914) | $ (126,817) | $ (69,707) |
| Net loss per share, basic and diluted: | | | |
| Continuing operations | $ (3.27) | $ (4.62) | $ (2.77) |
| Discontinued operations | $ — | $ (0.03) | $ (0.04) |
| Total | $ (3.27) | $ (4.65) | $ (2.81) |
| Weighted average common shares outstanding, basic and diluted | 37,884 | 27,301 | 24,785 |

See accompanying notes to the consolidated financial statements.

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**Zogenix, Inc.**
**Consolidated Statements of Comprehensive Loss**
**(in thousands)**

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2018** | **2017** | **2016** |
| Net loss | $ (123,914) | $ (126,817) | $ (69,707) |
| Other comprehensive income: | | | |
| Net unrealized gains on marketable securities, net of tax | 3 | — | — |
| Comprehensive loss | $ (123,911) | $ (126,817) | $ (69,707) |

See accompanying notes to the consolidated financial statements.

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**Zogenix, Inc.**
**Consolidated Statements of Stockholders' Equity**
**(in thousands)**

| | Common Stock | | Additional Paid-in Capital | Accumulated Other Comprehensive Income | Accumulated Deficit | Total Stockholders' Equity |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| Balance at December 31, 2015 | 24,732 | $ 25 | $ 558,251 | $ — | $ (375,516) | $ 182,760 |
| Net loss | — | — | — | — | (69,707) | (69,707) |
| Issuance of common stock under employee equity plans | 41 | — | 350 | — | — | 350 |
| Stock-based compensation | — | — | 7,353 | — | — | 7,353 |
| Balance at December 31, 2016 | 24,812 | 25 | 565,954 | — | (445,223) | 120,756 |
| Net loss | — | — | — | — | (126,817) | (126,817) |
| Issuance of common stock, net of issuance costs of $18.1 million | 9,256 | 9 | 290,582 | — | — | 290,591 |
| Issuance of common stock upon net exercise of common stock warrants | 26 | — | — | — | — | — |
| Issuance of common stock under employee equity plans | 713 | 1 | 10,835 | — | — | 10,836 |
| Stock-based compensation | — | — | 6,155 | — | — | 6,155 |
| Balance at December 31, 2017 | 34,808 | 35 | 873,526 | — | (572,040) | 301,521 |
| Net loss | — | — | — | — | (123,914) | (123,914) |
| Net unrealized gain on marketable securities, net of tax | — | — | — | 3 | — | 3 |
| Issuance of common stock, net of issuance | 6,740 | 7 | 323,128 | — | — | 323,135 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| costs of $20.2 million | | | | | | | | | | |
| Issuance of common stock under employee equity plans | 563 | — | | 7,994 | | — | | — | | 7,994 |
| Shares repurchased for tax withholdings related to net share settlement of employee equity awards | (33) | — | | (1,430) | | — | | — | | (1,430) |
| Stock-based compensation | — | — | | 15,492 | | — | | — | | 15,492 |
| Balance at December 31, 2018 | 42,078 | $ | 42 | $ | 1,218,710 | $ | 3 | $ | (695,954) | $ 522,801 |

See accompanying notes to the consolidated financial statements.

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**Zogenix, Inc.**
**Consolidated Statements of Cash Flows**
**(in thousands)**

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2018** | **2017** | **2016** |
| **Cash flows from operating activities:** | | | |
| Net loss | $ (123,914) | $ (126,817) | $ (69,707) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Stock-based compensation | 15,492 | 6,155 | 7,353 |
| Depreciation | 155 | 425 | 1,402 |
| Amortization of debt issuance costs and debt discount | — | 887 | 991 |
| Net accretion and amortization of investments in marketable securities | (1,998) | — | — |
| Change in fair value of common stock warrant liabilities | (169) | (297) | (5,387) |
| Change in fair value of contingent consideration | 1,300 | 24,100 | 1,800 |
| Inventory write-down | — | 2,232 | — |
| Asset impairment charges | — | 1,116 | 8,431 |
| Loss on extinguishment of debt | — | 4,876 | — |
| Changes in operating assets and liabilities: | | | |
| Trade accounts receivable | — | 9,356 | (11,181) |
| Inventory | — | 2,583 | 4,983 |
| Prepaid expenses and other current assets | (9,335) | (801) | (3,394) |
| Other assets | 266 | (2,784) | 471 |
| Accounts payable, accrued and other liabilities | 6,545 | 4,340 | (1,778) |
| Deferred revenue | — | (1,245) | (5,839) |
| Deferred tax liability | — | — | (1,025) |
| | (111,658) | (75,874) | (72,880) |

| | | | |
|---|---|---|---|
| Net cash used in operating activities | | | |
| **Cash flows from investing activities:** | | | |
| Purchases of marketable securities | (569,515) | — | — |
| Proceeds from maturities of marketable securities | 125,783 | — | — |
| Purchases of property and equipment | (1,018) | (76) | (103) |
| Net cash used in investing activities | (444,750) | (76) | (103) |
| **Cash flows from financing activities:** | | | |
| Proceeds from borrowings | — | — | 2,167 |
| Principal repayments of long-term debt | — | (20,000) | (3,334) |
| Payment of fees to extinguish long-term debt | — | (1,865) | — |
| Proceeds from issuance of common stock under equity incentive plans | 9,654 | 9,176 | 350 |
| Taxes paid related to net share settlement of equity awards | (1,430) | — | — |
| Proceeds from issuance of common stock, net of issuance costs | 323,135 | 290,591 | — |
| Net cash provided by (used in) financing activities | $ 331,359 | $ 277,902 | $ (817) |
| Net (decrease) increase in cash, cash equivalents and restricted cash (1) | $ (225,049) | $ 201,952 | $ (73,800) |
| Cash, cash equivalents and restricted cash at beginning of period (1) | $ 293,503 | $ 91,551 | $ 165,351 |
| Cash, cash equivalents and restricted cash at end of period | $ 68,454 | $ 293,503 | $ 91,551 |

| | | | |
|---|---|---|---|
| **Supplemental disclosure of cash flow information:** | | | |
| Cash paid for interest | $ — | $ 1,475 | $ 1,470 |
| **Noncash investing and financing activities:** | | | |
| Purchases of property and equipment in accounts payable and accrued liabilities | $ 1,762 | $ — | $ — |
| Extinguishment of working capital advance note payable under the Supply Agreement through net settlement of balances owed to the Company (2) | $ — | $ 7,000 | $ — |

*(1) Amounts in 2016 have been retrospectively adjusted to reflect the adoption of new accounting guidance that was effective January 1, 2018. See Note 2 for further information.*
*(2) See Notes 3 and 8 for further information.*

See accompanying notes to the consolidated financial statements.

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**Zogenix, Inc.**

**Notes to Consolidated Financial Statements**

**1. Organization and Description of Business**

Zogenix, Inc. and subsidiaries (the Company) is a pharmaceutical company developing and commercializing transformative central nervous system (CNS) therapies for people living with serious and life-threatening rare CNS disorders and medical conditions. The Company is currently focused on developing and commercializing CNS therapies to address rare, or "orphan" childhood-onset epilepsy disorders.

The Company was incorporated as SJ2 Therapeutics, Inc. in May 2006 in the State of Delaware and changed its name to Zogenix, Inc. in August 2006. The Company is in the development stage and generates no revenue. Previously, the Company performed contract manufacturing services in supplying Sumavel DosePro to Endo International plc (Endo) under a long-term supply agreement (Supply Agreement), which was terminated in 2017.

**Future Funding Requirements**

Excluding gains from two discrete business divestitures, the Company has incurred significant net losses and negative cash flows from operating activities resulting in an accumulated deficit of $696.0 million as of December 31, 2018. Management expects to continue to incur significant operating losses and negative cash flows from operations as the Company continues to incur costs related to its ongoing Phase 3 clinical trials of Fintepla in North America and the European Union (EU) in Dravet syndrome and a Phase 3 clinical trial in Lennox-Gastaut syndrome (LGS), which commenced in November 2017. Additionally, upon acceptance of the Company's regulatory submissions or approval for Fintepla/ZX008 by the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA), if at all, the Company will owe milestone payments under an existing agreement in connection with the Company's prior acquisition of Fintepla. Through December 31, 2018, the Company has relied primarily on the proceeds from equity offerings to finance its operations. Until such time, if ever, the Company can generate a sufficient amount of revenue to finance its cash requirements, the Company may need to continue to rely on additional financing to achieve its business objectives. However, if such financing is not available at adequate levels when needed, the Company may be required to significantly delay, scale back or discontinue one or more of the product development programs or commercialization efforts or other aspects of its business plans, and its operating results and financial condition would be adversely affected.

**2. Summary of Significant Accounting Policies**

**Basis of Presentation**

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States (GAAP) and include the accounts of Zogenix and its wholly-owned subsidiaries. The functional currency of the Company's foreign subsidiaries is the U.S. dollar. All intercompany transactions have been eliminated in consolidation.

Certain reclassifications have been made to the prior period amounts to conform to the current year presentation. Specifically, "Accrued clinical trial expenses" and "Other accrued liabilities", which previously were reported as "Accrued expenses" on the consolidated balance sheet, are now reported as separate line items.

**Use of Estimates**

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results may differ materially from those estimates. The Company believes significant judgment is involved in determining and in estimating the valuation of stock-based compensation, accrued clinical expenses, and contingent consideration liabilities. These estimates form the basis for making judgments about the carrying values of assets and liabilities when these values are not readily apparent from other sources.

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**Business Combinations**

The Company measures all assets acquired and liabilities assumed, including contingent consideration, at fair value as of the acquisition date. Contingent consideration obligations incurred in connection with a business combination are remeasured to their estimated fair values at each reporting period with the change in fair value recorded in operating expenses until the related contingencies are resolved. 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.

**Fair Value of Financial Instruments**

The Company's financial instruments, including cash and cash equivalents, other current assets, accounts payable and accrued liabilities, are carried at cost which approximates their fair value because of the short-term nature of these financial instruments. See Notes 4 and 5 for information on fair value for marketable securities, contingent consideration liabilities and the Company's outstanding common stock warrant liabilities.

**Cash Equivalents and Marketable Securities**

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 at the date of purchase.

The Company invests its excess cash in marketable securities with high credit ratings including money market funds and certificates of deposit, securities issued by the U.S. government and its agencies, corporate debt securities and commercial paper, which are all classified as "available-for-sale". The Company considers all available-for-sale securities, including those with maturity dates beyond 12 months, as available to support current operational liquidity needs and, therefore, classifies all securities with maturity dates beyond three months at the date of purchase as current assets on the consolidated balance sheets. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income on the consolidated statements of operations and comprehensive loss. Realized gains and losses and declines in value determined to be other-than-temporary, if any, on marketable securities are included in other income (expense), net. The cost of securities sold is determined using the specific identification method.

The Company periodically evaluates whether declines in fair values of its marketable securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the marketable security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or it is more likely than not it will be required to sell any marketable securities before recovery of its amortized cost basis. Factors considered include quoted market prices, recent financial results and operating trends, implied values from any recent transactions or offers of investee securities, credit quality of debt instrument issuers, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and management's strategy and intentions for holding the marketable security. To date, the Company has not recorded any impairment charges on its marketable securities related to other-than-temporary declines in market value.

**Concentration of Risk**

Cash equivalents and marketable securities are financial instruments that potentially subject the Company to concentration of credit risk. The Company maintains amounts on deposit with various financial institutions, which may exceed federally insured limits. However, management periodically evaluates the credit-worthiness of those institutions, and the Company has not experienced any losses on such deposits. The Company invests its excess cash primarily in money market funds and certificates of deposit, securities issued by the U.S. government and its agencies, corporate debt securities and commercial paper. The Company has established guidelines relative to diversification and maturities to maintain safety and liquidity. The Company has not experienced any credit losses related to these financial instruments and does not believe it is exposed to any significant credit risk related to these instruments.

Certain materials and key components that the Company utilizes in its operations are obtained through single suppliers. Since the suppliers of key components and materials must be named in a New Drug Application (NDA)

filed with the FDA for a product, significant delays can occur if the qualification of a new supplier is required. If delivery of material from the

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Company's suppliers were interrupted for any reason, the Company may be unable to supply any of its product candidates for clinical trials.

**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 2018, 2017 and 2016 was $0.2 million, $0.4 million and $1.4 million, respectively.

**Goodwill and Indefinite-Lived Intangible Assets**

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 difference between the purchase price and the fair value of assets acquired and liabilities assumed in a business combination is allocated to goodwill. Goodwill is evaluated for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist.

As of October 1, 2018, the Company performed a quantitative test and determined the fair value of its single reporting unit significantly exceeded its carrying value. As such, the Company concluded that goodwill was not impaired. The Company has not recognized any goodwill impairment in any of the years presented.

*Indefinite-Lived Intangible Asset*

The Company's indefinite-lived intangible asset consists of IPR&D acquired in a business combination 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 IPR&D 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 performed a final test for impairment and 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 IPR&D intangible asset.

In performing each annual impairment assessment and any interim impairment assessment, the Company determines if it should qualitatively assess whether it is more likely than not that the fair value of its IPR&D asset is less than its carrying amount (the qualitative impairment test). If the Company concludes that is the case, or elect not to use qualitative impairment test, the Company would proceed with quantitatively determining the fair value of the IPR&D asset and comparing its fair value to its carrying value to determine the amount of impairment, if any (the quantitative impairment test).

In performing the qualitative impairment test, the Company considers the results of the most recent quantitative impairment test and identifies the most relevant drivers of the fair value for the IPR&D asset. The most relevant drivers of fair value identified are consistent with the assumptions used in the quantitative estimate of the IPR&D asset discussed below. Using these drivers of fair value, the Company identifies events and circumstances that may have an effect on the fair value of the IPR&D asset since the last time the IPR&D's fair value was quantitatively determined. The Company then weighs these factors to determine and conclude if it is not more likely than not that the IPR&D asset is impaired. If it is more likely than not that the IPR&D asset is impaired, the Company proceeds with

quantitatively determining the fair value of the IPR&D asset.

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The Company uses the income approach to determine the fair value of its IPR&D asset. 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. This estimate includes significant assumptions regarding the estimates that market participants would make in evaluating the IPR&D asset, including the probability of successfully completing clinical trials and obtaining regulatory approval to market the IPR&D asset, the timing of and the expected costs to complete IPR&D projects, future net cash flows from potential drug sales, which are based on estimates of the sales price of the drug, the number of patients who will be diagnosed and treated and our competitive position in the marketplace, and appropriate discount and tax rates. Any impairment to be recorded is calculated as the difference between the fair value of the IPR&D asset as of the date of the assessment with the carrying value of the IPR&D asset on its consolidated balance sheet.

For 2018, the Company performed a qualitative test and concluded that it is more-likely-than-not that the fair value of the Company's IPR&D asset exceeded the carrying value and no further testing was required. The Company did not recognize any IPR&D impairment in any of the years presented.

**Impairment of Long-Lived Assets**

The Company evaluates long-lived assets periodically for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset (group) may not be recoverable. An impairment loss would be recognized when the carrying amount of the assets (asset group) exceeds the estimated undiscounted net cash flows. The amount of the impairment loss to be recorded is calculated as the excess of the carrying value of the assets (asset group) over their fair value.

The Company recognized an impairment charge for long-lived assets of $6.4 million in 2016 as a result of the decision by Endo International plc (Endo) to discontinue the sale of Sumavel DosePro and terminate the long-term manufacturing and supply agreement (the Supply Agreement) with the Company. In 2017, the Company recorded an impairment charge of $0.8 million for long-lived manufacturing assets associated with the production of Sumavel DosePro. There was no impairment to long-lived assets in 2018.

**Common Stock Warrant Liabilities**

In accordance with accounting guidance for common stock warrants that may potentially require cash settlement under certain circumstances, the Company classifies such common stock warrants as current liabilities on the consolidated balance sheet. The Company adjusts the carrying value of these common stock warrants to their estimated fair value at each reporting date with the increases or decreases in the fair value of such warrants recorded as change in fair value of warrant liabilities in the consolidated statement of operations.

**Revenue Recognition**

In 2018, the Company had no revenue as it had no contracts with customers. In 2017 and 2016, the Company recognized revenue from contract manufacturing services provided under the Supply Agreement with Endo, which terminated in September 2017. Contract manufacturing revenue was recognized under the legacy revenue recognition standard when all of the following criteria for revenue recognition have been met: (1) persuasive evidence of an arrangement existed (2) delivery has occurred or services have been rendered; (3) the fee was fixed or determinable; and (4) collectability was reasonably assured.

**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. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received. Such payments are evaluated for current or long-term classification based on when they will be realized.

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 (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

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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.

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.

**Income Taxes**

Income taxes are accounted for under the asset and liability method of accounting. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, as well as for operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the results of operations in the period that includes the enactment date. 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.

**UK's Research and Development (R&D) Tax Relief Scheme**

The Company carries out extensive research and development activities that benefit from UK's small and medium-sized enterprises (SME) R&D tax relief scheme, whereby an entity has an option to receive an enhanced UK tax deduction on its eligible R&D activities or, when an SME entity is in a net operating loss position, elect to surrender net operating losses that arise from its eligible R&D activities in exchange for a cash payment from the UK tax authorities. As the tax incentives may be received without regard to an entity's actual tax liability, they are not subject to accounting for income taxes. Amounts realized under the SME R&D tax relief scheme are recorded as a component of other income after an election for tax relief in the form of cash payments has been made for a discrete tax year by submitting a claim and collectability is deemed probable and reasonably assured.

**Leases**

The Company leases office space facilities under non-cancelable operating lease agreements and recognizes related rent expense on a straight-line basis over the term of the lease. Landlord allowances and incentives received, including allowances for leasehold improvements and rent holidays, are recognized as reductions to rent expense on a straight-line basis over the term of the lease. Cash reimbursements for tenant improvement allowances not yet received are recorded in other current assets on the consolidated balance sheet. The Company does not assume renewals in its determination of the lease term unless they are deemed to be reasonably assured at the inception of the lease. The Company begins recognizing rent expense on the date it obtains the legal right to use and control the leased space. Deferred rent consists of the difference between cash payments and the rent expense recognized.

**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**

The Company recognizes stock-based compensation for all equity awards made to employees based upon the awards' estimated grant date fair value. For equity awards that vest subject to the satisfaction of service requirements, compensation expense is measured based on the fair value of the award on the date of grant and is recognized as expense on a straight-line basis over the requisite service period. For stock awards which have a performance component, compensation cost is measured based on the fair value on the grant date (the date performance targets are established) and is expensed over the service period for each separately vesting tranche when the achievement of the performance condition becomes probable. The Company recognizes forfeitures as they occur.

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*Valuation of Stock Options*

The fair value of each option granted was estimated on the date of grant using the Black-Scholes option-pricing model with the following assumptions:

•Expected term—The expected term of the option awards represents the period of time between the grant date of the option awards and the date the option awards are either exercised, converted or canceled, including an estimate for those option awards still outstanding. The Company used the simplified method, as permitted by the SEC for companies with a limited history of relevant stock option exercise activity, to determine the expected term for its option grants.

•Expected volatility—The expected volatility was calculated based on the Company's historical stock prices over the expected term, supplemented as necessary with historical volatility of the common stock of several peer companies with characteristics similar to those of the Company.

•Risk-free interest rate—The risk-free interest rate was based on the U.S. Treasury yield curve in effect at the time of grant and with a maturity that approximated the Company's expected term.

•Dividend yield—The dividend yield was based on the Company's dividend history and the anticipated dividend payout over its expected term.

*Valuation of Restricted Stock Units*

The fair value of each restricted stock unit was based on the Company's closing stock price on the date of grant. The Company is also required to make estimates as to the probability of achieving the specific performance criteria. If actual results are not consistent with the Company's assumptions and judgments used in making these estimates, the Company may be required to increase or decrease compensation expense, which could be material to the Company's results of operations.

**Loss from Continuing Operations per Share**

Basic net loss from continuing operations per share is calculated by dividing the net loss from continuing operations by the weighted average number of common shares outstanding for the period reduced by weighted average shares subject to repurchase, without consideration for common stock equivalents. Diluted net loss from continuing operations per share is computed by dividing the net loss from continuing operations 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 and warrants to purchase common stock are considered to be common stock equivalents and are only included in the calculation of diluted net loss from continuing operations per share when their effect is dilutive.

The calculation of diluted loss per share also requires that, to the extent the average market price of the underlying shares for the reporting period exceeds the exercise price of the warrants to purchase common stock and the presumed exercise of such securities are dilutive to loss per share for the period, adjustments to net income or net loss used in the calculation are required to remove the change in fair value of the common stock warrant liability for the period. Likewise, adjustments to the denominator are required to reflect the related dilutive shares.

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

| | 2018 | 2017 | 2016 |
|---|---|---|---|
| Numerator | | | |
| Net loss from continuing operations | $ (123,716) | $ (126,022) | $ (68,686) |
| Denominator | | | |
| Weighted average common shares outstanding, | 37,884 | 27,301 | 24,785 |

| | | | |
|---|---|---|---|
| basic and diluted | | | |
| Loss from continuing operations per share, basic and diluted | $ (3.27) | $ (4.62) | $ (2.77) |

The following table presents the potential common shares outstanding that were excluded from the computation of diluted loss from continuing operations per share of common stock for the periods presented because including them would have been antidilutive (in thousands):

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| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Shares subject to outstanding common stock options | 3,770 | 3,865 | 3,171 |
| Shares subject to outstanding restricted stock units | 289 | 237 | 85 |
| Shares subject to outstanding warrants to purchase common stock | 33 | 282 | 1,975 |
| | 4,092 | 4,384 | 5,231 |

**Segment Information**

The Company operates as a single segment, which is the business of developing and commercializing transformative therapies to improve the lives of patients living with rare diseases and their families. The Company's chief decision maker, the President and Chief Executive Officer, reviews the Company's operating results on an aggregate basis and manages the Company's operations as a single operating unit. Substantially all of the Company's long-lived assets are located in the U.S.

**Accounting Pronouncements Recently Adopted**

Accounting Standards Update (ASU) 2014-09, *Revenue from Contracts with Customers (Topic 606)* and subsequent amendments to the initial guidance, or collectively, Topic 606, amended the existing accounting standards for revenue recognition. 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. The Company adopted Topic 606 effective January 1, 2018 using the modified retrospective approach. The adoption of Topic 606 did not have a material impact on the Company's consolidated financial statements as the Company does not have any contracts with customers.

ASU 2016-15, *Statement of Cash Flows (Topic 230)* provides guidance on eight specific cash flow issues, thereby reducing the diversity in practice in how certain transactions are classified in the statement of cash flows. The amendments in this ASU should be applied retrospectively to all periods presented. The Company adopted ASU 2016-15 effective January 1, 2018. The adoption of this ASU did not have a material impact on the Company's consolidated financial statements.

ASU 2016-18, *Statement of Cash Flows (Topic 230), Restricted Cash,* amends Topic 230 to add or clarify guidance on the classification and presentation of restricted cash in the statement of cash flows. The guidance requires that the statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents rather than only cash and cash equivalents, as previously required. The Company adopted ASU 2016-18 effective January 1, 2018 on a retrospective basis to all periods presented. For the year ended December 31, 2016, the change in restricted cash due to the release from escrow of holdback funds related to the Company's divestiture of Zohydro ER of $10.0 million has been excluded from investing activity in the statement of cash flows as the amount has now been included in the beginning total cash, cash equivalents, and restricted cash balance. The adoption of the guidance did not have any impact on the Company's

financial position or result of operations. As of December 31, 2018 and 2017, the Company did not have any restricted cash.

ASU 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business* narrows the definition of a business and provides additional guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. This accounting standards update is required to be applied prospectively to transactions occurring after the date of adoption. The Company adopted ASU 2017-09 effective January 1, 2018. The adoption of this ASU did not have a material impact on the Company's consolidated financial statements.

ASU 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting* provides guidance on determining changes to the terms and conditions of share-based payment awards and require an entity to apply modification accounting under Topic 718 unless all of the following conditions are met: (1) the fair value of the modified award is the same as the fair value of the original award immediately before the original award is modified. If the modification does not affect any of the inputs to the valuation technique that the entity uses to value the award, the entity is not required to estimate the value immediately before and after the modification; (2) the vesting conditions of the modified award are the same as the vesting conditions of the original award immediately before the original award is modified; and (3) the classification of the modified award as an equity instrument or a liability instrument is the same as the classification of the original award immediately before the original award is modified. The amendments should be applied prospectively to an award modified on or after the adoption date. The Company adopted ASU 2017-09 effective January 1, 2018. The adoption of this ASU did not have a material impact on the Company's consolidated financial statements.

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ASU 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* simplifies the accounting for share-based payment awards issued to nonemployees for goods and services, including fixing the estimated fair value of the stock award at the date of grant. ASU 2018-07 expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from non-employees. Consequently, the accounting for share-based payments to nonemployees and employees will be substantially aligned. The adoption of ASU 2018-07 requires a modified retrospective transition approach, with a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year. ASU 2018-07 is effective for public companies for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. The Company early adopted ASU 2018-07 effective July 1, 2018. The adoption of this ASU did not have a material impact on the Company's consolidated financial statements.

In December 2017, the SEC issued Staff Accounting Bulletin No. 118 (SAB 118), *Income Tax Accounting Implications of the Tax Cuts and Jobs Act* to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Cuts and Jobs Act of 2017 (Tax Act). In accordance with SAB 118, the Company recorded provisional tax impacts related to the revaluation of deferred tax assets and liabilities and the effects of the transition tax on undistributed foreign earnings and profits in its consolidated financial statements for the year ended December 31, 2017. As of December 31, 2018, the Company completed its accounting for the impact of the Tax Act and determined there were no material changes to its analysis originally performed. See Note 12 to the consolidated financial statements for additional details.

In August 2018, the SEC adopted amendments to certain disclosure requirements in Securities Act Release No. 33-10532, Disclosure Update and Simplification. These amendments eliminate, modify, or integrate into other SEC requirements certain disclosure rules. Among the amendments is the requirement to present an analysis of changes in stockholders' equity in the interim financial statements included in quarterly reports on Form 10-Q. The analysis, which can be presented as a footnote or separate statement, is required for the current and comparative quarter and year-to-date interim periods. The amendments became effective for all filings made on or after November 5, 2018. In light of the anticipated timing of effectiveness of the amendments and expected proximity of effectiveness to the filing date for most filers' quarterly reports, the SEC's Division of Corporate Finance issued a Compliance and Disclosure Interpretation related to Exchange Act Forms (CDI) – Question 105.09, that provides transition guidance related to this disclosure requirement. CDI – Question 105.09 states that the SEC would not object if the filer's first presentation of the changes in shareholders' equity is included in its Form 10-Q for the quarter that begins after the effective date of the amendments. Except for the requirement to provide the annual disclosure changes in stockholders' equity for interim periods, which will be included beginning with the Company's quarterly report on Form 10-Q ending March 31, 2019, the Company has adopted all relevant disclosure requirements.

**Accounting Pronouncements Issued But Not Yet Effective**

ASU 2016-02, *Leases (Topic 842)* establishes a right-of-use (ROU) model that requires all lessees to recognize ROU assets and liabilities for leases with a duration greater than one year on the balance sheet as well as provide disclosures with respect to certain qualitative and quantitative information regarding the amount, timing and uncertainty of cash flows arising from leases. Both a ROU asset and liability will initially be measured at the present value of the future minimum lease payments over the lease term. Subsequent measurement, including the presentation of expenses and cash flows, will depend on the classification of the lease as either a finance or an operating lease. Initial costs directly attributable to negotiating and arranging the lease will be included in the ROU asset. The new standard is effective for fiscal years beginning after December 15, 2018, and interim periods therein. Early adoption is permitted. Originally, entities were required to adopt ASU 2016-02 using a modified retrospective approach, which required prior periods to be presented under this new standard with various practical expedients allowed. In July 2018, the Financial Accounting Standards Board (FASB) issued ASU 2018-11, Leases (Topic 842): Targeted Improvements, which allows for a new transition method that offers the option to use the effective date as the date of initial application. The Company intends to elect this alternative transition method and therefore will not adjust comparative-period financial information and will continue to present all prior periods under previous lease accounting guidance. In addition, the Company intends to utilize the practical expedient that allows the Company to not reassess whether an expired or

existing contract contains a lease, the classification of leases or initial direct costs. The Company has identified the population of its contracts subject to this guidance. While the Company is finalizing its evaluation of the impact of adopting this accounting standard update on its consolidated financial statements and related disclosures, the Company expects to recognize on its balance sheet for associated leases a new ROU asset ranging from $7.5 million to $9.5 million and lease liability ranging from $12.0 million to $14.0 million, with the difference between ROU assets and lease liability attributed to the elimination of remaining unamortized lease incentive obligations, deferred rent and a cease-use liability. The adoption of this standard are also expected to impact the Company’s consolidated financial statement disclosures.

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ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. This standard update requires that certain financial assets be measured at amortized cost net of an allowance for estimated credit losses such that the net receivable represents the present value of expected cash collection. In addition, this standard update requires that certain financial assets be measured at amortized cost reflecting an allowance for estimated credit losses expected to occur over the life of the assets. The estimate of credit losses must be based on all relevant information including historical information, current conditions and reasonable and supportable forecasts that affect the collectability of the amounts. This standard update is effective as of the first quarter of 2020; however, early adoption is permitted. The Company intends to adopt this standard update in the first quarter of 2020. The Company is currently evaluating the impact that this standard update will have on its consolidated financial statements upon adoption.

ASU 2017-04, *Intangibles-Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment* simplifies how an entity is required to test goodwill for impairment by eliminating Step 2 from the goodwill impairment test. Step 2 measures a goodwill impairment loss by comparing the implied fair value of a reporting unit's goodwill with the carrying amount of that goodwill. Under the amendments in ASU 2017-04, an entity should recognize an impairment charge for the amount by which the carrying amount of a reporting unit exceeds its fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to that reporting unit. The updated guidance requires a prospective adoption. ASU 2017-04 is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. Early adoption is permitted for goodwill impairment tests performed on testing dates after January 1, 2017. The Company is currently evaluating the timing and impact of adopting this ASU on its consolidated financial statements and related disclosures.

ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement* modifies the disclosure requirements in Topic 820 by removing certain disclosure requirements related to the fair value hierarchy, modifying existing disclosure requirements related to measurement uncertainty and adding new disclosure requirements, such as disclosing the changes in unrealized gains and losses for the period included in other comprehensive income for recurring Level 3 fair value measurements held at the end of the reporting period and disclosing the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements. This ASU is effective for public companies for fiscal years beginning after December 15, 2019, including interim periods within that fiscal year. Early adoption is permitted for any removed or modified disclosures. The Company is currently evaluating the timing and impact of adopting this ASU on its consolidated financial statements and related disclosures.

**3. Strategic and License Agreements**

**Fintepla (ZX008)**

In October 2014, the Company acquired Brabant Pharma Limited (Brabant) in a business combination and obtained worldwide development and commercialization rights to Fintepla (ZX008; low-dose fenfluramine), its lead product candidate. Under the terms of the sale and purchase agreement, the Company agreed to make future milestone payments to the former owners of Brabant for up to $95.0 million in the event the Company achieves certain milestones with respect to Fintepla, consisting of $50.0 million in regulatory milestones and $45.0 million in sales milestones. In February 2019, the Company completed a rolling submission of a NDA with the FDA and submitted a MAA to the EMA for Fintepla for the treatment of seizures associated with Dravet syndrome. The EMA has accepted the MAA, which triggered a $10.0 million development milestone payment. An additional $10.0 million milestone payment shall become due and payable if the NDA is accepted by the FDA.

In addition, the Company has a collaboration and license agreement with the Universities of Antwerp and Leuven in Belgium (the Universities) that runs through September 2045. Under the terms of the agreement, the Universities granted the Company an exclusive worldwide license to use the data obtained from a study related to low-dose fenfluramine for the treatment of Dravet syndrome, as well as certain other intellectual property. The Company is required to pay a mid-single-digit percentage royalty on net sales of products containing low-dose fenfluramine for the treatment of Dravet syndrome or, in the case of a sublicense of products containing low-dose fenfluramine for the treatment of Dravet syndrome, a percentage in the mid-twenties of the sub-licensing revenues. The agreement may be terminated by the Universities if the Company: (a) does not use commercially reasonable efforts to (i) develop and commercialize products containing low-dose fenfluramine for the treatment of Dravet syndrome or related conditions

stemming from infantile epilepsy, or (ii) seek approval of products containing low-dose fenfluramine for the treatment of Dravet syndrome in the United States; or (b) if the Company becomes insolvent or makes an assignment for the benefit of creditors or should any petition in bankruptcy, or similar relief, be filed by or against the Company. The Company can terminate the agreement upon specified prior written notice to the Universities.

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**Contract Manufacturing Supply Agreement with Endo and Associated Exit Activities**

In May 2014, the Company completed the sale of its Sumavel DosePro business. Concurrently with the sale, the Company entered into the Supply Agreement to be the exclusive supplier of Sumavel DosePro to Endo. The Supply Agreement was terminated in September 2017. The Company recorded a charge of $2.2 million in inventory write-down to reflect its current net realizable value as a result the termination agreement in 2017 and also recorded an impairment charge of $2.0 million in 2016 to write off the remaining carrying amount of a prepaid royalty associated with the Supply Agreement. These additional charges reflected ongoing negotiations over the course of finalizing the termination of the Supply Agreement and were included as a cost of contract manufacturing and a component of operating expenses, respectively, in the consolidated statements of operations.

Pursuant to the termination agreement, the Company also received cash consideration of $1.5 million from Endo for reimbursement of a portion of the Company's termination costs for its third-party suppliers and manufacturers related to Sumavel DosePro product. As part of the termination agreement, both parties also agreed to net settle outstanding accounts receivable of $4.7 million due from Endo and the Company's remaining purchased raw materials and other costs of $2.3 million against the $7.0 million working capital advance note payable due to Endo. In connection with the Endo termination agreement, the Company also executed termination agreements with its third-party suppliers and manufacturers related to the Sumavel DosePro product and incurred contract termination costs of $2.5 million. Excluding the non-cash loss on extinguishment of debt due to the write-off of unamortized discount related to imputed interest (see Note 8), these termination agreements resulted in a net loss on contract termination of $0.5 million, which was included in loss on contract termination within continuing operations in the consolidated statements of operations.

**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 research and development 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. Cash, Cash Equivalents and Marketable Securities**

The following table summarizes the amortized cost and fair value of the Company's cash, cash equivalents and marketable securities as of December 31, 2018 (in thousands):

| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Estimated Fair Value |
|---|---|---|---|---|
| Current assets: | | | | |
| Cash and cash equivalents: | | | | |
| Cash | $ 5,222 | $ — | $ — | $ 5,222 |
| Money market funds | 63,232 | — | — | 63,232 |
| Total cash and cash equivalents | $ 68,454 | $ — | $ — | $ 68,454 |
| Marketable securities: | | | | |
| Commercial paper | $ 152,940 | $ — | $ — | $ 152,940 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Corporate debt securities | 60,622 | | 58 | | (75) | | 60,605 | |
| Certificates of deposit | 128,647 | | — | | — | | 128,647 | |
| U.S. Treasuries | 103,521 | | 31 | | (11) | | 103,541 | |
| Total marketable securities | $ | 445,730 | $ | 89 | $ | (86) | $ | 445,733 |
| Total cash, cash equivalents and marketable securities | $ | 514,184 | $ | 89 | $ | (86) | $ | 514,187 |

The following table summarizes the amortized cost and fair value of marketable securities based on stated effective maturities as of December 31, 2018 (in thousands):

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| | Amortized Cost | Fair Value |
|---|---|---|
| Due within one year | $ 408,479 | $ 408,471 |
| Due between one and two years | 37,251 | 37,262 |
| Total | $ 445,730 | $ 445,733 |

As of December 31, 2017, cash and cash equivalents included $289.8 million of money market fund investments having a carrying value equaled to their fair value. The Company did not hold any marketable securities at December 31, 2017.

There have been no significant realized gains or losses on available-for-sale securities for the periods presented. Available-for-sale debt securities that were in a continuous loss position but were not deemed to be other than temporarily impaired were immaterial at December 31, 2018.

See Note 5 for further information regarding the fair value of the Company's financial instruments.

**5. Fair Value Measurements**

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. A three-level valuation hierarchy has been established under GAAP for disclosure of fair value measurements. The valuation hierarchy is based on the transparency of inputs to the valuation of an asset or liability as of the measurement date. The three levels are defined 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 following tables summarize assets and liabilities recognized or disclosed at fair value on a recurring basis at December 31, 2018 and 2017 (in thousands):

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| | Level 1 | Level 2 | Level 3 | Total |
|---|---|---|---|---|
| **December 31, 2018** | | | | |
| Assets: | | | | |
| Cash equivalents: | | | | |
| Money market funds | $ 63,232 | $ — | $ — | $ 63,232 |
| Marketable securities: | | | | |
| Commercial paper | — | 152,940 | — | 152,940 |
| Corporate debt securities | — | 60,605 | — | 60,605 |
| Certificates of deposit | — | 128,647 | — | 128,647 |
| U.S. Treasury securities | — | 103,541 | — | 103,541 |
| Total assets(1) | $ 63,232 | $ 445,733 | $ — | $ 508,965 |
| Liabilities: | | | | |
| Common stock warrant liabilities (2) | $ — | $ — | $ 343 | $ 343 |
| Contingent consideration liabilities (3) | — | — | 78,200 | 78,200 |
| Total liabilities | $ — | $ — | $ 78,543 | $ 78,543 |
| **December 31, 2017** | | | | |
| Assets: | | | | |
| Cash equivalents: | | | | |
| Money market funds (1) | $ 289,782 | $ — | $ — | $ 289,782 |
| Total assets | $ 289,782 | $ — | $ — | $ 289,782 |
| Liabilities: | | | | |
| Common stock warrant liabilities (2) | $ — | $ — | $ 512 | $ 512 |
| Contingent consideration liabilities (3) | — | — | 76,900 | 76,900 |
| Total liabilities | $ — | $ — | $ 77,412 | $ 77,412 |

(1) Fair value is determined by taking into consideration valuations obtained from third-party pricing services. The third-party pricing services utilize industry standard valuation models, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities; issuer credit spreads; benchmark securities; and other observable inputs.
(2) Represents the fair value of common stock warrants outstanding that may require cash settlement under certain circumstances. The Company estimated the fair value of the warrant liabilities using the Black-Scholes valuation model. As of December 31, 2018, common stock warrant liabilities consisted of warrants issued in July 2011 in connection with a debt financing arrangement. The warrants entitle the holder to purchase up to 28,125 shares of common stock at an exercise price of $72.00 per share and expires in July 2021.
(3) In connection with the acquisition of Brabant in 2014 (See Note 3), the Company may be required to pay future consideration that is contingent upon the achievement of specified development, regulatory approval or sales-based milestone events. The Company estimates the fair value of contingent purchase consideration liabilities using a probability-weighted income approach, which reflects the probability and timing of future payments. This fair value measurement is based on significant Level 3 inputs such as the anticipated timelines and probability of achieving development, regulatory approval or sales-based milestone events and projected revenues. The resulting probability-weighted cash flows are discounted at risk-adjusted rates. Subsequent to the acquisition date, at each reporting period prior to settlement, the Company revalues these liabilities by performing a review of the assumptions listed above and records an adjustment to reflect any changes in the estimated fair values of these contingent consideration liabilities. In the absence of any significant changes in key assumptions during a reporting period, the change in fair values of these contingent consideration liabilities would primarily reflect an increase in fair value from the passage of time. Significant judgment is used in determining Level 3 inputs and fair value measurements as of a reporting period. Updates to assumptions could have a significant impact on the Company’s results of operations in a reporting period and actual results may differ from estimates. For example, significant increases in the estimated probability of achieving a milestone or projected revenues

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would result in a significantly higher fair value measurement while significant decreases in the estimated probability of achieving a milestone or projected revenues would result in a significantly lower fair value measurement. Significant increases in the discount rate or in the anticipated timelines would result in a significantly lower fair value measurement while significant decreases in the discount rate or anticipated timelines would result in a significantly higher fair value measurement. The potential contingent consideration payments required upon achievement of development, regulatory approval and sales-based milestones related to the Company's acquisition of Brabant range from zero if none of the milestones are achieved to a maximum of $95.0 million (undiscounted). As of December 31, 2018, the Company classified $32.3 million of the total contingent consideration liabilities of $78.2 million as current liabilities. The classification was based upon the Company's reasonable expectation as to the timing of settlement of certain specified milestones.

There were no transfers between levels for all periods presented. See Note 4 for further information regarding the carrying value of the Company's financial instruments.

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, 2018 and 2017 (in thousands):

| | Contingent Purchase Consideration | Common Stock Warrant Liabilities |
|---|---|---|
| Balance at December 31, 2016 | $ 52,800 | $ 809 |
| Additions | — | — |
| Settlements | — | — |
| Changes in fair value | 24,100 | (297) |
| Balance at December 31, 2017 | 76,900 | 512 |
| Additions | — | — |
| Settlements | — | — |
| Changes in fair value | 1,300 | (169) |
| Balance at December 31, 2018 | $ 78,200 | $ 343 |

Changes in the estimated fair value of contingent purchase consideration are reflected as operating expenses in the consolidated statements of operations. Changes in the estimated fair value of common stock warrant liabilities are included within other income (expense) in the consolidated statements of operations.

**6. Balance Sheet Components**

The following tables provide details of selected balance sheet components (in thousands):

**Property and Equipment, Net**

Property and equipment, net consisted of the following:

| | December 31, 2018 | 2017 |
|---|---|---|
| Computer equipment and software | $ 216 | $ 141 |
| | 3,210 | 976 |

| | | |
|---|---|---|
| Leasehold improvements | | |
| Furniture and fixtures | 880 | 407 |
| Total | 4,306 | 1,524 |
| Less accumulated depreciation | (1,436) | (1,279) |
| Property and equipment, net | $ 2,870 | $ 245 |

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**Other Long-Term Liabilities**

Other long-term liabilities consisted of the following:

| | December 31, 2018 | 2017 |
|---|---|---|
| Deferred rent and lease incentive obligation | $ 3,685 | $ 244 |
| Other | 145 | 540 |
| | $ 3,830 | $ 784 |

**7. 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.

See Note 3 for the Company's commitments under collaboration, license and purchase agreements.

**Operating Leases**

In October 2018, the Company entered into a new lease agreement for new headquarters and amended its existing headquarter lease, both with the same landlord. The new lease agreement provides for 37,307 square feet of office and laboratory space also located in Emeryville, California under a noncancellable lease that expires on June 30, 2027 and has a renewal option for an additional five years. The cash expected to be paid for base rent over the term of the new lease is approximately $15.3 million beginning in June 2019. The lease provides for lease incentives for tenant improvements of $3.1 million, a rent free period, and scheduled rent increases over the term of the lease. The Company is also required to pay its proportionate share of costs related to common area maintenance, property taxes, and other operating costs. Upon completion of its relocation to its new headquarters, which is expected to be by the end of the second quarter of 2019, the lease agreement for its existing headquarters will be terminated.

The Company was provided access to the leased space upon lease execution and recorded a $3.1 million lease incentive receivable within other current assets, with a corresponding lease incentive obligation as a component of deferred rent, in accrued liabilities or long-term liabilities, as appropriate.

The Company also has a noncancellable operating lease expiring in March 2020 for office space in San Diego, California, which previously served as the Company's headquarters prior to its relocation to Emeryville, California. In 2017, the Company vacated the leased premises upon entering into a noncancellable sublease agreement with a sublessee for the remainder of the Company's lease term. Because amounts to be received under the sublease were less than the amounts the Company is required to pay its lessor, the Company recorded a loss on lease of $0.6 million, net of adjustments to derecognize the related deferred rent liability, as a component of general and administrative expenses in the consolidated statements of operations. As of December 31, 2018, accrued liabilities related to this lease arrangement was $0.5 million, of which $0.1 million was long-term.

Rent expense for 2018, 2017 and 2016 was $1.6 million, $1.8 million and $1.9 million, respectively.

Future minimum rental payments under the Company's noncancellable operating leases, net of sublease rental income, were as follows (in thousands):

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| | Gross Rental Payments | Sublease Rental Income | Net Rental Payments |
|---|---|---|---|
| 2019 | $ 1,777 | $ (576) | $ 1,201 |
| 2020 | 1,788 | (148) | 1,640 |
| 2021 | 1,839 | — | 1,839 |
| 2022 | 1,894 | — | 1,894 |
| 2023 | 1,951 | — | 1,951 |
| Thereafter | 7,296 | — | 7,296 |
| Total | $ 16,545 | $ (724) | $ 15,821 |

**8. Debt**

In December 2017, the Company used a portion of the proceeds from the Company's October 2017 common stock offering (see Note 9) and paid off its term loan with an outstanding principal balance of $20.0 million, plus accrued interest. The Company recognized a $1.5 million loss on early extinguishment of debt consisting of a noncash charge to write off the remaining unamortized debt issuance costs and debt discount. The Company also incurred $1.9 million in additional fees related to early extinguishment of the term loan, which had a scheduled maturity date of July 1, 2020.

In May 2014, the Company was provided with an interest-free working capital note payable of $7.0 million from Endo in connection with the Supply Agreement (See Note 3). The working capital advance note payable matured upon the termination of the Supply Agreement. The working capital advance note payable was initially recorded on the consolidated balance sheet net of a $4.7 million debt discount related to imputed interest. In September 2017, the Company and Endo terminated the Supply Agreement and the working capital advance note payable became due and payable in accordance with its terms. Pursuant to the termination agreement, the $7.0 million promissory note was extinguished to settle amounts owed to the Company for accounts receivable and purchased raw materials (See Note 5). In connection with the extinguishment, the Company recognized a non-cash charge upon debt extinguishment of $3.4 million to write off the remaining unamortized debt discount related to imputed interest. As of December 31, 2018 and 2017, the Company had no debt outstanding.

**9. Stockholders' Equity**

**Preferred Stock**

The Company has 10,000,000 shares of preferred stock authorized for issuance, par value of $0.001 per share. As of December 31, 2018 and 2017, no shares of preferred stock were issued and outstanding.

**Common Stock**

The Company has 50,000,000 shares of common stock authorized for issuance, par value of $0.001 per share. Holders of the Company's common stock are entitled to one vote per share. As of December 31, 2018 and 2017, there were 42,078,164 and 34,807,509 shares of common stock issued and outstanding.

The following table presents common stock reserved for future issuance for the following equity instruments as of December 31, 2018 and 2017 (in thousands):

| | December 31, 2018 | 2017 |
|---|---|---|
| Stock options and RSUs outstanding | 4,033 | 3,651 |
| Warrants to purchase common stock | 28 | 38 |
| | 1,684 | 872 |

| | | |
|---|---|---|
| Available for future issuance under employee equity plans | | |
| Total common stock reserved for future issuance | 5,745 | 4,561 |

**Sale of Common Stock**

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In the third quarter of 2017, the Company sold a total of 1,550,880 shares of its common stock pursuant to an at-the-market sales agreement with Cantor Fitzgerald & Co. (ATM Agreement) and received net proceeds of approximately $19.4 million, after deducting commissions and other offering expenses.

In October 2017, the Company completed an underwritten public offering for the sale of 7,700,000 shares of its common stock. The shares were sold to the public at an offering price of $37.50 per share. Net proceeds raised from the offering amounted to approximately $271.3 million, after deducting underwriting discounts and commissions and other offering expenses.

In the second quarter of 2018, the Company sold a total of 740,417 shares of its common stock pursuant to the ATM Agreement and received net proceeds of approximately $30.3 million, after deducting commissions and other offering expenses.

In August 2018, the Company completed an underwritten public offering for the sale of 6,000,000 shares of its common stock. The shares were sold to the public at an offering price of $52.00 per share. Net proceeds raised from the offering amounted to approximately $292.9 million, after deducting underwriting discounts and commissions and other offering expenses.

**10. Stock-Based Compensation**

**Summary of Equity Incentive Plans**

***2006 Plan***

The Company granted options under its 2006 Equity Incentive Award Plan, as amended (2006 Plan) until November 2010 upon adoption of the 2010 Plan (discussed below), which serves as the successor plan to the 2006 Plan. While no further grants may be made from the 2006 Plan, it continues to govern the terms of options that remain outstanding under the 2006 Plan. The 2006 Plan provided for the granting of incentive stock options, non-qualified stock options and rights to purchase restricted stock to eligible recipients. Stock options granted pursuant to the 2006 Plan had a contractual term of ten years and generally vest over four years.

***2010 Plan***

The Company's 2010 Equity Incentive Award Plan, which was amended in June 2012 (2010 Plan), became effective immediately prior to the completion of the Company's initial public offering in November 2010. The 2010 Plan provides for the granting of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock units and rights to purchase restricted stock to eligible recipients. Service-based options granted pursuant to the 2010 Plan has a contractual term of ten years and generally vest over four years. Performance-based awards are subject to the employee's continued service and become vested based on the completion of the applicable performance conditions. As amended in June 2012, the initial 280,459 shares reserved for issuance under the 2010 Plan was increased to 1,162,500 shares, plus any shares related to outstanding options granted under the 2006 Plan that are subsequently repurchased, forfeited, expire or are canceled. In addition, the 2010 Plan's evergreen provision was also amended such that, commencing on January 1, 2013, and on each January 1 through and including January 1, 2020, the aggregate number of shares available for issuance under the 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.

In March 2018, the Board approved an amendment and restatement of its non-employee director compensation policy. Under the amended and restated compensation policy, any non-employee director who is first elected to the board of directors is granted an option to purchase 20,000 shares of our common stock on the date of his or her initial election to the board of directors. In addition, on the date of each of the Company's Annual Meeting of Stockholders, each non-employee director is eligible to receive an option to purchase 15,000 shares of common stock.

As of December 31, 2018 and 2017, 1,550,351 and 756,524 shares of common stock were available for future issuance under the 2010 Plan, respectively.

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***Inducement Plan***

In December 2013, the Company's board of directors (Board) adopted the Employment Inducement Equity Incentive Award Plan (Inducement Plan). The terms of the Inducement Plan are substantially similar to the terms of the 2010 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 Code applicable at the time 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.

The Company has initially reserved 337,500 shares of the Company's common stock for issuance pursuant to awards granted under the Inducement Plan, which was subsequently increased to 637,500 shares in May 2018. 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, 2018 and 2017, there were 118,325 and 102,276 shares of common stock available for future issuance under the Inducement Plan, respectively.

***2010 ESPP***

In November 2010, the Board adopted the 2010 Employee Stock Purchase Plan (2010 ESPP), 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 ESPP 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 ESPP. 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 ESPP 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 ESPP 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 ESPP 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 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. As of December 31, 2018 and 2017, there were 15,243 and 16,672 shares of common stock available for issuance under the 2010 ESPP, respectively.

**Equity Incentive Plan Activity**

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

*Stock Options*

The following table summarizes the Company's stock option activity for 2018:

| | Shares (in thousands) | Weighted Average Exercise Price | Weighted Average Remaining Contractual Term (years) | Aggregate Intrinsic Value (in thousands) |
|---|---|---|---|---|
| Outstanding at December 31, 2017 | 3,392 | $ 14.41 | | |
| Granted | 889 | $ 43.19 | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Exercised | (434) | $ | 16.84 | | | |
| Canceled | (103) | $ | 24.16 | | | |
| Outstanding at December 31, 2018 | 3,744 | $ | 20.69 | 6.9 | $ | 64,906 |
| Exercisable at December 31, 2018 | 2,415 | $ | 16.66 | 6.0 | $ | 48,735 |

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The total intrinsic value of options exercised in 2018, 2017 and 2016 was $11.8 million, $14.3 million and $24,000, respectively.

*Restricted Stock Units (RSUs)*

The following table summarizes the Company's restricted stock unit activity for 2018:

| | Shares (in thousands) | Weighted Average Fair Value per Share at Grant Date |
|---|---|---|
| Nonvested at December 31, 2017 | 259 | $ 10.43 |
| Granted | 146 | $ 42.76 |
| Vested | (98) | $ 10.74 |
| Canceled | (18) | $ 27.89 |
| Nonvested at December 31, 2018 | 289 | $ 25.56 |

The total intrinsic value of RSUs vested in 2018 was $4.2 million. No RSUs vested in 2017 and 2016. As of December 31, 2018, outstanding RSUs included approximately 154,000 shares granted in March 2017 to employees and executives that are performance-based. These performance-based awards vest upon FDA approval of the Company's NDA for Fintepla, provided such approval occurs within five years following the grant date. Due to the uncertainties associated with the FDA approval process, approval is not yet probable, as such term is used for accounting purposes, prior to the occurrence of the event. Accordingly, no compensation expense has been recognized to date. As of December 31, 2018, total unrecognized compensation costs related to such awards were $1.6 million. As of December 31, 2018, nonvested restricted stock units outstanding not subject to a performance condition had a weighted average remaining contractual term of 1.7 years with an intrinsic value of $4.9 million.

*Employee Stock Purchase Plan*

Shares purchased by employees under the 2010 ESPP were 32,679 shares, 35,934 shares and 35,164 shares in 2018, 2017 and 2016, respectively. As of December 31, 2018 and 2017, 15,243 shares and 16,672 shares of common stock were reserved for issuance under the 2010 ESPP, respectively.

**Valuation of Equity Awards**

The Company used the Black-Scholes option-pricing model for determining the estimated fair value and stock-based compensation related to stock options and ESPP purchase rights granted. A summary of the assumptions used to estimate the fair values for the periods presented is as follows:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| *Stock Options* | | | |
| Risk free interest rate | 2.3% to 3.0% | 1.8% to 2.3% | 1.1% to 2.1% |
| Expected term | 5.3 to 6.1 years | 5.1 to 6.1 years | 5.1 to 6.1 years |
| Expected volatility | 80.1% to | 75.1% to 85.8% | 76.5% to |

| | | | |
|---|---|---|---|
| | 85.2% | | 78.1% |
| Expected dividend yield | —% | —% | —% |
| Weighted-average fair value of option on grant date | $30.87 | $7.43 | $6.69 |
| *Employee Stock Purchase Plan* | | | |
| Risk free interest rate | 2.1% to 2.7% | 1.1% to 1.6% | 0.5% to 0.8% |
| Expected term | 0.5 to 1.0 years | 0.5 to 1.0 years | 0.5 to 1.0 years |
| Expected volatility | 44.7% to 113.1% | 54.8% to 152.8% | 59.5% to 71.3% |
| Expected dividend yield | —% | —% | —% |

**Performance Stock Options**

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In October 2015, the Company granted employees certain performance-based stock options for retention purposes. The stock options would vest upon satisfaction of a specified regulatory milestone within three years of the date of grant. In 2017, management determined the achievement of the performance condition was no longer probable and the cumulative compensation expense previously recognized of $0.7 million was reversed. In September 2018, these awards were modified to allow for 90% of such options outstanding at the modification date to vest immediately. The remaining 10% of the awards were canceled in October 2018 since the performance condition was not met. This improbable to probable modification resulted in the calculation and recognition of incremental stock-based compensation expense of $3.5 million in 2018. The Company estimated the fair value of the modified stock options using the Black-Scholes model based on the following key assumptions:

| *Modification of Stock Options* | |
|---|---|
| Exercise price | $ 13.32 |
| Common stock price on date of modification | $ 49.60 |
| Expected term | 3.5 years |
| Expected volatility | 79.9% |
| Expected dividend yield | —% |

**Stock-Based Compensation Expense**

The following table summarizes the components of total stock-based compensation expense included in the consolidated statements of operations for the periods presented (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Cost of contract manufacturing | $ — | $ 71 | $ 386 |
| Research and development | 6,317 | 1,933 | 1,924 |
| Selling, general and administrative | 9,175 | 4,151 | 5,043 |
| Total | $ 15,492 | $ 6,155 | $ 7,353 |

As of December 31, 2018, there was approximately $29.6 million of total unrecognized compensation costs related to outstanding equity awards scheduled to be recognized over a weighted average period of 2.6 years.

**11. 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 2018, 2017 and 2016, the Company made discretionary matching contributions of $0.2 million, $0.2 million, $0.1 million, respectively.

**12. Income Taxes**

For financial reporting purposes, the components of loss from continuing operations before income taxes were as follows (in thousands):

| | December 31, 2018 | 2017 | 2016 |
|---|---|---|---|
| United States | $ (35,838) | $ (32,112) | $ (24,285) |
| Foreign | (87,878) | (93,910) | (45,349) |
| Total | $ (123,716) | $ (126,022) | $ (69,634) |

At December 31, 2018, the Company's federal, state, and foreign net operating loss carryforwards were approximately $286.3 million, $190.3 million and $191.8 million, respectively, which may be subject to limitations as described below. If not utilized, the federal tax loss carryforwards incurred prior to 2018 will begin to expire in 2029 and the state tax loss carryforwards incurred prior to 2018 will begin to expire in 2021. Under the Tax Cut and Jobs Act of 2017 (Tax Act), federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the Tax Act. In

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addition, the Company has federal and California research and development income tax credit carryforwards of approximately $3.4 million and $4.1 million, respectively. If not utilized, the federal research and development income tax credit carryforwards will begin to expire in 2027. The California research and development income tax credit carryforwards do not expire and can be carried forward indefinitely. Due to the net operating loss carryforwards, all years remain open for income tax examination by tax authorities in the United States, various states and foreign tax jurisdictions in which the Company files tax returns.

As of December 31, 2018, the Company has experienced at least 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 in September 2011 upon the issuance of common stock in a 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. In addition, 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 in January 2014, which did not result in any reductions of federal and California net operating loss carryforwards or research and development income tax credits. Based on the Company's most recent assessment through December 31, 2018, no reduction was made to the federal and state net operating loss carryforwards or federal and state tax income tax credit carryforwards under these rules. Pursuant to the IRC, the 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.

A reconciliation of the Company's income tax benefit from continuing operations compared to the income tax benefit computed at the federal statutory tax is was as follows (in thousands):

| | December 31, 2018 | 2017 | 2016 |
|---|---|---|---|
| Income tax at federal statutory rate | $ (26,022) | $ (42,846) | $ (23,675) |
| State taxes, net of federal benefit | (8) | (19) | (65) |
| Change in valuation allowance | 16,949 | (11,208) | 16,024 |
| Impact of U.S. statutory rate change on revaluing deferred tax assets | — | 36,085 | — |
| Permanent interest disallowed | (35) | (150) | (1,832) |
| Impact of foreign rate change on deferred taxes | 1,961 | 1,619 | 521 |
| Other permanent differences[(1)] | (666) | 8,236 | 630 |
| Research and development tax credits | (51) | (274) | (145) |

| | | | |
|---|---|---|---|
| State tax rate benefit | 169 | 56 | 578 |
| Foreign rate differential | 1,731 | 10,636 | 6,122 |
| Stock-based compensation[(1)] | (1,344) | (2,462) | 1,132 |
| Net operating losses surrendered under UK's R&D tax relief scheme | 6,322 | — | — |
| Credits and other[(1)] | 994 | 327 | (238) |
| Income tax benefit | $ — | $ — | $ (948) |

[(1)] Certain prior years' amounts in the table above have been reclassified to conform with current year's presentation.

The Tax Act has resulted in significant changes to the U.S. corporate income tax system. These changes include a federal statutory rate reduction from 35% to a flat rate of 21% for tax years beginning after December 31, 2017, limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, implementing a territorial tax system, and requiring a mandatory one-time tax on U.S. owned undistributed foreign earnings and profits known as the transition tax.

Pursuant to SAB 118, an entity may select between one of three scenarios to determine a reasonable estimate arising from the Tax Act. The scenarios are (i) a final estimate which effectively closes the measurement window; (ii) a reasonable estimate leaving the measurement window open for future revisions; and (iii) no estimate as the law is still being analyzed. The Company was able to provide a reasonable estimate for the revaluation of deferred taxes and the effects of the transition tax on undistributed foreign earnings and profits. As such, the Company has recorded a $36.1 million reduction in deferred tax assets for the revaluation of deferred taxes which was offset by a corresponding decrease to the Company's full valuation allowance. As of December 31, 2018, the Company completed its accounting for the impact of the Tax Act and determined there were no material changes to its analysis originally performed.

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Significant components of the Company's deferred tax assets are presented below. A valuation allowance of $118.1 million and $101.1 million as of December 31, 2018 and 2017, 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.

| | December 31, 2018 | 2017 |
|---|---|---|
| Deferred tax assets: | | |
| Net operating losses | $ 103,187 | $ 87,142 |
| Capitalized research and development | 1,537 | 2,155 |
| Accrued expenses | 1,300 | 1,310 |
| Research and development credits | 5,343 | 5,282 |
| Amortization | 528 | 630 |
| Depreciation | — | 163 |
| Stock-based compensation[(1)] | 5,868 | 4,334 |
| Other, net[(1)] | 775 | 98 |
| Total gross deferred tax assets | 118,538 | 101,114 |
| Less valuation allowance | (118,064) | (101,114) |
| Net deferred tax assets | $ 474 | $ — |
| Deferred tax liabilities: | | |
| IPR&D | $ (17,425) | $ (17,425) |
| Depreciation | (474) | — |
| Total deferred tax liabilities | (17,899) | (17,425) |
| Net deferred tax liability | $ (17,425) | $ (17,425) |

[(1)] Prior year's amounts have been reclassified to conform with current year's presentation.

In 2017 and 2018, no tax provision has been recognized because of the operating losses and the full valuation allowance provided on all deferred tax assets, including the net operating losses. In 2016, the Company recognized a tax benefit of $0.9 million primarily due to the impact of changes in tax laws (tax rate reductions) enacted in the UK, which decreased the Company's deferred tax liability.

The Company recognizes liabilities for uncertain tax positions based on a two-step process. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount which is more than 50% likely of being realized upon ultimate settlement.

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

| | December 31, 2018 | 2017 | 2016 |
|---|---|---|---|
| Beginning balance of unrecognized tax benefits | $ 2,030 | $ 1,248 | $ 1,132 |
| Gross increases based on tax positions related to current year | — | 633 | 116 |
| Gross decreases based on tax positions related to prior years | (634) | — | — |
| Gross increases based on tax positions related to prior years | 91 | 149 | — |
| Settlements with taxing authorities | — | — | — |
| Expiration of statute of limitations | — | — | — |
| Ending balance of unrecognized tax benefits | $ 1,487 | $ 2,030 | $ 1,248 |

As at December 31, 2018 and 2017, there were no unrecognized tax benefits that, if recognized, would affect the Company's effective tax rate as any tax benefit would increase a deferred tax asset, which is currently offset by a full valuation allowance.

The Company recognizes interest and, if applicable, penalties related to income tax matters as income tax expense. No interest or penalties have been recorded for all periods presented. The Company does not expect any significant increases or decreases to its unrecognized tax benefits in the next twelve months.

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**13. UK's R&D Tax Relief Scheme**

The Company carries out extensive research and development activities that benefit from UK's small and medium-sized enterprises (SME) R&D tax relief scheme. Under this tax relief scheme, a SME has an option to receive an enhanced UK tax deduction on its eligible R&D activities or, when an SME entity is in a net operating loss position, can elect to surrender net operating losses that arise from its eligible R&D activities in exchange for a cash payment from the UK tax authorities. As the tax incentives may be received without regard to an entity's actual tax liability, they are not subject to accounting for income taxes. Amounts recognized by the Company for cash payment claims under the SME R&D tax relief scheme are recorded as a component of other income after an election for tax relief has been made for a discrete tax year by submitting a claim and collectability is deemed probable and reasonably assured.

In 2018, other income included $10.1 million related to elections the Company made to surrender net operating losses that arose from eligible R&D activities in exchange for cash under the SME R&D tax relief scheme. The balance consisted of a $3.0 million claim submitted in December 2017 for the Company's 2015 tax year, which was received in July 2018, and a $7.1 million claim submitted in December 2018 for the Company's 2016 tax year, which was received in February 2019. As of December 31, 2018, other current assets included a $7.1 million receivable related to the submitted claim for the Company's 2016 tax year. As of December 31, 2017, the Company did not record a receivable related to the submitted claim for its 2015 tax year as collectability was not probable or reasonably assured. The Company has not submitted claims or made elections to receive enhanced UK tax deductions on its eligible R&D activities for its 2017 or 2018 tax years.

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**14. Selected Quarterly Financial Information (Unaudited)**

The following tables show a summary of the Company's quarterly financial information for each of the four quarters of 2018 and 2017 and have been prepared in accordance with GAAP for interim financial information. In the opinion of management, all adjustments (consisting of normal recurring accruals) considered necessary for a fair presentation have been included.

| | 2018 Quarter Ended | | | |
|---|---|---|---|---|
| | March 31 | June 30 | September 30 | December 31 |
| | (in thousands, except per share amounts) | | | |
| Revenue | $ — | $ — | $ — | $ — |
| Loss from continuing operations | $ (30,180) | $ (28,839) | $ (42,264) | $ (22,433) |
| Loss from discontinued operations | $ — | $ (198) | $ — | $ — |
| Net loss | $ (30,180) | $ (29,037) | $ (42,264) | $ (22,433) |
| Net loss per share, basic and diluted | $ (0.87) | $ (0.83) | $ (1.08) | $ (0.53) |

| | 2017 Quarter Ended | | | |
|---|---|---|---|---|
| | March 31 | June 30 | September 30 | December 31 |
| | (in thousands, except per share amounts) | | | |
| Revenue | $ 2,696 | $ 7,125 | $ — | $ — |
| Loss from continuing operations | $ (21,126) | $ (22,453) | $ (42,660) | $ (39,783) |
| (Loss) income from discontinued operations | $ (181) | $ (555) | $ (134) | $ 75 |
| Net loss | $ (21,307) | $ (23,008) | $ (42,794) | $ (39,708) |
| Net loss per share, basic and diluted | $ (0.86) | $ (0.93) | $ (1.68) | $ (1.17) |

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**EXHIBIT INDEX**

| | | Incorporated by Reference | | | | |
|---|---|---|---|---|---|---|
| **Exhibit No.** | **Description** | **Form** | **File Number** | **Date of Filing** | **Exhibit No.** | **Filed Herewith** |
| 2.1† | 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 | 8-K/A | 001-34962 | December 23, 2014 | 10.1 | |
| 3.1 | Fifth Amended and Restated Certificate of Incorporation | S-1/A | 333-169210 | October 27, 2010 | 3.5 | |
| 3.2 | Certificate of Amendment of Fifth Amended and Restated Certificate of Incorporation | 10-Q | 001-34962 | November 8, 2012 | 3.2 | |
| 3.3 | Certificate of Amendment of Fifth Amended and Restated Certificate of Incorporation | 10-Q | 001-34962 | August 10, 2015 | 3.3 | |
| 3.4 | Amended and Restated Bylaws | S-1/A | 333-169210 | October 27, 2010 | 3.7 | |
| 4.1 | Form of the Registrant's Common Stock Certificate | S-1/A | 333-169210 | November 4, 2010 | 4.1 | |
| 4.2 | Warrant dated July 18, 2011 issued by the Registrant to Cowen Healthcare Royalty Partners II, L.P. | 10-Q | 001-34962 | August 12, 2011 | 4.12 | |
| 10.1 | Form of Director and Executive Officer Indemnification | S-1/A | 333-169210 | October 27, 2010 | 10.1 | |

| | | | | | |
|---|---|---|---|---|---|
| | Agreement | | | | |
| 10.2# | 2006 Equity Incentive Plan, as amended, and forms of option agreements thereunder | S-1 | 333-169210 | September 3, 2010 | 10.3 |
| 10.3# | 2010 Equity Incentive Award Plan and forms of option and restricted stock agreements thereunder | S-1/A | 333-169210 | October 27, 2010 | 10.5 |
| 10.4# | 2010 Employee Stock Purchase Plan and form of Offering document thereunder | S-1/A | 333-169210 | October 27, 2010 | 10.6 |
| 10.5# | Form of Restricted Stock Unit Award Agreement under the 2010 Equity Incentive Award Plan | 10-Q | 001-34962 | August 8, 2013 | 10.1 |
| 10.6# | Employment Inducement Equity Incentive Award Plan and form of stock option agreement thereunder | 8-K | 001-34962 | December 5, 2013 | 10.1 |
| 10.7# | Annual Incentive Plan | 10-Q | 001-34962 | May 11, 2015 | 10.3 |
| 10.8# | Independent Director Compensation Policy as amended and restated effective March 14, 2018 | 10-Q | 001-34962 | May 9, 2018 | 10.1 |
| 10.9# | Amended and Restated Employment Agreement, dated April 27, 2015, by and between the Registrant and Stephen J. Farr, Ph.D. | 10-Q | 001-34962 | August 10, 2015 | 10.4 |
| 10.10# | Employment Agreement, dated June 29, 2015, by and between the Registrant and | 10-Q | 001-34962 | August 10, 2015 | 10.5 |

| | | | | | |
|---|---|---|---|---|---|
| | Gail M. Farfel, Ph.D. | | | | |
| 10.11# | Employment Agreement dated December 17, 2013 by and between the Registrant and Bradley S. Galer, M.D. | 10-K | 001-34962 | March 7, 2014 | 10.44 |
| 10.12# | Employment Agreement dated January 16, 2017, by and between the Registrant and Michael P. Smith | 10-Q | 001-34962 | May 4, 2017 | 10.2 |
| 10.13# | Employment Agreement dated July 2, 2018, by and between the Registrant and Ashish Sagrolikar | 10-Q | 001-34962 | November 8, 2018 | 10.1 |

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| | | Incorporated by Reference | | | | |
|---|---|---|---|---|---|---|
| **Exhibit No.** | **Description** | **Form** | **File Number** | **Date of Filing** | **Exhibit No.** | **Filed Herewith** |
| 10.14† | 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-Q | 001-34962 | November 6, 2014 | 10.5 | |
| 10.15 | Lease dated October 31, 2006 by and between the Registrant and Emery Station Joint Venture, LLC | S-1 | 333-169210 | September 3, 2010 | 10.1 | |
| 10.16 | First Amendment to Lease dated July 10, 2007 by and between the Registrant and Emery Station Joint Venture, LLC | S-1 | 333-169210 | September 3, 2010 | 10.11 | |
| 10.17 | Second Amendment to Lease dated October 20, 2009 by and between the Registrant and Emery Station Joint Venture, LLC | S-1 | 333-169210 | September 3, 2010 | 10.12 | |
| 10.18 | Third Amendment to Office Lease, dated July 20, 2015, by and between the Registrant and Emery Station Joint Venture, LLC | 10-Q | 001-34962 | August 10, 2015 | 10.8 | |
| 10.19 | Lease Termination Agreement, dated October 1, 2018, by and between | | | | | X |

| | | | | | | |
|---|---|---|---|---|---|---|
| | the Registrant and Emery Station Joint Venture, LLC | | | | | |
| 10.20 | Office Lease dated August 5, 2014 by and between the Registrant and Kilroy Realty, L.P. | 10-Q | 001-34962 | November 6, 2014 | 10.6 | |
| 10.21 | Lease Agreement, dated October 1, 2018, by and between the Registrant and Emery Station West, LLC | | | | | X |
| 10.22 | Controlled Equity Offering Sales Agreement, dated May 10, 2016, by and between the Registrant and Cantor Fitzgerald & Co. | S-3 | 333-211265 | May 10, 2016 | 1.2 | |
| 21.1 | Subsidiaries of the Company | 10-K | 001-34962 | March 10, 2017 | 21.1 | |
| 23.1 | Consent of Independent Registered Public Accounting Firm | | | | | X |
| 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) | | | | | X |
| 31.2 | Certification of Chief Financial Officer pursuant to Section 302 of the Public Company Accounting | | | | | X |

| | | | |
|---|---|---|---|
| | 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) | | X |
| 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) | | X |
| 101.INS | XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document. | | |
| 101.SCH | XBRL Taxonomy Extension Schema Document. | | X |

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| | | Incorporated by Reference | | | | |
|---|---|---|---|---|---|---|
| **Exhibit No.** | **Description** | **Form** | **File Number** | **Date of Filing** | **Exhibit No.** | **Filed Herewith** |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase Document. | | | | | X |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase Document. | | | | | X |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document. | | | | | X |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase Document. | | | | | X |

† 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.

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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: | February 28, 2019 | By: | /s/ Stephen J. Farr |
| | | | President and Chief Executive Officer |
| Date: | February 28, 2019 | 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.<br>**Stephen J. Farr, Ph.D.** | President and Chief Executive Officer (Principal Executive Officer) | February 28, 2019 |
| /S/ MICHAEL P. SMITH<br>**Michael P. Smith** | Executive Vice President, Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer) | February 28, 2019 |
| /S/ CAM L. GARNER<br>**Cam L. Garner** | Chairman of the Board | February 28, 2019 |
| /S/ LOUIS C. BOCK<br>**Louis C. Bock** | Director | February 28, 2019 |
| /S/ JAMES B. BREITMEYER, M.D., Ph.D.<br>**James B. Breitmeyer, M.D., Ph.D** | Director | February 28, 2019 |
| /S/ ROGER L. HAWLEY<br>**Roger L. Hawley** | Director | February 28, 2019 |
| /S/ ERLE T. MAST<br>**Erle T. Mast** | Director | February 28, 2019 |
| /S/ RENEE TANNENBAUM, Pharm.D.<br>**Renee Tannenbaum, Pharm.D.** | Director | February 28, 2019 |

| | | |
|---|---|---|
| /S/ MARK WIGGINS<br>**Mark Wiggins** | Director | February 28, 2019 |