UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2021

or

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

For the transition period from _____ to _____

Commission file number: 001-34962

ZOGENIX, INC.

Delaware	**20-5300780**
(State of Incorporation)	**(I.R.S. Employer Identification No.)**
5959 Horton Street, Suite 500 **Emeryville, California**	**94608**
(Address of principal executive offices)	**(Zip Code)**

(510) 550-8300
(Registrant's telephone number, including area code)

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

Title of each class	Trading symbol	Name of exchange registered
Common Stock, $0.001 par value per share	ZGNX	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

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

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 ☒

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 ☒ 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). Yes ☒ ☐ No

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	☒	Accelerated Filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 USC. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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

As of June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates was approximately $863.0 million.

As of February 25, 2022, there were 56,227,441 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 2022 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, 2021.

ZOGENIX, INC.

FORM 10-K

For the Year Ended December 31, 2021

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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:

- our ability to achieve the complete, or realize the anticipated benefits of, the Merger (as defined below) with UCB S.A. (referred to as Parent below);
- the potential payment of the CVR (as defined below);
- the extent of disruption to our business caused by the pending Merger and its effect, if any with our current plans and operations;
- our ability to commercialize Fintepla;
- the progress and timing of clinical trials of Fintepla and MT-1621;
- the safety and efficacy of our product candidates;
- the impact of the COVID-19 pandemic;
- the timing of submissions to, and decisions made by the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) 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,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “ongoing” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. 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.

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

Unless the context requires otherwise, references in this Annual Report on Form 10-K to "Zogenix," "we," "us" and "our" refer to Zogenix Inc., a Delaware corporation, and its consolidated subsidiaries.

SUMMARY OF RISK FACTORS

Investing in our common stock is subject to numerous risks and uncertainties, including those described in Part I, Item 1A, "Risk Factors" of this Annual Report on Form 10-K. The principal risks and uncertainties affecting our business include the following:

- The conditions under the Merger Agreement to Parent's consummation of the Offer and our subsequent Merger with Purchaser may not be satisfied at all or in the anticipated timeframe.
- While Parent's Offer and the proposed Merger are pending, we are subject to business uncertainties and contractual restrictions that could disrupt our business.
- Litigation filed or that may be filed against us and/or the members of our board of directors could prevent or delay the consummation of the Merger.
- In the event that the Merger is not consummated, the trading price of our common stock and our future business and results of operations may be negatively affected.
- If the Merger Agreement is terminated, we may, under certain circumstances, be obligated to pay a termination fee to Parent. These costs could require us to use available cash that would have otherwise been available for other uses.
- We may not be successful in executing our sales and marketing strategy for the commercialization of Fintepla.
- If Fintepla or MT-1621, if approved, does not achieve broad market acceptance or coverage by third-party payors, the revenues that we generate will be limited.
- 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 may 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 success depends substantially on Fintepla as a commercial product and as a product candidate in other indications as well as our product candidate MT-1621. We cannot be certain that Fintepla will receive

additional regulatory approvals, or be successfully commercialized, or whether MT-1621 or any future product candidates will receive regulatory approval or be successfully commercialized.

- We depend on a sole specialty distributor, our customer, for distribution of Fintepla in the United States, and the failure of this specialty distributor to distribute Fintepla effectively would adversely affect sales of Fintepla.
- Our business is subject to risks arising from epidemic diseases, such as the COVID-19 pandemic.
- Fintepla, MT-1621 and any of our future product candidates are subject to extensive regulation.
- We may not be able to maintain orphan drug designation or obtain or maintain orphan drug exclusivity for Fintepla or MT-1621.
- Our clinical trials may fail to demonstrate acceptable levels of safety and efficacy for our product candidates, which could prevent or significantly delay their regulatory approval.
- 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.
- 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 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.
- 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.
- 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.

ITEM 1. BUSINESS

Overview

Zogenix Inc. is a global biopharmaceutical company committed to developing and commercializing therapies with the potential to transform the lives of patients and their families living with rare diseases. We are primarily focused on developing and commercializing two therapeutic product opportunities: Fintepla, a low-dose fenfluramine, for rare, devastating, difficult-to-treat pediatric epilepsy disorders and MT-1621 for a rare, life-threatening mitochondrial depletion disease, thymidine kinase 2 deficiency (TK2d).

Fintepla is approved for marketing in the U.S., the European Union (EU) and in the United Kingdom and is under late-stage development in Japan for the treatment of seizures associated with Dravet syndrome, a rare and devastating pediatric epilepsy disorder.

We own and control worldwide development and commercialization rights to Fintepla. We currently market and commercialize Fintepla for the adjunctive treatment of seizures associated with Dravet syndrome in the U.S., Germany and France through our highly specialized and focused commercial team. We plan to utilize this self-commercialization strategy for other major markets in Europe. In March 2019, we entered into an exclusive distribution agreement with Nippon Shinyaku Co., Ltd. to support the sales and distribution of Fintepla in Japan, if approved for marketing in that country. In December 2021, we submitted a New Drug Application to the Japanese Ministry of Health, Labour & Welfare (MHLW) for the marketing approval of Fintepla for the treatment of seizures associated with Dravet syndrome in Japan. We plan to seek regulatory approvals and make Fintepla available to patients in other select international markets through our commercial team or work with partners in other parts of the world. In the fourth quarter of 2021, we submitted applications in the U.S. and in the EU for regulatory approvals to market Fintepla for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), a rare and devastating form of childhood-onset epilepsy. In September 2021, we initiated a Phase 3 Study of Fintepla in patients with a genetic epilepsy called CDKL5 Deficiency Disorder (CDD). We continue to explore Fintepla for other potential indications associated with epilepsy disorders through on-going and new Investigator Initiated Studies.

In September 2019, we acquired all the outstanding equity interests of Modis Therapeutics, Inc. (Modis), a privately-held biopharmaceutical company. Through our Modis acquisition, we hold exclusive worldwide license from Columbia University in New York City (Columbia) to certain intellectual property rights owned or controlled by Columbia to develop and commercialize MT-1621. MT-1621 is an investigational deoxynucleoside-combination substrate enhancement therapy in development for the treatment of TK2d, an inherited mitochondrial DNA depletion disease that predominantly affects children and is often fatal. MT-1621 is currently in late-stage development and we are in active discussions with regulatory authorities in the U.S. and in the EU regarding the potential submission of new drug applications (NDAs) for MT-1621 as a treatment for patients with TK2d.

Merger Agreement

On January 18, 2022, we entered into a definitive Agreement and Plan of Merger (the “Merger Agreement”), with UCB S.A., a société anonyme formed under the laws of Belgium (“Parent”) and Zinc Merger Sub, Inc., a Delaware corporation and an indirect wholly owned subsidiary of Parent (“Purchaser”), pursuant to which, on the terms and subject to the conditions set forth therein, and in accordance with the relevant provisions of the Delaware General Corporation Law, as amended (the “DGCL”), Purchaser will be merged with and into the Company (the “Merger”). Purchaser commenced a tender offer (the “Offer”) on February 1, 2022 to acquire all of the Company’s outstanding shares of common stock, par value $0.001 per share (the “Company Shares”), at a purchase price of (i) $26.00 per Company Share (the “Closing Amount”), net to the seller thereof in cash, subject to reduction for any applicable withholding taxes and without interest, plus (ii) one non-transferrable contingent value right per Company Share representing the right to receive a contingent payment of $2.00 (each, a “CVR”, and the Closing Amount plus one CVR, collectively, or any greater amount per Company Share that may be paid pursuant to the Offer, being hereinafter referred to as the “Offer Price”), net to the holder thereof in cash, subject to reduction for any applicable withholding taxes and without interest, upon the achievement of the milestone specified in, and on the other terms and subject to the other conditions set forth in, the CVR Agreement (as defined in the Merger Agreement).

Each CVR represents a non-transferable contractual contingent right to receive a cash payment of $2.00, without interest and less any applicable withholding taxes (the “Milestone Payment”), if, and only if, no later than December 31, 2023, the European Commission approves Zogenix’s product Fintepla® as an orphan medicinal product for treatment of seizures associated with Lennox-Gastaut syndrome, following an opinion rendered by the Committee for Orphan Medicinal Products of the European Medicines Agency (“EMA”) recommending that

fenfluramine hydrochloride for the treatment of Lennox-Gastaut syndrome not be removed from the Community Register of Orphan Medicinal Products (the “Milestone”).

Completion of the Offer is subject to the satisfaction or waiver of customary conditions, including (i) (i) there having been validly tendered in accordance with the terms of the Offer and not validly withdrawn, as of immediately prior to the expiration of the Offer, a number of Company Shares that, together with the Company Shares then owned by Parent or Merger Sub, represents at least a majority of the Company Shares then outstanding; (ii) the accuracy of the representations and warranties of the Company contained in the Merger Agreement, subject to certain materiality qualifications; (iii) the Company’s compliance in all material respects with its covenants and agreements contained in the Merger Agreement; (iv) the expiration or termination of any waiting period (and any extension thereof) applicable to the Offer or the Merger under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and the receipt of any other clearance, approval or consent applicable to Offer or the Merger (as defined below) under any applicable antitrust law; (v) the absence of a Company Material Adverse Effect (as defined in the Merger Agreement) that is continuing; and (vi) the absence of any law, regulation, order, injunction or ruling issued or enacted by any government authority of competent jurisdiction that would prohibit or make illegal the consummation of the Offer or the Merger, or that would impose certain remedies or restrictions on the ability of Parent to fully own or operate the Company, its businesses or assets.

We expect the Merger to close in the first half of 2022, subject to the regulatory approvals and other customary closing conditions described above and in the Merger Agreement.

Additional information about the Merger and related transactions is set forth in our filings with the Securities and Exchange Commission, or the SEC.

Our Strategy

Our mission is to develop and commercialize therapies with the potential to transform the lives of patients and their families living with rare diseases. The critical components of our business strategy include the following:

- ***Successfully launch and commercialize Fintepla for the treatment of patients with Dravet syndrome in the U.S. and Europe, and obtain regulatory approval and commence commercialization in Japan and multiple select geographies throughout the world.*** In June 2020, we announced FDA approval for Fintepla for the adjunctive treatment of seizures associated with Dravet syndrome in the U.S., in combination with other drugs including stiripentol, clobazam, and valproate. Shortly thereafter, in July 2020 we launched Fintepla and made the therapy available to patients in the U.S. through our specialized commercial team, including our care coordination team at Zogenix Central. In December 2020, we received marketing approval for Fintepla for the adjunctive treatment of seizures in Dravet syndrome from the European Commission and currently have commercial sales in Germany and France. We plan to launch and commercialize Fintepla in other major European markets with country-based commercial teams once we are able to secure appropriate reimbursement approvals. In Japan, we are pursuing regulatory approval for Fintepla with our commercial partner, Nippon Shinyaku. In Israel, we are currently pursuing regulatory approval for Fintepla with our commercial partner, Medison Pharma, Ltd., and we will seek to make Fintepla available to patients in other select international markets through our own commercial teams or partnerships. We have entered into manufacturing and supply agreements for Fintepla and are continuing to build our internal commercial capabilities for potential commercialization in other select international markets.
- ***Seek regulatory approval of Fintepla for the treatment of seizures associated with LGS.*** In February 2020, we reported positive top-line results from our global Phase 3 clinical trial (Study 1601) of Fintepla for the treatment of seizures associated with LGS. The trial met its primary objective of demonstrating that Fintepla at a dose of 0.7 mg/kg/day was statistically superior to placebo in reducing the frequency of drop seizures and demonstrated statistically significant improvements versus placebo in key secondary efficacy measures, including the proportion of patients with a greater than 50% reduction in drop seizure frequency. In September and December 2021, we submitted a supplemental new drug application (sNDA) for LGS to the FDA and an application for a Type II Variation Marketing Authorization Application (MAA) with the European Medicine Agency (EMA), respectively, for Fintepla for the treatment of seizures associated with LGS. If approved, we plan to commercialize Fintepla as a potential treatment for patients with LGS in the U.S., the EU and the United Kingdom with a similar self-commercialization approach that we are taking in Dravet syndrome.

- ***Advance the development of MT-1621 for the treatment of TK2d.*** In October 2019, we announced positive top-line results from our global, retrospective Phase 2 study (the RETRO study) at the World Muscle Society congress in Copenhagen. 94.7% of treated patients had either improved (68%) or stabilized (26%) overall responses in major functional domains. A survival analysis using a time-dependent Cox regression model showed that the difference in probability of survival between treated patients and untreated natural history control patients was statistically significant ($p<0.0006$). Among clinical responders, a subset demonstrated profound responses, in some cases re-acquiring previously lost motor milestones such as ambulation, respiratory function and feeding. Safety data from RETRO indicated that MT-1621 was generally well-tolerated. We held several meetings with the FDA and EMA in 2020 and 2021 to discuss regulatory requirements and the scope of information needed for NDA and MAA submissions, respectively. We are targeting an NDA to the FDA submission in the second half 2022. We anticipate submitting an MAA to obtain marketing authorization in Europe thereafter.
- ***Pursue development of Fintepla for additional indications****.* In addition to Dravet syndrome and LGS, we believe that the unique mechanism of action of Fintepla has the potential to treat other serious epileptic encephalopathies where there is a significant unmet medical need. In September 2021, we initiated a Phase 3 trial of Fintepla for the treatment of CDKL5 deficiency disorder (CDD), an infant-onset genetic seizure disorder. We continue to explore Fintepla as a potential treatment for additional severe, treatment-resistant rare epilepsies through the initiation of other investigator-initiated clinical studies.

Fintepla for Patients with Dravet Syndrome

Fintepla is a low-dose, oral solution formulation of fenfluramine, a small molecule with unique serotonergic and positive sigma-1 receptor modulation activity, approved in the U.S. for adjunctive therapy in the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older. To ensure safe use, Fintepla was approved to be available in the U.S. only through a restricted distribution program called the Fintepla Risk Evaluation and Mitigation Strategy (REMS) Program. Under the Fintepla REMS Program, echocardiogram assessments of patients are required before, during, and after treatment with Fintepla. Fintepla is approved in the EU for the treatment of seizures associated with Dravet syndrome as an add-on therapy to other anti-epileptic medicines for patients two years of age and older and is available via a controlled access program.

In support of the approvals, Fintepla, when used in adjunctive therapy, demonstrated positive safety and efficacy results from two randomized, international, multi-center, placebo-controlled Phase 3 trials (Study 1 and Study 2), as well as data from a long-term, open-label extension study in 330 Dravet syndrome patients treated up to 3 years. The Study 1 trial met its primary objective of demonstrating that Fintepla, at a dose of 0.7 mg/kg/day (26 mg/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 ($p<0.001$). The Study 2 trial successfully met the primary objective of demonstrating that Fintepla, at a dose of 0.4 mg/kg/day, when administered to patients on a stiripentol treatment regimen, 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 ($p<0.001$). Across both Study 1 and Study 2, Fintepla was generally well-tolerated and no case of valvular heart disease or pulmonary arterial hypertension was observed in any patients.

Dravet syndrome is a rare, lifelong form of pediatric-onset epilepsy, marked with severe, debilitating seizures with life threatening consequences for patients and for which current treatment options are limited. The exact number of people with Dravet syndrome is unknown but has been estimated to be between 1 in 15,700 to 1 in 40,000 people.

Recent Developments

In December 2021, we submitted a New Drug Application to the Japanese Ministry of Health, Labour & Welfare (MHLW) for the marketing approval of Fintepla for the treatment of epileptic seizures associated with Dravet syndrome in Japan. Fintepla received Orphan Drug Designation from Japan's MHLW in August 2021. The filing was based on results from Studies 1, 2, and 1503 described above. Additional data from an additional randomized, international, multi-center, placebo-controlled Phase 3 trial, or Study 3, was included in this filing. The Study 3 trial met its primary objective of demonstrating that Fintepla, at a dose of 0.7 mg/kg/day (26 mg/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 ($p<0.001$). Study 3 included patients from Japan, as well as North America, Europe and the UK. As in Studies 1 and 2, Fintepla was well-tolerated in Study 3 and no cases of pulmonary arterial hypertension or valvular heart disease were observed.

Our Clinical Product Candidates

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.

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). The study included a total of 263 patients between the ages of 2 and 35 years whose seizures were currently uncontrolled while on one or more anti-epileptic drugs (AEDs) randomized into three treatment groups: Fintepla 0.7 mg/kg/day (26 mg maximum daily dose; n=87), Fintepla 0.2 mg/kg/day (n=89), and placebo (n=87). The median age of patients was 13 years, with 29% being 18 years or older. Patients entering the study were taking between one and four AEDs and previously had tried and discontinued an average of seven other AEDs. The median baseline drop seizure frequency across the study groups was 77 seizures per month. After establishing baseline seizure frequency for 4 weeks, randomized patients were titrated to their dose over a 2-week titration period, followed by a 12-week fixed dose maintenance period. Patients who completed Part 1 were eligible to enter Part 2 of the clinical trial, an ongoing 12-month open label extension (OLE) study to evaluate the long-term safety, tolerability and effectiveness of Fintepla.

Study 1601 met its primary endpoint of showing a highly statistically significant reduction from baseline compared to placebo in the median percent change in monthly drop seizure frequency. Patients taking Fintepla 0.7 mg/kg/day achieved a median reduction of 26.5% compared to a median reduction of 7.8% in patients taking placebo ($p=0.0012$). Using a parametric analysis, patients taking Fintepla 0.7 mg/kg/day demonstrated a 26.5% greater reduction in mean monthly drop seizure frequency compared to placebo ($p=0.0034$). The median percent reduction in monthly drop seizures between baseline and the treatment period for the lower study dose of Fintepla (0.2 mg/kg/day), a secondary endpoint, was 13.2% and did not reach statistical significance compared to placebo ($p=0.0915$). Additional secondary endpoints of the study were also positive as the proportion of study patients treated with Fintepla 0.7 mg/kg/day who achieved a (≥50%) reduction in monthly drop seizures was superior to placebo ($p=0.0165$). Also, with regard to Clinical Global Impression of Improvement ratings (CGI-I, a measure of improvement of worsening relative to baseline) as assessed by the investigator, patients who received the Fintepla 0.7 mg/kg/day dose demonstrated a superiority to placebo in terms of the proportion of patients who much improved or very much improved ($p=0.0007$).

In Study 1601 Fintepla was generally well-tolerated, with the adverse events consistent with those observed in our two prior Phase 3 trials in Dravet syndrome. incidence of patients who experienced at least one treatment emergent adverse event was 89.7% of patients in the Fintepla 0.7 mg/kg/day group, 76.4% in the Fintepla 0.2 mg/kg/day group and 79.3% in the placebo group. The most common adverse events (≥10%) in the Fintepla-treated groups were decreased appetite, somnolence, fatigue, vomiting, diarrhea, and pyrexia. The incidence of serious treatment emergent adverse events was 11.5% (n=10) in the 0.7 mg/kg/day group, 4.5% (n=4) in the 0.2 mg/kg/day group, and 4.6% (n=4) in the placebo group. Six patients in the 0.7 mg/kg/day group had an adverse event leading to study discontinuation compared to four subjects in the 0.2 mg/kg/day group and one patient in the placebo group; the majority of these were considered treatment-related. There was one death during the trial (0.7 mg/kg/day group) caused by SUDEP, which was assessed by the investigator to be unrelated to the study drug. No cases of valvular heart disease or pulmonary hypertension have been observed in Study 1601. A total of 247 (93.9%) patients entered the OLE phase.

Recent Developments

In September 2021, we submitted a supplemental New Drug Application (sNDA) to the FDA for Fintepla for the treatment of seizures associated with LGS. In December 2021, Zogenix announced that the FDA accepted for filing the sNDA, granted our request for Priority Review, and set a Prescription Drug User Fee Act (PDUFA) goal date of March 25, 2022. FDA may grant Priority Review designation to NDAs for drugs that are intended to treat serious conditions and, if approved, would provide significant improvements in safety or effectiveness.

In December 2021, we submitted a Type II Variation Market Authorization Application to the EMA for Fintepla for the treatment of seizures associated with LGS. If approved, the application would expand the use of Fintepla in the European Union and the United Kingdom beyond patients with Dravet syndrome to include patients with LGS.

Fintepla for CDD

In December 2020 at the annual American Epilepsy Society Meeting, clinical investigators from the New York University Langone Medical Center reported interim results from the first six patients of an open-label, investigator-initiated study of Fintepla in CDD patients between ages 2 and 35 that patients taking Fintepla at a dose of up to 0.7/mg/kg day experienced a clinically meaningful reduction in both generalized clonic-tonic seizures (90%) and tonic seizures (55%). CDD is a genetic neurological disorder that presents clinically with persistent seizures starting at infancy, followed by severe impairment in neurological development. Based on the reported interim results of the open-label, investigator-initiated study, we initiated a two-arm, fixed-dose Phase 3 trial to investigate the efficacy and safety of FINTEPLA in controlling convulsive seizure frequency at a dose of 0.7 mg/kg/day in September 2021. Based on feedback from the FDA, we believe a single Phase 3 study, if successful, would be sufficient to support an sNDA submission for Fintepla for CDD.

Fintepla for Other Potential Indications

We also plan to continue to explore Fintepla as a potential treatment for additional severe, treatment-resistant rare epilepsies through other investigator-initiated clinical studies.

MT-1621 for Patients with TK2d

TK2d is a rare, debilitating, and often fatal genetic disorder that primarily affects infants and children and for which there are currently no approved therapies. As of September 6, 2019, the date we acquired Modis, Modis had completed the RETRO study of MT-1621 in patients with TK2d and commenced a Phase 2 prospective, OLE study of patients with TK2d, Study MT-1621-101. MT1621 has received Breakthrough Therapy designation from the FDA and access to the PRIME scheme by the EMA and we intend to seek accelerated regulatory review pathways in both the United States and Europe.

RETRO was a global retrospective study of MT-1621, a fixed combination treatment of two pyrimidine nucleosides deoxycytidine and deoxythymidine (dC/dT), in 38 pediatric and adult patients with TK2d (median age of disease onset, 2.5 years) treated at eight clinical sites in the United States, Spain and Israel.

Subjects received MT-1621 for a median of 71 weeks (range 92 days – 7 years). Each subject was scored across motor, respiratory, and feeding domains according to pre-defined response criteria and was compared to pre-treatment status to assess whether responses improved, remained stable, or worsened. Parallel to RETRO, we compiled a comprehensive, global TK2d Natural History dataset from published studies and individual case reports to document untreated patients' disease course. From this natural history dataset, 68 patients reflecting the range of disease severity, age, and age of disease onset, were selected as a control group for treated patients in the RETRO study.

In October 2019 we announced positive top-line results from the pivotal Phase 2 RETRO study at the World Muscle Society congress in Copenhagen. 94.7% of treated patients had either improved (68%) or stabilized (26%) overall responses in major functional domains. A survival analysis using a time-dependent Cox regression model showed that the difference in probability of survival between treated patients and untreated natural history control patients was statistically significant ($p<0.0006$). Among clinical responders, a subset demonstrated profound responses, in some cases re-acquiring previously lost motor milestones such as ambulation, respiratory function and feeding. Safety data from RETRO indicated that MT-1621 was generally well-tolerated. Most reported adverse events were considered not related to study drug (199 of 292), with mild or moderate diarrhea being the most common treatment-related adverse event (AE), occurring in 63% of patients. Serious AEs (SAEs) were reported in 14 subjects (37%). The majority of SAEs were deemed related to TK2d; two patients experienced three events

related to study drug alone (kidney stone, kidney stone removal, diarrhea). Two adult-onset patients stopped treatment due to asymptomatic increases in aminotransferase liver enzymes (no increase in bilirubin levels), which resolved upon discontinuation of treatment.

In April 2020, we held an End-of-Phase 2 meeting with the FDA and in June 2020, we met with the FDA to discuss chemistry, manufacturing, and controls (CMC) for MT1621. In the meetings, the FDA outlined the additional clinical and non-clinical information needed for an NDA submission. In July 2021, we had a Type B Meeting with the FDA where the FDA confirmed the adequacy of the proposed data packages for an NDA submission due to the rare and serious nature of TK2d and the unmet medical need.

Based on this feedback, we are targeting an NDA submission to the FDA for TK2d in the second half of 2022. In addition, we are conducting a Phase 1 pharmacokinetic (PK) study in renal impairment, as recommended by the FDA, to provide dosing recommendations in the setting of impaired renal function and include the results in the NDA submission. The FDA also concurred with our proposed CMC plan for the prospective NDA submission.

In December 2021, we received Scientific Advice feedback from the EMA supportive of our clinical and non-clinical plan to pursue marketing authorization for the treatment of TK2d patients with the age of onset of TK2d younger than 12 years of age. We are targeting an MAA submission after our anticipated NDA submission.

Preclinical Pipeline

Tevard Gene Therapy Collaboration for Genetic Epilepsies

In December 2020, we entered into a collaboration with Tevard Biosciences, Inc. for the research, development and commercialization of gene therapies for the treatment of Dravet syndrome and other epilepsy disorders. The collaboration is at the research and discovery stage and will leverage Tevard' s pioneering and novel t-RNA-based technology to treat genetic disorders not amenable to traditional types of gene therapies, such as Dravet Syndrome.

Please see "Strategic and License Agreements" section for a more detailed description of the terms of our Tevard collaboration.

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 and 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 products, 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. GW's CBD was subsequently approved for the treatment of Dravet syndrome and LGS by the European Commission (as Epidyolex®) in September of 2019. Epidyolex must be prescribed with clobazam in Europe. 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 clobazam.

Fintepla has a novel biological mechanism of action (selective serotonin and sigma-1 receptor activity) that is different from the other antiepileptic drugs currently available and in clinical development in the United States and

Europe 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.

Multiple companies are developing clinical-stage product candidates for the potential treatment of Dravet syndrome. Takeda Pharmaceutical Company Limited is currently evaluating its product candidate TAK-935/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. Additional clinical stage candidates for the treatment of Dravet syndrome include LP352 from Longboard Pharmaceuticals, Inc.(Phase 1), clemizole (Phase 2) being evaluated by Epygenix Therapeutics, Inc., Huperzine-A from Supernus Pharmaceuticals (Phase 1/2), STK-001 from Stoke Therapeutics (Phase 1), and NBI-921352 from Neurocrine Biosciences (Phase 1).

Several other companies, including Encoded Therapeutics, Inc., Neucyte, Inc., NeuroCycle Therapeutics and Sarepta Therapeutics, Inc., have disclosed that they are evaluating preclinical drug candidates, including gene therapies and small molecules, for the potential treatment of Dravet syndrome.

MT-1621

Currently, we are not aware of any pharmaceutical products that have been approved for the treatment of a primary mitochondrial disease. Similarly, we are not aware of any pharmaceutical companies who are developing a pharmaceutical product candidate for the treatment of TK2d.

Beyond TK2d, a number of pharmaceutical companies are developing clinical-staged product candidates for the potential treatment of other mitochondrial diseases, including Metro International Biotech LLC, PTC Therapeutics, Inc., Reata Pharmaceuticals, Inc., Reneo Pharmaceuticals, Inc., Stealth BioTherapeutics, Inc., and Wellstat Therapeutics Corp.

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, MT-1621 or any future product candidates.

Fintepla

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 fenfluramine hydrochloride, the active pharmaceutical ingredient (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. In July 2019, we entered into a supply agreement (PCI Pharma Agreement) with Penn Pharmaceutical Services Limited, trading as PCI Pharma Services (PCI Pharma), pursuant to which PCI Pharma will procure the raw materials (other than the active pharmaceutical ingredient) for, formulate, fill, test and release an oral solution of Fintepla. Pursuant to the PCI Pharma Agreement, at a specified time prior to the anticipated receipt of the first marketing authorization by a regulatory agency to market Fintepla, and then each month following such receipt, we are required to deliver a rolling forecast of our expected commercial orders, a portion of which will be considered a binding, firm order.

The term of the PCI Pharma Agreement is five years, which term shall be automatically extended for successive two-year periods thereafter, unless terminated earlier. After the second anniversary of the Effective Date, either party may terminate the PCI Pharma Agreement at any time without cause following a specified notice period applicable to the respective party. In addition, either party may terminate the agreement (1) upon written notice if the other party has failed to remedy a material breach of any of its representations, warranties or other obligations under the PCI Pharma Agreement within a specified period following receipt of written notice of such breach, (2) immediately in the event of a material breach of the other party's representations, warranties or other obligations under the PCI Pharma Agreement and in the event that such breach is not capable of remedy and (3) in the event that the other party files for bankruptcy, reorganization, liquidation, administration or receivership proceedings, or a substantial portion of the assets of such party is assigned for the benefit of such party's creditors. We may also terminate the PCI Pharma Agreement immediately in the event PCI Pharma is unable to supply Fintepla at specified quantities and within certain times. PCI Pharma may also terminate the Agreement upon notice if it determines its performance of services would violate applicable law. PCI Pharma's manufacturing services under the PCI Pharma

Agreement will also terminate automatically if Fintepla is withdrawn as a result of regulatory review or we decide to cease development activities of Fintepla.

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 necessary to manufacture our product candidates. Third-party manufacturers are and will be used to formulate, fill, label, package, test, release, 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 of our products.

MT-1621

As a part of our acquisition of Modis in September 2019, we assumed a manufacturing supply agreement with ST Pharm Co. LTD (ST Pharm), pursuant to which ST Pharm will be our clinical materials manufacturer and supplier of both 2'-deoxycytidine and 2'-deoxythymidine APIs used in MT1621. The term of the supply agreement is five (5) years from the date of agreement (October 2017), which term can be extended for successive two-year periods thereafter, unless terminated earlier. ST Pharm has been providing the API for the clinical trial material supply needs and registration batches since the beginning of MT1621 clinical trials. In addition, we also assumed a supply agreement with Catalent Pharma Solutions (Catalent), pursuant to which Catalent will procure all materials other than the API, fill into drug product packs, and package, test, and release the MT-1621 powder for oral solution finished product.

Strategic and License Agreements

Fintepla

As a result of our acquisition of Brabant, 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 Agreement), the Universities granted us an exclusive worldwide license to use the data obtained from a study related to low-dose fenfluramine for the treatment of Dravet syndrome or certain related conditions stemming from infantile epilepsy such as LGS, as well as certain other intellectual property. Under the Universities Agreement, net product sales of Fintepla are subject to royalties in the mid-single-digit percentage, or in the case of a sublicense, a percentage in the mid-twenties of the sub-licensing revenues.

In December 2021, we executed an amendment to the Universities Agreement, which provided for a one-time payment of $7.0 million related to our previous collaboration activities and consideration received to date under the Shinyaku Agreement. The amendment clarified that the Universities' are entitled to 15% of any regulatory or sales-based milestones under the Shinyaku Agreement, if achieved, as well as the method of calculating royalties due for supplying Fintepla, if approved for marketing, to Shinyaku, the exclusive distributor of Fintepla for Japan.

MT-1621

As a result of our acquisition of Modis, we became party to the Exclusive License Agreement, by and between Modis and Columbia, dated as of September 26, 2016 (the Columbia Agreement), related to MT-1621. We are required to use commercially reasonable efforts to develop and commercialize licensed products worldwide, including to meet certain development and commercialization milestones within specified periods of time. Upon the achievement of certain regulatory and commercial milestones, we are required to pay Columbia up to $2.9 million and $25.0 million, respectively, as well as tiered royalties on sales for each licensed product, at percentages ranging from the mid-single digits to the high single-digits. The royalty obligations and Columbia Agreement will expire on a country-by-country and product-by-product basis upon the later of (i) 15 years after the first bona fide commercial sale of a licensed product, (ii) the expiration of the last to expire valid patent claim covering a licensed product in a country or (iii) expiration of any regulatory exclusivity covering such licensed product. The Columbia Agreement may be terminated either by Columbia or by us in the event of an uncured material breach by the other party, or by Columbia in the event we are subject to specified bankruptcy, insolvency or similar circumstances. We can

terminate the Columbia Agreement either in its entirety or on a product-by-product and country-by-country basis, upon specified prior written notice to Columbia, provided we are not exploiting licensed products in such countries.

We also became party to a license agreement between two other research institutions related to MT1621 where we may be required to pay up to $3.0 million for research, development and regulatory milestone events and up to $10.0 million for certain sales milestone events. We are also required to pay tiered royalties ranging from low to mid-single digits on net sales of licensed product.

Tevard Collaboration, Option and License Agreement

In October 2019, we entered into an option agreement with Tevard Biosciences (Tevard), a privately-held company focused on tRNA-based gene therapies. Under the agreement, Tevard granted us an option to license exclusive rights related to a preclinical development program to identify and develop novel tRNA-based gene therapies for Dravet syndrome. During 2020, we extended the option period to exercise our license rights prior to entering into a collaboration, option and license agreement with Tevard. Payments made under the option agreement were nonrefundable, but may be credited against the upfront payment due if we exercise our option on the preclinical development program.

In December 2020, we exercised the option on the Dravet syndrome program and entered into a collaboration, option and license agreement with Tevard (the Tevard Agreement). The financial terms of the Tevard Agreement included an upfront payment of $5.2 million. In connection with the transaction, we also purchased a convertible promissory note issued by Tevard in the amount of $5.0 million. The note matures in December 2022 and carries interest at 3.5% per year. The note will automatically convert into equity securities issued by Tevard in their next equity financing transaction at a conversion price equal to the price paid per share by other investors of the financing transaction.

In addition to the upfront payments, we have agreed to fund Tevard's early discovery activities under the licensed Dravet syndrome program in accordance with the development plan as determined by the parties to the agreement. Once Tevard completes the early discovery activities for a program, we will be responsible for any potential future development and commercialization activities. Tevard is also eligible to receive additional development, regulatory and commercial-related milestone payments of up to $100.0 million for the Dravet program, as well as tiered single digit royalties on future net sales that result from the collaboration. On a country-by-country and product-by-product basis, royalty payments would commence on our first commercial sale of a product and terminate on the later of: (a) the expiration of patent-based exclusivity of such product in such country; (b) the expiration of regulatory based exclusivity of such product in such country; and (c) 10 years from the first commercial sale of the product in such country. Tevard has the option with respect to the Dravet syndrome program to elect to reimburse us for certain of our development costs for the Dravet syndrome program in exchange for receiving tiered royalties on future net sales ranging from low double digits to not more than 20% for products from the Dravet syndrome program.

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.

Fintepla

Currently, we have included 11 patents in FDA's list of Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"). As of December 31, 2021, we have rights to six issued and Orange Book-listed U.S. patents and eight issued foreign patents. One European patent was upheld in an opposition proceeding, and is now pending an appeal. A second European patent was recently opposed. These patents, entitled "Method for the Treatment of Dravet Syndrome," have claims covering methods for treatment of seizures associated with Dravet syndrome with Fintepla as adjunctive therapy 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 are assignees of an additional five Orange Book-listed patents covering: controlled distribution systems, and treatment of patients thereunder, for Fintepla; increasing patient exposure to Fintepla when co-administered with cannabidiol; and high purity fenfluramine compositions (API) used in our product that are expected to provide protection in the U.S. and which will reach their 20-year terms between 2036 and 2038.

MT1621

We have certain patent rights that we obtained through our acquisition of Modis. In September 2016, Modis entered into a license agreement with Columbia University under which Modis was granted an exclusive worldwide license and sublicense to certain intellectual property rights owned or controlled by Columbia to develop and commercialize MT-1621 and certain backup compounds for any claimed indication or purpose. These licensed patent rights include patents owned by Columbia and patents jointly owned by Columbia and Vall d'Hebron Research Institute (VHIR). VHIR delegated to Columbia the rights to enter into the Columbia Agreement on VHIR's behalf. The patent family jointly owned by Columbia and VHIR is directed to the use of MT-1621 to treat TK2 deficiency disorder and includes two issued patents in each of these jurisdictions; the U.S., the European Patent Office, Israel, Japan, Australia and Brazil, all of which will reach their 20-year terms in 2036. Further, pending applications in Mexico and Russia were recently allowed. In addition, there are pending patent applications in Canada, China, Hong Kong, India, Korea, as well as continuing applications in Australia, Brazil, the U.S., Israel, Japan, Russia and Europe. There are no patents covering the composition of matter in MT-1621, although there are pending applications claiming low residual solvent compositions of one of the MT-1621 components.

We have pending, in appropriate jurisdictions, foreign patent applications corresponding to our U.S. patents and US and Patent Cooperation Treaty patent applications for both Fintepla and MT1621. We cannot assure you that any of our patent applications will result in the issuance of patents, that any issued patent will include claims of the breadth we are seeking, or that competitors or other third-parties will not successfully challenge or circumvent our patents if they are issued.

Our ability to maintain and solidify our proprietary and intellectual property position for our products and product candidates will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, pending patent applications we have filed or licensed from third parties may not result in the issuance of patents.

We believe our patents are valid and do not infringe the patents or other proprietary rights of others. Accordingly, we believe we are not obligated to pay royalties relating to the use of intellectual property to any third parties except Catholic University of Leuven, University Hospital Antwerp, Columbia University and VHIR from which we have licensed certain 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:

- completion of pre-clinical laboratory and animal testing and formulation studies in compliance with the FDA's good laboratory practice (GLP) regulations and other applicable regulations;
- submission to the FDA of an IND for human clinical testing which must become effective before human clinical trials may begin in the United States;
- approval by an independent institutional review board (IRB) or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice (GCP) regulations, to establish the safety and efficacy of the proposed drug product for each intended use;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;

- 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 to ensure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quantity and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the U.S.

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. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. 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, 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. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

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: The drug is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

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.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2

trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, pre-clinical studies and clinical trials are submitted to the FDA as part of an NDA. NDAs must also contain extensive information relating to the product's pharmacology, CMC and proposed labeling, among other things.

The submission of an NDA may be subject to a substantial application user fee, and the 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. Under the PDUFA goals that are currently in effect, the FDA has a standard review goal of ten months from the date of filing of a NDA for a new molecular entity, and ten months from the date of receipt for an NDA for a non-new molecular entity, to review and act on the submission. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. 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 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.

For some drugs, the FDA may determine that a Risk Evaluation and Mitigation Strategy (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.

In addition, the Pediatric Research Equity Act (PREA) requires a sponsor to conduct pediatric clinical trials for most drugs for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Expedited Development and Review Programs

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing drug products that meet certain criteria. Specifically, 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. For a fast track designated 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.

A sponsor may also seek FDA designation of a product candidate as a “breakthrough therapy” if the product candidate 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 candidate 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.

Any product candidate submitted to the FDA for approval, including a product with a fast track designation or breakthrough therapy designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. An NDA is eligible for priority review if the product candidate is intended to treat a serious condition, and if approved, would provide 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 designated for priority review in an effort to facilitate the review. Under its current review goals, 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, and within six months of the receipt date for non-new molecular entity NDA.

In addition, a product candidate 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. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing clinical trials or if such trials fail to verify the predicted clinical benefit. 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, breakthrough therapy designation, priority review, and accelerated approval do not change the standards for approval but may expedite the development or approval process. 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.

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. The FDA may also 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. In addition, the FDA may also require a REMS for an approved product when new safety information emerges.

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. 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 impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product;
- 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.

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 marketing 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.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan 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 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. However, competitors, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of one of our product candidates for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. In addition, if an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity.

In the EU, medicinal products: (a) that are used to treat or prevent life-threatening or chronically debilitating conditions that affect no more than five in ten thousand people in the EU when the application is made; or (b) that are used to treat or prevent life-threatening or chronically debilitating conditions and that, for economic reasons, would be unlikely to be developed without incentives; and (c) where no satisfactory method of diagnosis, prevention or treatment of the condition concerned exists, or, if such a method exists, the medicinal product would be of significant benefit to those affected by the condition, may be granted an orphan designation. The application for orphan designation must be submitted to the EMA and approved before an application is made for marketing authorization for the product. Once authorized, orphan medicinal products are entitled to up to ten years of market exclusivity (which may be extended for an additional two years if pediatric data have been produced in accordance with an agreed pediatric investigational plan). During this ten year period, with a limited number of exceptions, neither the competent authorities of the EU Member States, the EMA, or the EC are permitted to accept applications or grant marketing authorization for other similar medicinal products with the same therapeutic indication. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this latter product is safer, more efficacious or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the criteria for orphan designation are no longer met or if the orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Rare Pediatric Disease Priority Review Voucher Program

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the United States within one year following the date of approval.

For purposes of this program, a “rare pediatric disease” is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare diseases or conditions within the meaning of the Orphan Drug Act. Congress has only authorized the Rare Pediatric Disease Priority Review Voucher program until September 30, 2024. Consequently, sponsors of marketing applications approved after that date will not receive the voucher unless Congress reauthorizes the Rare Pediatric Disease Priority Review Voucher program. However, even if the program is not reauthorized, if a drug candidate receives Rare Pediatric Disease Designation before October 1, 2024, the sponsor of the marketing application for such drug will be eligible to receive a voucher if the application for the designated drug is approved by the FDA before October 1, 2026.

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.

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 Schedule IV 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.

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.

Foreign Regulation of Drug Development and Approval

In addition to regulations in the U.S., we are subject to a variety of foreign regulatory requirements including those governing drug development, pre-clinical and clinical studies, marketing authorization, manufacturing, pharmacovigilance and post-marketing regulation for drugs. The foreign regulatory approval process includes all of the risks associated with FDA approval set forth above, as well as additional country-specific regulations. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. The approval process varies from country to country, can involve additional testing beyond that required by FDA, and may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing, promotion, and reimbursement vary greatly from country to country.

Non-clinical studies and clinical trials

Similarly to the United States, the various phases of non-clinical and clinical research in the European Union (EU) are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice (GLP) as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization (ICH) guidelines on Good Clinical Practices (GCP) as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide ‘no fault’ compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation (CTR) which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states

without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application (CTA) to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice (GMP). Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our future product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization (MA). To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application (MAA). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MA" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Product for Human Use (CHMP) of the European Medicines Agency (EMA) and are valid throughout the EU. The centralized procedure is mandatory for certain types of product candidates, such as: (i) medicinal products derived from biotechnology processes, such as genetic engineering, (ii) designated orphan medicines, (iii) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases and (iv) advanced therapy medicinal products (ATMPs) such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure is optional for product candidates containing a new active substance not yet authorized in the EU, or for product candidates that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state 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. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the EU regulatory system, we may submit applications for marketing authorizations in more than one EU member state either under the centralized, decentralized, or mutual recognition procedure.

Under the above described procedures, before granting the MA, the competent authorities make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days. In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines (PRIME) scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. In 2016, the EMA launched its Priority Medicines (PRIME) scheme. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. The scheme focuses on medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options. These medicines are considered priority medicines by the EMA. To be accepted for PRIME, a medicine has to show its potential to benefit patients with unmet medical needs based on early clinical data. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a "standard" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, MA may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable.

Data and marketing exclusivity

The EU also provides opportunities for market exclusivity. Upon receiving MA, reference products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product can be designated as an orphan if its sponsor can establish that: (1) the product

is intended for the diagnosis, prevention or treatment of a life threatening or chronically debilitating condition (2) either (a) such condition affects not more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from the orphan status, would not generate sufficient return in the EU to justify the necessary investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized for marketing in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

In the EU, an application for designation as an orphan product can be made any time prior to the filing of the application for MA. Orphan drug designation entitles a party to incentives such fee reductions or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of a MA, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that the competent authorities cannot accept another MAA, or grant a MA, or accept an application to extend a MA for a similar product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan (PIP). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The orphan exclusivity period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan drug destination, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity, or where the prevalence of the condition has increased above the threshold. Granting of an authorization for another similar orphan medicinal product where another product has market exclusivity can happen at any time if: (i) the second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior, (ii) inability of the applicant to supply sufficient quantities of the orphan medicinal product or (iii) where the applicant consents to a second orphan medicinal product application. A company may voluntarily remove a product from the orphan register.

Pediatric Development

In the EU, MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a PIP agreed with the EMA's Pediatric Committee (PDCO). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which an MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all member states and study results are included in the product information, even when negative, the product is eligible for a six-months supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

Controlled Substances

Controlled substances are not regulated at EU level and the EU legislation does not establish different classes of narcotic or psychotropic substances. However, the United Nations, or UN, Single Convention on Narcotic Drugs of 1961 and the UN Convention on Psychotropic Substances of 1971, or the UN Conventions, codify internationally applicable control measures to ensure the availability of narcotic drugs and psychotropic substances for medical and scientific purposes. The individual EU member states are all signatories to these UN Conventions. All signatories have a dual obligation to ensure that these substances are available for medical purposes and to protect populations against abuse and dependence.

The UN Conventions regulate narcotic drugs and psychotropic substances as Schedule I, II, III, IV substances with Schedule II substances presenting the lowest relative risk of abuse among such substances and Schedule I and IV substances considered to present the highest risk of abuse.

The UN Conventions require signatories to require all persons manufacturing, trading (including exporting and importing) or distributing controlled substances to obtain a license from the relevant authority. Each individual export or import of a controlled substance must also be subject to an authorisation. Before the relevant authority can issue an export authorisation for a particular shipment, the exporter must provide the authority with a copy of the import

authorisation issued by the relevant authority of the importing country. Implementation of the obligations provided in the UN Conventions and additional requirements are regulated at national level and requirements may vary from one member state to another.

Post-Approval Requirements

Similar to the U.S., both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA the European Commission and/or and the competent authorities of the EU member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports (PSURs).

All new MAA must include a risk management plan (RMP) describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Failure by us or by any of our third party partners, including suppliers, manufacturers, marketers and distributors to comply with EU laws and the related national laws of EU member states governing the conduct of clinical trials, manufacturing approval, MA of medicinal products, pre-approval promotion of products, reporting of adverse health events, both before and after grant of MA, and marketing/promotion of such products following grant of authorization may result in administrative, civil, or criminal penalties. These penalties could include delays in or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, suspension, or variation of the MA, total or partial suspension of production, distribution, manufacturing, or clinical trials, operating restrictions, injunctions, suspension of licenses, fines, and criminal penalties.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom (UK) left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the UK during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement (TCA) and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as “retained EU law”. However, new legislation such as the EU CTR will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an ‘appropriate authority’ to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) is the UK’s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will

apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain (GB); broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the UK. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019 (the "Exit Regulations).

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt-out. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore after Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the UK. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a GB authorization; or use the MHRA's decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB.

There will be no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB.

Regulation of Combination Products in the EU

The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. EU guidance has been published to help manufacturers select the right regulatory framework.

Drug-delivery products intended to administer a medicinal product where the medicinal product and the device form a single integral product are regulated as medicinal products in the EU. The EMA is responsible for evaluating the quality, safety and efficacy of MAAs submitted through the centralized procedure, including the safety and performance of the medical device in relation to its use with the medicinal product. The EMA or the EU member state national competent authority will assess the product in accordance with the rules for medicinal products described above but the device part must comply with the Medical Devices Regulation (including the general safety and performance requirements provided in Annex I). MAA must include – where available – the results of the assessment of the conformity of the device part with the Medical Devices Regulation contained in the manufacturer's EU declaration of conformity of the device or the relevant certificate issued by a notified body. If the MAA does not include the results of the conformity assessment and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required, the competent authority must require the applicant to provide a notified body opinion on the conformity of the device.

By contrast, in case of drug-delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product (but are e.g. co-packaged), the medicinal product is regulated in accordance with the rules for medicinal products described above while the device part is regulated as a medical device and will have to comply with all the requirements set forth by the Medical Devices Regulation.

The characteristics of non-integral devices used for the administration of medicinal products may impact the quality, safety and efficacy profile of the medicinal products. To the extent that administration devices are co-packaged with the medicinal product or, in exceptional cases, where the use of a specific type of administration device is specifically provided for in the product information of the medicinal product, additional information may need to be provided in the MAA for the medicinal product on the characteristics of the medical device(s) that may impact on the quality, safety and/or efficacy of the medicinal product. The MA holder of the medicinal product is responsible for the co-packaged medicinal product and its traceability (including the co-packaged device).

The requirements regarding quality documentation for medicinal products when used with a medical device, including single integral products, co-packaged and referenced products, are outlined in the EMA guideline of July 22, 2021, which became applicable as of January 1, 2022.

The aforementioned EU rules are generally applicable in the European Economic Area.

Healthcare Fraud and Abuse Laws

We are subject to various federal, state, local and foreign laws targeting fraud and abuse in the healthcare industry. These laws are applicable to manufacturers of products regulated by the FDA or foreign regulatory authorities, 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.

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. 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. 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 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.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, (collectively, the ACA) also imposed new reporting and disclosure requirements on drug manufacturers for any "transfer of value" made or distributed to teaching hospitals and physicians (defined to include any doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives), and any ownership or investment interested held by such physicians and their immediate family members during the preceding calendar year. Failure to submit required information may result in civil monetary penalties for any payments, transfers of value or ownership or investment interests not reported in an annual submission, and additional penalties for "knowing failures". 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.

Violations of any of these laws or other governmental regulations may result in civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal or foreign healthcare programs, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements or oversight if the drug manufacturer becomes subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of its operations.

Data Privacy and Security Laws

We and our collaborators and third-party providers may be subject to federal, state and foreign data privacy and security laws and regulations. In the United States, numerous federal and state laws and regulations, including health information privacy laws, data breach notification laws, and consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), 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 and third-party service providers. For example, we may be subject to, or our marketing activities may be limited by, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and regulations implemented thereunder, which establishes a set of national privacy and security standards for the protection of protected health information by "covered entities" (health plans, health care clearinghouses and certain health care providers) and the "business associates" with whom such covered entities contract for services that involve creating, receiving, maintaining or transmitting protected health information.

In addition, certain state and non-U.S. laws, such as the California Consumer Privacy Act of 2018 (CCPA), the California Privacy Rights Act (CPRA) and the EU General Data Protection Regulation (GDPR), govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. In addition, the GDPR increases the scrutiny of transfers of personal data from clinical trial sites located in the EEA to the United States and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws; in July 2020, the Court of Justice of the EU (CJEU) limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield and imposing further restrictions on use of the standard contractual clauses (SCCs), which could increase our costs and our ability to efficiently process personal data from the EEA. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving,

may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Government Drug Pricing Reporting

Medicaid is a joint federal and state program for low-income and disabled beneficiaries. Under the Medicaid Drug Rebate Program ("MDRP"), as a condition of having federal funds available for our covered outpatient drugs under Medicaid and under Medicare Part B, we must enter into, and have entered into, an agreement with the Secretary of Health and Human Services to pay a rebate to state Medicaid programs for each unit of our covered outpatient drugs dispensed to a Medicaid beneficiary and paid for by the state Medicaid program. Medicaid rebates are based on pricing data that we are required to report on a monthly and quarterly basis to the U.S. Centers for Medicare & Medicaid Services ("CMS"), the federal agency that administers the MDRP and Medicare programs. For the MDRP, these data include the average manufacturer price ("AMP") for each drug and, in the case of innovator products, the Best Price, which represents the lowest price available from the manufacturer to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the United States in any pricing structure, calculated to include all applicable sales and associated rebates, discounts and other price concessions. If we become aware that our MDRP submissions for a prior period were incorrect or have changed as a result of recalculation of the pricing data, we must resubmit the corrected data for up to three years after those data originally were due. If we fail to provide information timely or are found to have knowingly submitted false information to CMS, we may be subject to civil monetary penalties and other sanctions, including termination from the MDRP.

Federal law requires that a manufacturer that participates in the MDRP also participate in the Public Health Service's 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program is administered by the Health Resources and Services Administration ("HRSA") and requires us to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for our covered outpatient drugs when used in an outpatient setting. 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. A drug that is designated for a rare disease or condition by the Secretary of Health and Human Services is not subject to the 340B ceiling price requirement with regard to the following covered entities: rural referral centers, sole community hospitals, critical access hospitals, and free-standing cancer hospitals. The 340B ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP. In general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price requirement. We must report 340B ceiling prices to HRSA on a quarterly basis, and HRSA publishes them to 340B covered entities. HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B-eligible drugs. HRSA has also finalized an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges. In addition, legislation may be introduced that, if passed, would further expand the 340B program, such as adding further covered entities or requiring participating manufacturers to agree to provide 340B discounted pricing on drugs when used in an inpatient setting.

In order to be eligible to have drug products paid for with federal funds under Medicaid and Medicare Part B and purchased by certain federal agencies and grantees, we must also participate in the U.S. Department of Veterans Affairs ("VA") Federal Supply Schedule ("FSS") pricing program. Under the VA/FSS program, we must report the Non-Federal Average Manufacturer Price ("Non-FAMP") for our covered drugs to the VA and charge certain federal agencies no more than the Federal Ceiling Price, which is calculated based on Non-FAMP using a statutory formula. These four agencies are the VA, the U.S. Department of Defense, the U.S. Coast Guard, and the U.S. Public Health Service (including the Indian Health Service). We must also pay rebates on products purchased by military personnel and dependents through the TRICARE retail pharmacy program. If a manufacturer participating in the FSS program fails to provide timely information or is found to have knowingly submitted false information, the manufacturer may be subject to civil monetary penalties.

Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number

of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers for the untimely, inaccurate, or incomplete reporting of drug pricing information or for otherwise failing to comply with drug price transparency requirements.

Third-Party Payor Coverage and Reimbursement

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

Changes in third-party payor coverage and reimbursement rules can impact our business. For example, the ACA's changes include expanded manufacturer Medicaid rebate liability to include utilization by beneficiaries enrolled in Medicaid managed care organizations; increasing the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; modifying the Average Manufacturer Price ("AMP") definition under the MDRP for drugs that are inhaled, infused, instilled, implanted, or injected; and establishing a new Medicare Part D coverage gap discount program, in which manufacturers must now provide 70% 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.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15, 2021 through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. More recently, on March 11, 2021, President Biden signed into law the American Rescue Plan Act of 2021, which eliminates the statutory cap on the Medicaid drug rebate, currently set at 100% of a drug's AMP, beginning January 1, 2024.

Other legislative changes have also been proposed and adopted in the United States since the ACA 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 2030, with the exception of a temporary suspension from May 1, 2020 through July 1, 2022 (with a 1% payment reduction from April 1 to June 30, 2022), 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, the Build Back Better Act, if enacted, would introduce substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, and the establishment of rebate payment requirements on manufacturers under Medicare Parts B and D. If the Build Back Better Act is not enacted, similar or other drug pricing proposals could appear in future legislation.

The likelihood of implementation of these and other reform initiatives is uncertain. Moreover, in the coming years, additional legislative and regulatory changes could be made to governmental health programs that could significantly impact pharmaceutical companies and the success of our product candidates. 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, and/or continue to put pressure on pharmaceutical pricing, as well as increase our regulatory burdens and operating costs, any of 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.

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 and foreign regulatory authorities have 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.

Human Capital

As of December 31, 2021, we had 327 full-time employees, consisting of 250 employed in the United States, 73 employed in the United Kingdom and other European countries and four in Japan. Of these employees, 154 were engaged primarily in product development, quality assurance and clinical development and regulatory activities, 89 were engaged primarily in sales and commercialization activities, nine were engaged primarily in manufacturing, and the remaining 75 were engaged primarily in management and general and administrative activities.

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.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, and incentivizing our management team and our clinical, scientific and other employees and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and motivate personnel through the granting of stock-based and cash-based compensation awards, in order to align our interests and the interests of our stockholders with those of our employees and consultants.

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 5959 Horton Street, Suite 500, 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 free of charge 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 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.

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 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 the Merger Agreement

The conditions under the Merger Agreement to Parent's consummation of the Offer and our subsequent Merger with Purchaser may not be satisfied at all or in the anticipated timeframe.

Under the terms of the Merger Agreement, the consummation of Parent's pending Offer and subsequent Merger is subject to customary conditions. Satisfaction of certain of the conditions is not within our control, and difficulties in otherwise satisfying the conditions may prevent, delay, or otherwise materially adversely affect the consummation of the pending Offer and subsequent Merger. These conditions include, among other things, (i) there having been validly tendered in accordance with the terms of the Offer and not validly withdrawn, as of immediately prior to the expiration of the Offer, a number of Company Shares that, together with the Company Shares then owned by Parent or Merger Sub, represents at least a majority of the Company Shares then outstanding; (ii) the accuracy of the representations and warranties of the Company contained in the Merger Agreement, subject to certain materiality qualifications; (iii) the Company's compliance in all material respects with its covenants and agreements contained in the Merger Agreement; (iv) the expiration or termination of any waiting period (and any extension thereof) applicable to the Offer or the Merger under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and the receipt of any other clearance, approval or consent applicable to Offer or the Merger (as defined below) under any applicable antitrust law; (v) the absence of a Company Material Adverse Effect (as defined in the Merger Agreement) that is continuing; and (vi) the absence of any law, regulation, order, injunction or ruling issued or enacted by any government authority of competent jurisdiction that would prohibit or make illegal the consummation of the Offer or the Merger, or that would impose certain remedies or restrictions on the ability of Parent to fully own or operate the Company, its businesses or assets. We cannot predict with certainty whether and when any of the required conditions will be satisfied. If the Merger does not receive, or timely receive, the required regulatory approvals and clearances, or if another event occurs delaying or preventing the Merger, such delay or failure to complete the Merger may create uncertainty or otherwise have negative consequences that may materially and adversely affect our financial condition and results of operations, as well as the price per share for our common stock.

While Parent's Offer and the proposed Merger are pending, we are subject to business uncertainties and contractual restrictions that could disrupt our business.

Whether or not the pending Offer and subsequent Merger is consummated, the Merger may disrupt our current plans and operations, which could have an adverse effect on our business and financial results. The pendency of the pending Offer and subsequent Merger may also divert management's attention and our resources from ongoing business and operations, and our employees and other key personnel may have uncertainties about the effect of the pending Offer and subsequent Merger, and the uncertainties may impact our ability to retain, recruit, and hire key personnel while the Merger is pending or if it fails to close.

The preparations for the consummation of the Merger have placed and we expect will continue to place a significant burden on many of our management, employees and on our internal resources. The diversion of management's attention away from operating our business in the ordinary course could adversely affect our financial results. Also, if, despite our efforts, key personnel depart because of these uncertainties and burdens, or because they do not wish to remain with the combined company, our business and results of operations may be adversely affected. We have incurred and will continue to incur significant expenses due to legal, advisory, printing and financial services fees related to the Merger. These expenses must be paid regardless of whether the Merger is consummated, which may materially and adversely affect our financial condition and results of operations.

Furthermore, we cannot predict how our business partners will view or react to the pending Offer and subsequent Merger upon consummation. If we are unable to reassure our business partners to continue transacting business with us, our financial condition and results of operations may be adversely affected.

In addition, the Merger Agreement generally requires us to operate our business and operations in the ordinary course pending consummation of the Merger and also restricts us from taking certain actions without Parent's prior written consent during the interim period between the execution of the Merger Agreement and the effective time of the Merger (or the date on which the Merger Agreement is earlier terminated). For these and other reasons, the pendency of the proposed Merger could adversely affect our business and results of operations.

Our executive officers and directors may have interests that are different from, or in addition to, those of our stockholders generally.

Our executive officers and directors may have interests in the tender offer and merger that are different from, or are in addition to, those of our stockholders generally. These interests include direct or indirect ownership of our common stock and stock options, the acceleration of stock options upon consummation of the transactions and other interests. Such interests of our directors and executive officers are set forth in further detail in the Schedule 14D-9 filed by the Company with the SEC on February 1, 2022.

Litigation filed or that may be filed against us and/or the members of our board of directors could prevent or delay the consummation of the Merger.

Lawsuits filed, or that may be filed, could delay or prevent our acquisition by Parent, divert the attention of our management and employees from our day-to-day business and otherwise adversely affect us financially. The outcome of any lawsuit filed or that may be filed challenging the Merger is uncertain. One of the conditions to the closing of the Merger is that there shall not be in effect any temporary restraining order, preliminary or permanent injunction or other order, in each case issued by a Governmental Authority of competent jurisdiction, that prohibits or makes illegal the consummation of the Merger. Accordingly, if any lawsuit (including but not limited to the legal proceedings discussed in this report in Part I, Item 3 — "Legal Proceedings") is successful in obtaining an order enjoining the Merger, then the Merger may not be consummated within the expected time frame, or at all, and could result in substantial costs, including but not limited to, costs associated with the indemnification of our directors and officers.

Our stockholders may not receive any payment on the CVRs and the CVRs may otherwise expire valueless.

If the Merger is completed, we and certain other parties will enter into the CVR Agreement pursuant to which, for each share of our common stock held, our stockholders of record as of immediately prior to the effective time of the Merger will receive one non-transferrable CVR entitling such holders to receive the Milestone Payment if, and only if, no later than December 31, 2023, the Milestone is achieve. Parent is obligated only to use commercially reasonable efforts to achieve the Milestone following the closing of the Merger and there can be no assurance that the Milestone will be achieved or that the Milestone Payment will be made. In addition, the CVRs will not be transferable, will not have any voting or dividend rights, and interest will not accrue on any amounts potentially payable on the CVRs. Accordingly, the right of any of our stockholders to receive any future payment on or derive any value form the CVRs will be contingent solely upon the achievement of the Milestone Event within the time periods specified in the CVR Agreement and if these events are not achieved for any reason within the time periods specified in the CVR Agreement, no payments will be made under the CVRs, and the CVRs will expire valueless.

In the event that the Merger is not consummated, the trading price of our common stock and our future business and results of operations may be negatively affected.

The conditions to the consummation of the pending Offer and subsequent Merger may not be satisfied, as noted above. If the Merger is not consummated, we would remain responsible for significant transaction costs, and the focus of our management would have been diverted from seeking other potential strategic opportunities, in each case without realizing any benefits of the Merger. For these and other reasons, not consummating the Merger could adversely affect our business and results of operations.

Furthermore, if the pending Offer and subsequent Merger are not consummated, the price of our common stock may decline significantly from the current market price, which we believe reflects a market assumption that the Merger will be consummated. Additionally, a failure of the Merger may result in negative publicity and a negative impression of us in the investment community, and have a negative impact on our ability to raise additional financing

in the future. Finally, any disruptions to our business resulting from the announcement and pendency of the Merger, including any adverse changes in our relationships with our business partners and employees or recruiting and retention efforts, could continue or accelerate in the event of a failed transaction.

The Merger Agreement imposes restrictions on the operation of our business prior to closing, which could adversely affect our business.

Pursuant to the terms of the Merger Agreement, we are subject to certain restrictions on the conduct of our business, which may adversely affect the Company's businesses, including by delaying or preventing the Company from pursuing non-ordinary course opportunities that may arise or precluding actions that may be advisable if the Company were to remain an independent public company.

If the Merger Agreement is terminated, we may, under certain circumstances, be obligated to pay a termination fee to Parent. These costs could require us to use available cash that would have otherwise been available for other uses.

If the Merger is not completed, in certain circumstances, we could be required to pay a termination fee of $59.0 million to Parent. If the Merger Agreement is terminated, the termination fee we may be required to pay, if any, under the Merger Agreement may require us to use available cash that would have otherwise been available for general corporate purposes or other uses. For these and other reasons, termination of the Merger Agreement could materially and adversely affect our business, results of operations or financial condition, which in turn would materially and adversely affect the price per share of our common stock.

Risks Related to Our Business and Industry

Our success depends substantially on Fintepla as commercial product and as a product candidate in other indications as well as our product candidate MT-1621. We cannot be certain that Fintepla will receive additional regulatory approvals we may pursue, or be successfully commercialized, or whether MT-1621 or any future product candidates will receive regulatory approval or be successfully commercialized.

Our business depends substantially on the successful commercialization of Fintepla, and the development and commercialization of Fintepla for additional indications or other changes and of MT-1621. Although Fintepla has been approved in the United States and the EU for the treatment of seizures associated with Dravet syndrome in patients two years of age and older, we may not be able to obtain supplemental approvals for Fintepla or obtain initial approvals for MT-1621 in the future. Accordingly, Fintepla, MT-1621 and any future product candidates will require additional clinical and pre-clinical development, regulatory review and approval in multiple jurisdictions, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenues from product sales. The research, testing, manufacturing, labeling, approval, sale, marketing, distribution and promotion of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, whose regulations differ from country to country.

We are not permitted to market our product candidates in the United States until we receive approval of an NDA or NDA supplement 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.

For example, MT-1621 has been evaluated in a Phase 2 retrospective treatment clinical study called RETRO, which demonstrated increased survival probability and improved functional abilities for patients treated with MT-1621 compared with untreated natural history control patients. However, the FDA or European Medicines Agency (EMA) may disagree with the design of the RETRO and the reliance on a natural history dataset as the comparator, and we may be required to conduct additional trials prior to seeking regulatory approval.

Obtaining regulatory approval for a product candidate is a lengthy, expensive and uncertain process, and may not be successful. Any failure to obtain regulatory approvals for MT-1621 or any future product candidate, and any supplemental approvals for Fintepla, 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 MT-1621 and would have a material and adverse impact on our business.

Even if we successfully obtain additional regulatory approvals to market Fintepla, or initial approvals to market MT-1621, 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.

We may not be successful in executing our sales and marketing strategy for the commercialization of Fintepla.

We have built a highly specialized and focused commercial sales and marketing organization, including sales, marketing and customer support functions, to commercialize Fintepla in the United States and Germany, our first market in Europe. We will need to build a commercial sales and marketing organization to launch and commercialize Fintepla in other markets if we are able to secure appropriate marketing and reimbursement approvals. Prior to commercial launch of Fintepla, we had no prior experience in the marketing and sale of a rare disease product, and there are significant risks involved in managing a sales organization, including our ability to retain and incentivize qualified individuals, provide adequate training to sales and marketing personnel, generate sufficient sales leads, effectively manage a sales and marketing team, and handle any unforeseen costs and expenses. In addition, even if our self-commercialization strategy works in one market, such strategy may not be successful in other markets. If we are unable to successfully maintain our sales and marketing organization, implement our commercialization plans and facilitate adoption by patients and physicians of Fintepla, then we will not be able to generate significant revenue which will have a material adverse effect on our business, results of operations, financial condition and prospects.

We depend on a sole specialty distributor, our customer, for distribution of Fintepla in the United States, and the failure of this specialty distributor to distribute Fintepla effectively would adversely affect sales of Fintepla.

We rely on our only customer, a specialty distributor for the distribution of Fintepla in the United States. Our customer subsequently resells our product through its related specialty pharmacy provider to patients and health care providers. A specialty pharmacy is a pharmacy that specializes in the dispensing, and a specialty distributor is a distributor that specializes in the distribution, of medications for complex or chronic conditions, which often require a high level of patient education, physician administration and ongoing management. The use of a specialty distributor who distributes Fintepla through its related specialty pharmacy provider to patients and health care providers involves certain risks, including, but not limited to, risks that our customer will:

- not provide us accurate or timely information regarding their inventories, the number of patients who are using our product or complaints about our product;
- reduce or discontinue their efforts to sell or support or otherwise not effectively sell or support our product;
- not devote the resources necessary to sell our products in the volumes and within the time frames that we expect;
- engage in unlawful or inappropriate business practices that result in legal or regulatory enforcement activity which could result in liability to us or damage the goodwill within the Dravet syndrome community associated with Fintepla; and
- be unable to satisfy financial obligations to us or others.

In the event that our customer does not fulfill its contractual obligations to us or refuses to or fails to adequately perform distribution of Fintepla to patients and healthcare providers, or the agreements with us are terminated without adequate notice, shipments of Fintepla, and associated revenues, would be adversely affected.

Further, if our customer becomes subject to bankruptcy, is unable to pay us for our products or is acquired by a company that wants to terminate the relationship with us, or if we otherwise lose our relationship with our customer, our revenue, results of operations and cash flows would be adversely affected. If our customer cannot perform as agreed or the relationship is otherwise terminated, we may be unable to replace them on a timely basis or at all. Even if we are able to replace our customer with a different specialty distributor/customer, such transition could result adversely affect our results of operations and cash flows.

Our business is subject to risks arising from epidemic diseases, such as the COVID-19 pandemic.

The current COVID-19 worldwide pandemic has presented substantial public health and economic challenges and is affecting our employees, patients, communities and business operations, as well as the U.S. and global economy and financial markets. International and U.S. governmental authorities in impacted regions are taking

actions to slow the spread of COVID-19, including issuing varying forms of “stay-at-home” orders, and restricting business functions outside of one’s home. In response, we closed our offices for all but the most essential activities and have implemented a policy allowing all employees to work from across all locations, following the guidelines or directives issued by federal, state and local government agencies in the U.S. as well as the U.K. government. As a result of these restrictions, our sales force has not been able to conduct in-person interactions with physicians and healthcare providers and have been restricted to primarily conducting educational and promotional activities for Fintepla virtually, which may impact our ability to market Fintepla. To date, we have been able to continue to supply Fintepla commercially to our patients in the U.S. and Germany and both Fintepla and MT-1621 to our patients currently enrolled in our clinical trials and we do not currently anticipate any interruptions in clinical or commercial supply. In addition, while we are continuing the clinical trials we have underway in sites across the globe, we expect that COVID-19 precautions may directly or indirectly impact the timeline for some of our clinical trials. As the COVID-19 pandemic continues to spread around the globe, we may experience disruptions that could severely impact our business, clinical trials and manufacturing and supply chains, including:

- an inability to effectively market Fintepla or interruptions in patient site access as part of our REMS program;
- further delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems, including interruption of commercial supply;
- delays or inability of us or our independent registered public accounting firm to count and/or observe the counts of our physical inventories;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials and interruption in global shipping that may affect the transport of clinical trial materials;
- limitations on employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- delays in receiving feedback or approvals from the FDA or other regulatory authorities with respect to future clinical trials or regulatory submissions, including for MT-1621;
- changes in local regulations as part of a response to COVID-19 which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- refusal of the FDA or EMA to accept data from clinical trials in certain geographies; and
- difficulties launching or commercializing products, including due to reduced access to doctors as a result of social distancing protocols.

In addition, the spread of COVID-19 has had and may continue to severely impact the trading price of shares of our common stock and could further severely impact our ability to raise additional capital on a timely basis or at all.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the COVID-19 may impact our business, including our commercial sales, clinical trials, manufacturing and supply chains and financial condition will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the

geographic spread of certain variants of the disease that may be less susceptible to available vaccines, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

To the extent the COVID-19 pandemic adversely affects our business and financial results, many of the other risks described in this “Risk Factors” section may be heightened.

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

Our product candidates are prone to the risks of failure inherent in drug development. Before obtaining U.S. regulatory approval for a product candidate 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 our product candidates are not shown to be safe and effective in clinical trials, the programs could be delayed or terminated, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

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 our product candidates may not necessarily be predictive of the results of future clinical trials or preclinical studies. The results of prior clinical trials of our product candidates may not be replicated in any future clinical trials of these product candidates. Clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in prior clinical trials nonetheless have failed to obtain FDA or foreign regulatory approval. If we fail to produce positive results in our clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates and our business and financial prospects, would be adversely affected.

Further, Fintepla may not be approved for the treatment of seizures associated with LGS even though recent, positive topline results from our ongoing Phase 3 trial of Fintepla for LGS showed that Fintepla met its primary and certain key secondary endpoints. Similarly, MT1621 may not be approved even though the RETRO data demonstrated improved survival probability of patients treated with MT1621 compared with a natural history patient control group. 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, including with the design of the Phase 2 retrospective study comparing the outcomes from the MT-1621 active treatment group against outcomes from a natural history dataset. 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.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our clinical studies, which are based on preliminary analyses of then-available data. Such preliminary results and related findings and conclusions are subject to change following more comprehensive reviews 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 topline 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. Topline 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, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our clinical studies. Interim data from this clinical trial and future clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, and as more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses of data from preclinical studies or clinical trials of its product candidates, or may interpret or weigh the importance of data differently, which could impact the value of the particular product candidate, the approvability or prospects for commercialization of the product candidate, or our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and stockholders and others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Information that we decide not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business. If the interim, topline or preliminary data that we disclose differ from actual results, or if others, including regulatory authorities, disagree with the conclusions we reach based on our analyses of such data, 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 MT-1621 or pre-clinical or clinical testing for any future product candidates could result in increased costs to us and delay or limit our ability to pursue regulatory approvals 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 MT-1621 or pre-clinical or clinical testing for any future product candidates could significantly affect our product development costs and business plan.

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 IRB or ethics committee 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 or MT-1621 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, DEA or other regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- discovery of serious or unexpected toxicities or side effects experienced by study participants or other unforeseen safety issues;
- lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties;
- lack of effectiveness of any product candidate during clinical trials;
- slower than expected rates of subject recruitment and enrollment rates in clinical trials;
- inability of our CROs or other third-party contractors to comply with all contractual requirements or to perform their services in a timely or acceptable manner;
- inability or unwillingness of medical investigators to follow our clinical protocols; and
- unfavorable results from on-going clinical trials and pre-clinical studies.

Additionally, changes in applicable regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to the FDA or foreign regulatory authorities and IRBs or ethics committees 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, MT-1621 and any future product candidates may be harmed, which may have a material adverse effect on our business, results of operations, financial condition and prospects.

In addition, additional government regulation with respect to clinical trials may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation (CTR) which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application (CTA) to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

It is currently unclear to what extent the UK will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the UK Medicines and Healthcare products Regulatory Agency (MHRA) launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closes on 14 March 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation will be closely watched and will determine whether the UK chooses to align with the regulation or diverge from it to maintain regulatory flexibility. A decision by the UK not to closely align its regulations with the new approach that will be adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and/or make it harder to seek a marketing authorization in the EU for our product candidates on the basis of clinical trials conducted in the UK.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

We face intense competition, and if our competitors market and/or develop treatments for any of our product candidates' indications 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 marketing products and obtaining regulatory approvals for product candidates and other resources than we do.

For example, Fintepla competes against other products and product candidates approved and in development for the treatment of Dravet syndrome. In June 2018, the FDA approved the first treatment for 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. GW's CBD was subsequently approved for the treatment of Dravet syndrome and LGS by the European Commission (as Epidyolex®) in September of 2019. 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. Multiple companies are developing clinical-staged product candidates for the potential treatment of Dravet syndrome. Takeda Pharmaceutical Company Limited is currently evaluating its product candidate TAK-935/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. Additional clinical stage candidates for the treatment of Dravet syndrome include LP352 from Longboard Pharmaceuticals, Inc.(Phase 1), Huperzine-A from Supernus Pharmaceuticals (Phase 1/2), and clemizole (Phase 1) being evaluated by Epygenix Therapeutics, Inc.

We expect Fintepla 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. While we currently are not aware of any pharmaceutical companies who are developing a pharmaceutical product candidate for the treatment of TK2d that would compete against MT-1621, 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 or MT-1621, if approved, 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 in the treatment of seizures associated with Dravet syndrome or, if approved, in other indications, or of MT1621, 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 are critical for commercial success. The degree of market acceptance of Fintepla or any product candidates for which we may receive regulatory approval will depend on a number of factors, including:

- acceptance by physicians and patients of the product as a safe and effective treatment;
- any negative publicity or political action related to our or our competitors' products;
- the relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- demonstration to authorities of the pharmacoeconomic benefits;
- demonstration to authorities of the improvement in burden of illness;
- limitations or warnings contained in a product's FDA-approved or 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.

Breakthrough therapy designation and access to the PRIME scheme for MT-1621 may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that MT1621 or any of our product candidates will receive marketing approval.

In February 2019, the FDA granted breakthrough therapy designation for MT1621 in the United States for the treatment of TK2d. 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. 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 though MT1621 qualifies as a breakthrough therapy, the FDA may later decide that MT-1621, or any of our other product candidates that may qualify as a breakthrough therapy, 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 rescinded breakthrough therapy designation for Fintepla for Dravet syndrome due to the existence of two recently approved therapies for Dravet syndrome and, therefore, the administrative criteria for designation were no longer met.

In November 2018, the EMA admitted MT-1621 to the PRIME scheme for the treatment of patients with TK2d. In the EU, innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the Breakthrough Therapy designation in the United States. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. The benefits of a PRIME designation include the appointment of a rapporteur before submission of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

Even though we have access to PRIME for MT-1621, this may not result in a materially faster development process, review or approval compared to conventional EMA procedures. The EMA may later decide that MT-1621 no longer meets the conditions for qualification or decide that the time period for review or approval will not be shortened. Further, obtaining access to PRIME does not assure or increase the likelihood of grant of a marketing authorization by the European Commission.

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 have sought and may seek FDA approval in the future 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 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 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 $1.6 billion as of December 31, 2021. During the year ended December 31, 2021, net cash used in operating activities was $185.3 million. 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 and MT-1621. Additionally, in the event that MT-1621 is approved in the United States or the EU, we will owe milestone payments related to our acquisition of development and commercialization rights to MT-1621. Our ability to generate revenues from Fintepla or MT-1621, if approved, will depend on a number of factors including our ability to successfully complete clinical trials, obtain necessary regulatory approvals in target countries 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 or MT-1621, if approved, or any future 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 and planned Phase 3 programs for Fintepla and our clinical development program of MT-1621. We rely heavily on these parties for the execution of our clinical trials and pre-clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and regulatory requirements. We and our CROs are required to comply with GCP requirements for clinical studies of our product candidates, and GLP requirements for certain pre-clinical studies. The FDA and foreign regulatory authorities enforce 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 or foreign regulatory authorities 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 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 September 2019, we completed the acquisition of Modis, which owns worldwide development and commercialization rights to MT-1621. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

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

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

We are dependent on numerous third parties in our 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 do not own or operate manufacturing facilities and have no plans to build our own clinical or commercial scale manufacturing capabilities. We outsource all manufacturing and packaging of the clinical trial materials for Fintepla and MT-1621 to third parties and will rely on third parties for commercial manufacturing and packaging of Fintepla, and for MT-1621, if approved. In February 2019, we entered into a master supply agreement with Aptuit, pursuant to which Aptuit became our commercial manufacturer and supplier of the fenfluramine API. In addition, in July 2019 we entered into the PCI Pharma Agreement, pursuant to which PCI Pharma became our commercial manufacturer and supplier for Fintepla. We may never be able to establish additional sources of supply for Fintepla.

The facilities used by third-party manufacturers to manufacture our product candidates must be approved by the FDA or other regulatory agencies pursuant to inspections that will be conducted after we submit a an NDA to the

FDA or their equivalent to other regulatory agencies. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP or similar foreign requirements for manufacture of our drug products. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, including requirements related to the manufacturing of high potency and pure compounds or other products, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates, or if regulatory authorities withdraw any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market Fintepla or our other product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Our or a third-party's failure to execute on our manufacturing requirements, to do so on commercially reasonable terms, or to comply with cGMP or similar foreign requirements could adversely affect our business in a number of ways, including an inability to initiate or continue clinical trials of any future product candidates under development, delays in submitting regulatory applications, or receiving marketing approvals, for our product candidates, requirements to cease development or to recall batches of our product candidates, and an inability to meet commercial demands for Fintepla or our other products, if approved. In addition, 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, 2021, we had 327 full-time employees, consisting of 250 employed in the United States, 73 employed in the United Kingdom and other European countries and four in Japan. Of these employees, 154 were engaged primarily in product development, quality assurance and clinical development and regulatory activities, 89 were engaged primarily in sales and commercialization activities, nine were engaged primarily in manufacturing, and the remaining 75 were engaged primarily in management and general and administrative activities. 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 have our headquarters. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercialization objectives, our ability to raise additional capital, our ability to implement our business strategy and our ability to maintain effective internal controls for financial reporting and disclosure controls and procedures as required by the Sarbanes-Oxley Act of 2002 (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 continued development and commercialization of Fintepla and our other 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.

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.

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

Successful sales of Fintepla and 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 (CSA) and could result in harm to patients relating to its potential for abuse. Although we no longer sell Zohydro ER following the sale of the Zohydro ER business in April 2015, we retain all liabilities associated with the Zohydro ER business arising prior to such sale, including possible product liability exposure in connection with sales of Zohydro ER made prior to the sale of the Zohydro ER business. In addition, a liability claim may be brought against us even if our products or product candidates merely appear to have caused an injury.

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

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

We have obtained product liability insurance coverage for commercial product sales and clinical trials with a $20 million per occurrence and annual aggregate coverage limit. Our insurance coverage may not be sufficient to cover all of our product liability related expenses or losses and may not cover us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost, in sufficient amounts or upon adequate terms to protect us against losses due to product liability. If we determine that it is prudent to increase our product liability coverage based on approval of 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 be unable to obtain regulatory approvals for or commercialize MT-1621 or any future product candidates outside of the United States.

We market Fintepla and if approved, we intend to market MT-1621 outside of the United States. 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" and those disclosed in Part I, Item 1A of our 2018 Annual Report on Form 10-K regarding FDA approval in the United States, as well as other risks.

In the EU, 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.

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

The UK left the EU on January 31, 2020, following which existing EU legislation continued to apply in the UK during a transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to global trade deals negotiated by the EU

on behalf of its members and provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement, which became effective on the January 1, 2021.

The long term effects of UK's withdrawal from the EU on our business in the UK, the EU and worldwide will depend on the effects of the implementation and application of the Trade and Cooperation Agreement and any other relevant agreements between the UK and the EU. EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". However, new legislation will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an 'appropriate authority' to amend or supplement existing regulations in the area of medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps. There is a possibility that over time, national laws will be amended and that consequently the regulatory framework in Great Britain will diverge from that of the EU. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) is the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

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 may significantly reduce global market liquidity, restrict the ability of key market participants to operate in certain financial markets or restrict our access to capital. In addition, 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. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and reduce the price of our common stock.

Risks Related to Our Financial Position and Capital Requirements

We have incurred significant operating losses and negative cash flows from operations since inception and are dependent upon external sources of financing to fund our business and development.

We currently have limited collaboration revenue under an arrangement with Nippon Shinyaku Co., Ltd. We commenced the commercial launch of Fintepla in the United States in July 2020 and in Germany in February 2021, which have produced limited revenue to date. We have financed our operations primarily through the proceeds from the issuance of equity securities and debt, and have incurred negative cash flow from operations in each year since our inception. For the years ended December 31, 2021, 2020 and 2019, we incurred net losses of $227.4 million, $209.4 million and $419.5 million, respectively, and our cash used in operating activities was $185.3 million, $167.5 million and $111.5 million, respectively. As of December 31, 2021, we had an accumulated deficit of $1.6 billion. The net 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.

We may 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 Fintepla and any other 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.

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 indebtedness and liabilities could limit the cash flow available for our operations, expose us to risks that could adversely affect our business, financial condition and results of operations and impair our ability to satisfy our obligations under the Convertible Senior Notes.

In September 2020, we issued $200.0 million aggregate principal amount of our Convertible Senior Notes in a private offering exempt from registration under the Securities Act of 1933. In connection with the offering, we granted the initial purchasers an option to purchase up to an additional $30.0 million in principal amount of Convertible Senior Notes, which was exercised in full in October 2020. We may also incur additional indebtedness to meet future financing needs. Our indebtedness could have significant negative consequences for our security holders and our business, results of operations and financial condition by, among other things:

- increasing our vulnerability to adverse economic and industry conditions;
- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our cash flow from operations to service our indebtedness, which reduces the amount of cash available for other purposes;
- limiting our flexibility to plan for, or react to, changes in our business;
- diluting the interests of our existing stockholders as a result of issuing shares of our common stock upon conversion of the Convertible Senior Notes; and

- placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital.

Our business may not generate sufficient funds, and we may otherwise be unable to maintain sufficient cash reserves, to pay amounts due under our indebtedness, including the Convertible Senior Notes, and our cash needs may increase in the future. In addition, any future indebtedness that we may incur may contain financial and other restrictive covenants that limit our ability to operate our business, raise capital or make payments under our other indebtedness. If we fail to comply with these covenants or to make payments under our indebtedness when due, then we would be in default under that indebtedness, which could, in turn, result in that and our other indebtedness becoming immediately payable in full.

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. Concerns over inflation, energy costs, geopolitical issues, public health emergencies, the availability and cost of credit, and the U.S. financial markets have in the past contributed to, and may continue in the future to contribute to, increased volatility and diminished expectations for the economy and the markets. For example, the COVID-19 pandemic has impacted the global economy, including limiting global travel, impacting our operations and the operations of the third-parties we work with. The extent to which the COVID-19 pandemic will impact our results of operations will depend on future developments, which are highly uncertain and cannot be predicted, including the progress on the distribution of vaccinations in the locations where we operate, new information which may emerge concerning the severity of any variants of COVID-19 and the actions to contain COVID-19 or treat its impact, among others. In addition, domestic and international equity and debt markets have experienced and may continue to experience heightened volatility and turmoil based on domestic and international economic conditions and concerns. In the event these economic conditions and concerns continue or worsen and the markets continue to remain volatile, our results of operations and liquidity could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary, and our stock price may decline. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are not federally insured. If economic instability continues, we cannot provide assurance that we will not experience losses on these investments.

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

We may need to raise additional funds through public or private equity offerings, debt financings, receivables or royalty financings or corporate collaboration and licensing arrangements. For example, in May 2016, we entered into an at-the-market sales agreement (the ATM Sales Agreement), with Cantor Fitzgerald & Co. (Cantor), pursuant to which Cantor agreed to act as a sales agent in connection with sale of our common stock from time to time pursuant to an effective registration statement. In June 2020, we filed a prospectus supplement (the 2020 ATM Prospectus), to our automatic “shelf” registration statement on Form S-3 registering the offering, issuance and sale of up to $200.0 million in gross aggregate proceeds of common stock pursuant to the 2016 Sales Agreement. As of December 31, 2020, there was $194.9 million remaining for future sales under the 2020 ATM Prospectus. 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 U.K. tax legislation.

As a company that carries out extensive research and development activities, we benefit from the U.K.’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 U.K. 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 U.K. 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 U.K.'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 U.K.'s SME R&D tax relief scheme in the future as we increase our personnel and expand our business because we may no longer qualify as an SME. In order to qualify as an SME for R&D tax credits, we must continue to be a company with fewer than 500 employees and also have either an annual turnover not exceeding €100 million or a balance sheet not exceeding €86 million. We may also benefit in the future from U.K.'s R&D Expenditure Credit scheme, or the RDEC scheme, available to larger companies. However, the RDEC scheme has a significantly lower credit than the SME scheme. In addition, changes in U.K. tax legislation may reduce or limit any future claims. For example, a policy paper was published on October 29, 2018 setting out HMRC's intention from April 2020 to cap the amount of cash rebate that a qualifying loss-making business can receive in any one year under the research and development tax credit regime for SMEs at three times the company's total liability for National Insurance contributions and income tax under the Pay As You Earn system.

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 (the Code), 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 disallowed business interest deductions) (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 rolling 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. Although we have experienced several ownership changes in the past, we do not anticipate that the limitations arising from prior ownership changes will significantly impact our ability to utilize our net operating losses and tax credit carryforwards. We may also experience ownership changes in the future, however, which could limit the use of our tax attributes and have an adverse effect on our consolidated results of operations. In addition, pursuant to the Tax Cuts and Jobs Act of 2017 (Tax Act), as modified by the Coronavirus Aid, Relief and Economic Security Act, we may not use net operating loss carryforwards arising in taxable years beginning after December 31, 2017 to reduce our taxable income by more than 80% in any taxable year beginning after December 31, 2020. These limitations may require us to pay federal income taxes in future years despite generating a loss for federal income tax purposes in prior years.

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

As of December 31, 2021, our cash, cash equivalents and marketable securities totaled $301.7 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 is approved in the United States, the EU and the UK for the treatment of seizures associated with Dravet syndrome in patients two years and older, and we currently are developing Fintepla for the treatment of seizures associated with LGS and CDKL5 Deficiency Disorder (CDD), and are developing MT-1621 for the treatment of TK2d. 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 and outside 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 or similar approval from foreign regulatory authorities. 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.

The FDA and foreign regulatory authorities have 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 and foreign regulatory authorities may not deem a product candidate safe and effective for its proposed indication;
- the FDA and foreign regulatory authorities may not find the data from pre-clinical studies and clinical trials sufficient to support approval;
- the FDA and foreign regulatory authorities may require additional pre-clinical studies or clinical trials;
- the FDA and foreign regulatory authorities may not approve of our third-party manufacturers' processes and facilities; or
- the FDA and foreign regulatory authorities may change its approval policies or adopt new regulations. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. A proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration of regulatory exclusivity, eligibility for expedited pathways, etc.) is expected to be adopted by the European Commission by the end of 2022. The proposed revisions, once they are agreed and adopted by the European Parliament and European Council (not expected before the end of 2024) may have a significant impact on the pharmaceutical industry in the long term.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or foreign regulatory authorities approval. We cannot guarantee that the FDA foreign regulatory authorities will interpret trial results as we do, and more trials could be required before we are able to submit applications seeking approval of our product candidates. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Of the large number of drugs in development, only a small percentage successfully complete the regulatory approval processes and are commercialized. This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain additional regulatory approvals to market Fintepla, or our failure to obtain initial regulatory approvals to market MT1621 or any other product candidate, which would significantly harm our business, results of operations and prospects.

In addition, the FDA or foreign regulatory authorities may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or foreign regulatory authorities may approve a product candidate with a REMS or a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate or other risk management measures. For example, the FDA approved Fintepla for the treatment of seizures associated with Dravet syndrome subject to the Fintepla REMS program, which requires echocardiogram assessments of patients before, during, and after treatment with Fintepla. The FDA or foreign regulatory authorities may also grant approval contingent on the performance of costly post-marketing clinical trials. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

We may not be able to maintain orphan drug designation or obtain or maintain orphan drug exclusivity for Fintepla or MT-1621.

We have obtained orphan drug designation for Fintepla in the United States and the European Union for both the treatment of Dravet syndrome and LGS. We have also received orphan drug designation for MT1621 for the treatment of TK2d. 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 disease or condition can be recovered by sales in the United States. In the EU, orphan drug designation is granted by the European Commission based on a scientific opinion of the EMA's Committee for Orphan Medicinal Products. A medicinal product may be designated as orphan if its sponsor can establish that (i) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (ii) either (a) such condition affects no more than 5 in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the medicinal product

will be of significant benefit to those affected by the condition. The application for orphan designation must be submitted before the application for marketing authorization. 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, access to the centralized procedure and fee reductions.

If a product with an orphan drug designation subsequently receives the first marketing approval for the disease or condition for which it has such designation, the product is eligible for a period of marketing exclusivity, which precludes the FDA or foreign regulatory authorities 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 the EU. Also, we are only able to attain orphan drug designation in the EU if we are able to demonstrate to the competent authorities that our product candidates have incremental benefit over any other approved product for that orphan disorder.

The European exclusivity period can be reduced to six years if, at this end of the fifth year, 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 foreign regulatory authorities determine 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 or the EU because different drugs can be approved for the same condition. Even after an orphan drug is approved and granted exclusivity, the FDA and foreign regulatory authorities can subsequently approve the same or a similar drug for the same condition during the exclusivity period if the FDA or foreign regulatory authorities conclude 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.

Use of our product candidates could be associated with side effects, adverse events or other properties or safety risks, which could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon a product candidate, limit the commercial profile of the label for an approved product candidate, or result in other significant negative consequences that could severely harm our business, prospects, operating results and financial condition.

Results of our clinical trials could reveal a high and unacceptable severity and prevalence, or unexpected characteristics of side effects. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials, result in a more restrictive label for the product candidate, or delay or cause the denial of regulatory approval of the product candidate by the FDA or comparable foreign regulatory authorities. The drug-related side effects could also affect patient recruitment for our clinical trials, or the ability of enrolled patients to complete the trials, or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, if our product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial prospects for the product candidate if approved. We may also be required to modify our plans for future studies based on findings in our ongoing clinical trials. Many compounds that initially showed promise in early-stage testing have later been found to cause side effects that prevented further development of the compound. In addition, regulatory authorities may draw different conclusions or require additional testing to confirm these determinations.

Additionally, if we or others identify undesirable side effects, or other previously unknown problems, caused by Fintepla, or by MT1621 or any of our future product candidates, if approved, a number of potentially significant negative consequences could result, including:

- regulatory authorities may not approve, or may withdraw their approval of 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 implement a REMS or create a Medication Guide outlining the risks of such side effects for distribution to patients or other risk management measures;
- 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 or similar risk management measures;
- the FDA or foreign regulatory authorities may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety or efficacy of the product;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

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.

Even though we have obtained regulatory approval for Fintepla, and even if we obtain approval for MT-1621 or any other product candidate, we will remain subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Following potential approval of any of our product candidates, the FDA or foreign regulatory authorities may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time-consuming post-approval studies, post-market surveillance or clinical trials to monitor the safety and efficacy of the product. The FDA or foreign regulatory authorities may also require a REMS or similar risk management measure as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. For example, the FDA approved Fintepla for the treatment of seizures associated with Dravet syndrome subject to the Fintepla REMS program, which among other things, requires echocardiogram assessments of patients before, during, and after treatment with Fintepla. Fintepla is also subject to a similar monitoring in the EU. In addition, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our products will be subject to extensive and ongoing regulatory requirements following approval. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs or similar foreign requirements and GCP requirements for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our products, including adverse events of unanticipated type, severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- fines, restitutions, disgorgement of profits or revenues, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications we filed or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our products; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

In addition, the product labeling, advertising and promotion for Fintepla, and for any of our product candidates that may receive approval, will be subject to regulatory requirements and continuing regulatory review. The FDA or and foreign regulatory authorities strictly regulate the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA or foreign regulatory authorities as reflected in the product's approved labeling. For example, the FDA-approved label for Fintepla is limited to the treatment of seizures associated with Dravet syndrome in patients two years of age and older. Physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. 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 sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

The FDA and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities 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, such as the EMA following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs or modifications to approved drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, 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.

Separately, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state of inspectional operations, and in July 2021, the FDA resumed standard inspectional operations of domestic facilities and was continuing to maintain this level of operation as of September 2021. More recently, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

The successful commercialization of Fintepla and our product candidates will depend in part on the extent to which third-party payors, including governmental authorities and private health insurers, provide funding, establish favorable coverage and pricing policies, and set adequate reimbursement levels. Failure to obtain or maintain coverage and adequate reimbursement for Fintepla or any of our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

Our ability to commercialize Fintepla and any of our product candidates successfully, particularly in orphan or rare disease indications, will depend in part on the availability of favorable coverage and the adequacy of reimbursement for the product and alternative treatments from third-party payors (e.g., governmental authorities, private health insurers and other organizations). Obtaining coverage and adequate reimbursement is contingent on our ability to:

- obtain clinical data that supports payor value/benefit assessments;
- execute formal payor value/benefit assessment processes;
- obtain coverage that enables use in populations reflected in any product candidate's approved product label; and
- effectively negotiate favorable pricing and reimbursement terms.

While in some markets, there is a single payor, in other markets there are multiple payors that can have different ways of assessing prescription drugs. To commercialize our product candidates successfully, we will be required to have sufficient expertise and resources to execute on the respective product candidate's coverage and reimbursement strategy, which we cannot be certain we will be able to do.

Governmental authorities, private health insurers and other third-party payors have attempted to control costs by delaying the time to reimbursement, and by restricting the breadth of patient-coverage and limiting the amount of reimbursement for particular products in terms of lower pricing and increasing the proportion of the cost for which the patient is responsible. There may be significant delays in obtaining reimbursement for newly approved products or product indications, coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside the United States, and reimbursement rates may vary according to the use of the product and the clinical setting in which it is used. Coverage and reimbursement barriers by payors may materially impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available, or available only at limited levels, or if such coverage will require patient out-of-pocket costs that are unacceptably high, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. Moreover, any coverage or reimbursement that may be obtained may be decreased or eliminated in the future.

Third-party payors continue to introduce new tactics to contain costs, including more rigorous value/benefit assessment processes and criteria. It is possible that third-party payors will change the clinical comparators that serve as benchmarks for determining relative value. The result of such a change would be a more challenging value/benefit assessment caused by a more challenging basis for comparison and the potential for a worse relative outcome. Third-party payors may determine that we have failed to generate sufficient evidence to support a value/benefit assessment and refuse to provide coverage and reimbursement, thereby impacting or preventing the progression to a price negotiation. The potential of third-party payors to introduce more rigorous value/benefit assessment processes and criteria could have a negative impact on our ability to commercialize our product candidates successfully.

Third-party payors are also introducing more challenging price negotiation tactics, including in re-visiting established coverage and reimbursement in cases when new competitors, including brands, generics and biosimilars enter the market. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to cover the cost of the alternative product. Even if we show improved efficacy or improved convenience of administration with Fintepla or any our product candidates, if approved, pricing of competitive products may limit the amount we will be able to charge for our product candidates. Third-party payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our products. In some cases, when new competitor generic and biosimilar products enter the market, there are mandatory price reductions for the innovator compound, in other cases, payors employ "therapeutic category" price referencing and seek to lower the reimbursement levels for all treatment in the respective therapeutic category. In other cases, new competitor brand drugs can trigger therapeutic category reviews in the interest of modifying coverage and or

reimbursement levels. The potential of third-party payors to introduce more challenging price negotiation tactics could have a negative impact on our ability to commercialize our product candidates successfully.

Evolving health policy and associated legislative changes aimed at lowering healthcare expenditure could impact the commercialization of Fintepla and our product candidates. Pharmaceutical pricing has been, and likely will continue to be, a central component of these efforts.

The regulations that govern regulatory approvals, pricing and reimbursement for new pharmaceutical products vary widely from country to country. In markets of some countries we may pursue outside of the United States for any of our product candidates, the products may be subject to extensive governmental price control or other price regulations. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price negotiations that delay our commercial launch of the product candidate, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product candidate in that country. Adverse pricing and reimbursement limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Net prices for products may be reduced by mandatory discounts or legislated rebates that must be paid in order to participate in government healthcare programs or paid to other third-party payors. Mandatory discounts can be legislated at any time in any market. Similarly, some markets currently have pricing legislation that sets the price of a pharmaceutical product in their market by referencing the price of that product in other markets, known as international reference pricing. International reference pricing has the potential to impact price cuts in individual countries and the countries that reference the pricing of certain other individual countries. Expansion of mandatory discounts and international reference pricing, including into the United States, presents a material risk to our ability to achieve favorable pricing and adequate reimbursement.

Drug importation and cross-border trade, both sanctioned and unsanctioned, occurs when a pharmaceutical product from a market where the official price is set lower is shipped and made commercially available in a market where the official price is set higher. Any future relaxation of laws that presently restrict or limit drug importation or cross-border trade, including in the United States, could have a material negative impact on our ability to commercialize our product candidates, if approved.

We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, we may not be able to achieve or sustain favorable pricing for our product candidates and adequate reimbursement.

If we fail to comply with reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We participate in governmental programs that impose drug price reporting, payment, and other compliance obligations on pharmaceutical manufacturers. Medicaid is a joint federal and state program that for low-income and disabled beneficiaries. Under the Medicaid Drug Rebate Program (“MDRP”), as a condition of having federal funds available for a manufacturer’s covered outpatient drugs under Medicaid and under Medicare Part B, we must enter into, and have entered into, an agreement with the Secretary of Health and Human Services to pay a rebate to state Medicaid programs for each unit of our covered outpatient drugs dispensed to a Medicaid beneficiary and paid for by the state Medicaid program. Medicaid rebates are based on pricing data that we are required to report on a monthly and quarterly basis to the U.S. Centers for Medicare & Medicaid Services (“CMS”), the federal agency that administers the MDRP and Medicare programs. For the MDRP, these data include the average manufacturer price (“AMP”) for each drug and, in the case of innovator products, the Best Price, which represents the lowest price available from the manufacturer to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the United States in any pricing structure, calculated to include all applicable sales and associated rebates, discounts and other price concessions. If we become aware that our MDRP submissions for a prior period were incorrect or have changed as a result of recalculation of the pricing data, we must resubmit the corrected data for up to three years after those data originally were due. If we fail to provide information timely or

are found to have knowingly submitted false information to CMS, we may be subject to civil monetary penalties and other sanctions, including termination from the MDRP.

Federal law requires that any company that participates in the MDRP also participate in the Public Health Service's 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program is administered by the Health Resources and Services Administration ("HRSA") and requires us to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for our covered drugs when used in an outpatient setting. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. A drug that is designated for a rare disease or condition by the Secretary of Health and Human Services is not subject to the 340B ceiling price requirement with regard to the following covered entities: rural referral centers, sole community hospitals, critical access hospitals, and free-standing cancer hospitals. The 340B ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP. In general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price requirement. We must report 340B ceiling prices to HRSA on a quarterly basis, and HRSA publishes them to 340B covered entities. HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B-eligible drugs. HRSA has also finalized an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges. In addition, legislation may be introduced that, if passed, would further expand the 340B program, such as adding further covered entities or requiring participating manufacturers to agree to provide 340B discounted pricing on drugs when used in an inpatient setting.

In order to be eligible to have drug products paid for with federal funds under Medicaid and Medicare Part B and purchased by certain federal agencies and grantees, we must also participate in the U.S. Department of Veterans Affairs ("VA") Federal Supply Schedule ("FSS") pricing program. Under the VA/FSS program, we must report the Non-Federal Average Manufacturer Price ("Non-FAMP") for our covered drugs to the VA and charge certain federal agencies no more than the Federal Ceiling Price, which is calculated based on Non-FAMP using a statutory formula. These four agencies are the VA, the U.S. Department of Defense, the U.S. Coast Guard, and the U.S. Public Health Service (including the Indian Health Service). We must also pay rebates on products purchased by military personnel and dependents through the TRICARE retail pharmacy program. If a manufacturer participating in the FSS program fails to provide timely information or is found to have knowingly submitted false information, the manufacturer may be subject to civil monetary penalties.

Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers for the untimely, inaccurate, or incomplete reporting of drug pricing information or for otherwise failing to comply with drug price transparency requirements. If we are found to have violated state law requirements, we may become subject to penalties or other enforcement mechanisms, which could have a material adverse effect on our business.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies, and the courts, which can change and evolve over time. Such pricing calculations and reporting, along with any necessary restatements and recalculations, could increase costs for complying with the laws and regulations governing the MDRP and other governmental programs, and under the MDRP could result in an overage or underage in Medicaid rebate liability for past quarters. Price recalculations under the MDRP also may affect the ceiling price at which manufacturers are required to offer products under the 340B program. Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. CMS could also terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. We cannot assure you that our submissions will not be found by CMS or other governmental agencies to be incomplete or incorrect.

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 Fintepla or any of our product candidates that may be approved by the FDA or foreign regulatory authorities.

In the United States and internationally, 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, state and foreign 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 ACA, was signed into law, which included measures to significantly change the way health care is financed by both governmental and private insurers. Among the provisions of the ACA 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 23.1% and 13.0% of the average manufacturer price for most branded and generic drugs, respectively;
- a modification of the Average Manufacturer Price definition under the Medicaid Drug Rebate Program for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer point-of-sale discounts of 70% 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;
- 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.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15, 2021 through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

Other legislative changes have also been proposed and adopted in the United States since the ACA 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 2030, with the exception of a temporary suspension from May 1, 2020 through July 1, 2022 (with a 1% payment reduction from April 1 to June 30,

2022), 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. More recently, on March 11, 2021, President Biden signed into law the American Rescue Plan Act of 2021, which eliminates the statutory cap on the Medicaid drug rebate, currently set at 100% of a drug's AMP, beginning January 1, 2024.

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, the Build Back Better Act, if enacted, would introduce substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, and the establishment of rebate payment requirements on manufacturers under Medicare Parts B and D. If the Build Back Better Act is not enacted, similar or other drug pricing proposals could appear in future legislation. The likelihood of implementation of these and other reform initiatives is uncertain. In the coming years, additional legislative and regulatory changes could be made to governmental health programs that could significantly impact pharmaceutical companies and the success of our products and product candidates.

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 governmental 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 EU, 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 EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, 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 EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU 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 EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In December, 2021, Regulation No 2021/2282 on Health Technology Assessment (HTA) amending Directive 2011/24/EU, was adopted. This regulation which entered into force in January 2022 intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period and will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be

responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

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. Similar risks exist in foreign jurisdictions.

If we do not comply with federal, state and foreign healthcare laws, including fraud and abuse 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 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;
- federal civil and criminal false claims laws, including the False Claims Act, 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. 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 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;
- 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;
- federal "sunshine" requirements that require drug manufacturers to report and disclose any "transfer of value" made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives), and teaching hospitals, and any investment or ownership interests held by 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

- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

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.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. To the extent that any product we make is sold in a foreign country, we may be subject to similar foreign laws and regulations. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in 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.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly regulated under HIPAA, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information.

Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, the California Consumer Privacy Act of 2018 (CCPA) went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for

violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act (CPRA) recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

In the EU, the GDPR went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. In addition, the GDPR increases the scrutiny of transfers of personal data from clinical trial sites located in the EEA to the United States and other jurisdictions that the European Commission does not recognize as having “adequate” data protection laws; in July 2020, the CJEU limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield and imposing further restrictions on use of SCCs. The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the UK; the UK’s Information Commissioner’s Office launched a public consultation on its draft revised data transfers mechanisms in August 2021 and laid its proposal before Parliament, with the UK SCCs expected to come into force in March 2022, with a two-year grace period. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Further, from January 1, 2021, we are subject to the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, e.g. fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection law remains unclear, and it is unclear how UK data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the United Kingdom will be regulated in the long term. The European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EU member states to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews/extends that decision, and remains under review by the Commission during this period. In September 2021, the UK government launched a consultation on its proposals for wide-ranging reform of UK data protection laws following Brexit. There is a risk that any material changes which are made to the UK data protection regime could result in the Commission reviewing the UK adequacy decision, and the UK losing its adequacy decision if the Commission deems the UK to no longer provide adequate protection for personal data. These changes will lead to additional costs and increase our overall risk exposure.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

Risks Related to Our 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 (the Universities).

Prior to receiving rights to four 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. With respect to our MT-1621 product candidate, we have certain patent rights that we obtained through our acquisition of Modis. In September 2016, Modis entered into a license agreement (the Columbia Agreement), with Columbia, under which Modis was granted an exclusive worldwide license and sublicense to certain intellectual property rights owned or controlled by Columbia to develop and commercialize MT-1621 and certain backup compounds for any application or purpose. These licensed patent rights include patents owned by Columbia and patents jointly owned by Columbia and Vall d'Hebron Research Institute (VHIR). VHIR delegated to Columbia the rights to enter into the Columbia Agreement on VHIR's behalf. The patent family jointly owned by Columbia and VHIR is directed to the use of MT-1621 to treat TK2d and includes a granted U.S. patent and a granted European patent application, pending applications in Australia, Brazil, Canada, China, Hong Kong, Israel, India, Japan, Korea, Mexico and Russia, as well as continuing applications in the United States and Europe. There are no patents covering the API in MT-1621.

The initial applications covering MT1621 or the 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 Fintepla and MT-1621 matters 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 these matters may not have been completely familiar with U.S. patent law or the patent law in various countries, possibly resulting in inadequate disclosure, improperly claiming inventions 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 and MT-1621 did not and may still not have sufficient knowledge relating to preferred procedures and the legal requirements related to the protection of intellectual property. They published papers which adversely affected our licensed rights, particularly in jurisdictions without a grace period for inventors' own disclosures. 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. Even if additional patents issue, such issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts.

In 2021, we initiated three patent infringement actions on Orange Book-listed patents under The Drug Price Competition and Patent Term Restoration Act ("Hatch-Waxman Act") in the United States District Court for the District of Delaware against filers of Abbreviated New Drug Applications ("ANDAs") for fenfluramine products referencing Fintepla. The defendants, Lupin Ltd., Apotex Inc., and Apotex Corp., have raised common defenses and counterclaims of noninfringement and/or invalidity. Depending on the outcome of these actions, some of our patents could be held not infringed or invalid, permitting generic competition prior to their original expiration.

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 (USPTO), and Congress have recently made significant changes to the patent system. There have been three U.S. Supreme Court decisions that now show a trend of the Supreme Court which is distinctly negative on patents. The trend of these decisions along with 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 may soon become commercially available in generic drug products, and no patent protection will be available without regard to formulation or method of use;
- the APIs in MT-1621 are well-known and available commercially from many sources, and no patent protection claiming the APIs as a composition of matter will be available;
- 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 and MT-1621 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 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 and Columbia 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 and MT-1621. 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 (i) patent applications filed only in the United States may be maintained in secrecy until the patents are issued, (ii) other United States patent applications and patent applications filed in many foreign jurisdictions are typically not published until eighteen months after their filing date, (iii) 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 filed a U.S. patent application prior to March 16, 2013 on inventions similar to those owned or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such proceedings may be decided against us if the other party had independently arrived at the same or similar invention prior to our own or, if applicable, our licensor's invention, resulting in a loss of our U.S. patent position with respect to such inventions. In addition, if another party has reason to assert a substantial new question of patentability against any of our claims in our owned and in-licensed U.S. patents, the third party can request that the USPTO reexamine the patent claims, which may result in a loss of scope of some claims or a loss of the entire patent. We are currently defending an opposition to one of our patents in the European Patent Office, and in the future 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. In any such proceedings, a court or other administrative body may decide that a patent of ours is invalid, in whole or in part or construe our patent's claims narrowly resulting in a loss of our patent position. 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.

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.

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, 2021, the price per share for our common stock on The Nasdaq Global Market has ranged from a low sale price of $11.25 to a high sale price of $23.43. 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 MT-1621;
- the development status of Fintepla or MT-1621, including the results from our clinical trials;
- variations in the level of expenses related to Fintepla or MT-1621 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;
- 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, public health crises, pandemics such as COVID-19 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 the risk factors described in this section of this Annual Report on Form 10-K, 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 and MT-1621 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:

- timing and level of commercial sales of Fintepla;
- variations in the level of development and/or regulatory expenses related to Fintepla and MT-1621 development programs;
- results of clinical trials for Fintepla or MT1621;
- any intellectual property infringement lawsuit in which we may become involved;
- 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.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. We commenced the commercial launch of Fintepla in the United States in July 2020 and in Germany in February 2021. Additionally, from time to time, in addition to the existing Shinyaku Agreement, we may enter into collaborative arrangements with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. Accordingly, our revenue may depend on development funding and the achievement of development and clinical milestones under current and any potential future collaborative arrangements and sales of Fintepla and our other products, if approved. Furthermore, revenues may consist of the recognition of deferred revenue from upfront, nonrefundable payments that we received from Shinyaku or payments we may receive under future collaboration agreements and the timing of recognizing deferred revenue is subject to significant management judgments,

including estimating total costs at completion. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next. As a result, any period-to-period comparisons of our operating results may not be meaningful. Accordingly, the results of any one period should not be relied upon as an indication of future performance.

We have been involved in securities class action litigation and may become involved in future 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 have in the past and may in the future become involved in securities class action litigation. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business. Any adverse determination in any such litigation or any amounts paid to settle any such actual or threatened litigation could require that we make significant payments.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. As of December 31, 2020, we had research coverage by only nine 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, 2021, we had approximately 56.1 million 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 or executive officers and directors, or the perception that those sales may occur, could have a material adverse effect on the trading price of our common stock.

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

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

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than 66 2/3% of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than 66 2/3% of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of 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.

General Risk Factors

As a result of operating as a public company, we incur significant legal and accounting compliance costs and we are subject to the Sarbanes-Oxley Act, and we can provide no assurance that we will, at all times, in the future be able to report that our internal controls over financial reporting are effective.

As a public company, we incur significant legal, accounting and other expenses. 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. 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. In addition, we currently do not have an internal audit function, and we may in the future need to hire additional accounting and financial staff to establish such a function. Moreover, effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent fraud. If we cannot conclude that we have effective internal controls over our financial reporting, or our independent registered public accounting firm is unable to provide an unqualified opinion regarding the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements. In addition, 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.

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.

Our business and operations may suffer in the event of system failures, which could materially affect our results.

Despite the implementation of security measures, our information technology systems and those of our current and our partners, contractors and consultants are vulnerable to attack and damage from cyber-attacks, computer viruses and malware (e.g., ransomware), unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage or disrupt, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. For example, we have been the target of cyber-attacks seeking to misappropriate our funds and have also experienced failures in our information systems and computer servers. We cannot be sure that similar cyber-attacks or 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 due to the delays in the development of our product candidates and/or due to reputational harm, litigation, regulatory investigations and enforcement, fines and penalties, or increased costs of compliance and system remediation. Any losses, costs or liabilities may not be covered by, or may exceed the coverage limits of, any or all applicable insurance policies.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

As of December 31, 2021, our corporate headquarters, which includes executive offices and research and development and business operations, consist of approximately 37,307 square feet of leased office and laboratory space in Emeryville, California. In Maidenhead, United Kingdom, we lease approximately 7,331 square feet of office space. We also maintain limited office space for our subsidiaries in Ireland, Germany, Italy and Japan.

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

On July 21, 2021, we received a letter dated July 20, 2021, notifying us that Apotex Inc. and Apotex Corp. submitted to FDA an ANDA for a generic 2.2 mg base/ml fenfluramine hydrochloride drug product. The letter indicated that Apotex's ANDA included "Paragraph IV" certifications (pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV)) as to Apotex's position that two of our Orange Book-listed patents covering Fintepla, U.S. Patent Nos. 10,603,290, expiration date August 2, 2037, and 10,452,815, expiration date June 29, 2038, were invalid and/or would not be infringed by the manufacture, use or sale of Apotex's fenfluramine hydrochloride oral solution, 2.2 mg base/ml product. On August 30, 2021, we filed a complaint against Apotex Inc. and Apotex Corp. for patent infringement under the Hatch-Waxman Act in the United States Court for the District of Delaware. On October 13, we received a letter dated October 12, 2021, notifying us that Apotex had amended its ANDA and submitted additional certifications with respect to two additional Orange Book-listed patents covering Fintepla, U.S. Patent Nos. 10,950,331, expiration date September 28, 2035, and 10,947,183, expiration date December 20, 2036. The letter included a statement setting forth the basis for Apotex's opinion that these two additional patents are also invalid and/or will not be infringed by the manufacture, use or sale of Apotex's fenfluramine hydrochloride oral solution, 2.2 mg base/ml product. On October 28, 2021, we filed a second complaint against Apotex Inc. and Apotex Corp. for infringement based on these additional certifications in the United States District Court for the District of Delaware. These cases have since been consolidated.

On August 31, 2021, we received a letter dated August 27, 2021, notifying us that Lupin Limited ("Lupin") submitted to FDA an ANDA for a generic 2.2 mg base/ml fenfluramine hydrochloride drug product. The letter indicated that Lupin's ANDA included Paragraph IV certifications with respect to seven of our Orange Book-listed patents covering Fintepla, U.S. Patent Nos. 9,549,909, expiration date May 3, 2033, 9,603,814, expiration date May 3, 2033, 9,603,815, expiration date May 3, 2033, 9,610,260, expiration date May 3, 2033, 10,478,441, expiration date May 3, 2033, 10,478,442, expiration date May 3, 2033; and 10,947,183, expiration date December 20, 2036 (collectively, "the Asserted Patents"). The letter included a statement setting forth the basis for Lupin's opinion that these patents are invalid and/or will not be infringed by the manufacture, use or sale of Lupin's fenfluramine hydrochloride oral solution, 2.2 mg base/ml product. On October 6, 2021, we filed a complaint against Lupin for patent infringement under the Hatch-Waxman Act in the United States District Court for the District of Delaware.

Merger-Related Litigation

Following the announcement of the execution of the Agreement and Plan of Merger, dated January 18, 2022, by and among UCB S.A., Zinc Merger Sub, Inc. and Zogenix, Inc. and through the date hereof, several complaints related to the merger have been filed. The complaints are captioned: *Wang v. Zogenix, Inc.*, Case No. 1:22-cv-00900, which was filed by a purported Zogenix stockholder in the United States District Court for the Southern District of New York on February 2, 2022; *Barman v. Zogenix, Inc.*, Case No. 4:22-cv-00719, which was filed by a purported Zogenix stockholder in the United States District Court for the Northern District of California on February 3, 2022; *Ciccotelli v. Zogenix, Inc.*, Case No. 1:22-cv-00172, which was filed by a purported Zogenix stockholder in

the United States District Court for the District of Delaware on February 7, 2022 (the "Ciccotelli Action"); *Finuliar v. Zogenix, Inc.*, Case No. 1:22-cv-01051, which was filed by a purported Zogenix stockholder in the United States District Court for the Southern District of New York on February 7, 2022 (the "Finuliar Action"); *Hansen v. Zogenix, Inc.*, Case No. 1:22-cv-00679, which was filed by a purported Zogenix stockholder in the United States District Court for the Eastern District of New York on February 7, 2022; *Eiden v. Zogenix, Inc.*, Case No. 1:22-cv-01108, which was filed by a purported Zogenix stockholder in the United States District Court for the Southern District of New York on February 8, 2022; *Wheeler v. Zogenix, Inc.*, Case No. 1:22-cv-00183, which was filed by a purported Zogenix stockholder in the United States District Court for the District of Delaware on February 9, 2022; *Justice v. Zogenix, Inc.*, Case No. 2:22-cv-00545, which was filed by a purported Zogenix stockholder in the United States District Court for the Eastern District of Pennsylvania on February 10, 2022; *Wilhelm v. Zogenix, Inc.*, Case No. 1:22-cv-00185, which was filed by a purported Zogenix stockholder in the United States District Court for the District of Delaware on February 10, 2022; and *Kelly v. Zogenix, Inc.*, Case No. 1:22-cv-01184, which was filed by a purported Zogenix stockholder in the United States District Court for the Southern District of New York on February 11, 2022 (collectively, the "Complaints"). The Complaints name as defendants Zogenix and members of our board of directors, and the complaint in the Ciccotelli Action also names Parent and Purchaser as defendants.

The Complaints generally allege that the defendants violated Section 14(d), 14(e) and 20(a) of the Securities Exchange Act of 1934, as well as Rules 14a-9 and 14d-9 promulgated thereunder. Specifically, one or more of the Complaints allege that the Schedule 14D-9 (as amended or supplemented from time to time), the "Schedule 14D-9" filed on February 1, 2022 with the SEC by Zogenix fails to disclose material information and/or materially misrepresents information concerning the sales process leading up to the merger, potential conflicts of interest of BofA Securities and Zogenix insiders, our financial projections, the financial analyses of BofA Securities, and the financial analyses of SVB Leerink. The complaint in the Finuliar Action also asserts state law claims against the members of our board of directors alleging that they breached their fiduciary duty of candor/disclosure by causing or permitting the Schedule 14D-9 to be filed. The relief sought in one or more of the Complaints includes enjoining the consummation of the merger, enjoining defendants from filing any amendment to the Schedule 14D-9 unless certain allegedly material information is included, directing defendants to disseminate an amended Schedule 14D-9 that does not contain any untrue statements of material fact and that states all material facts required in it or necessary to make the statements therein not misleading, declaring that defendants violated Sections 14(d), 14(e), and 20(a) of the Exchange Act and Rules 14a-9 and 14d-9 promulgated thereunder, rescinding, to the extent already consummated, the merger and awarding rescissory damages, directing defendants to account for all alleged damages suffered as a result of defendants' alleged wrongdoing, awarding the plaintiffs their respective costs and disbursements, and granting other and further equitable relief as the Court may deem just and proper.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

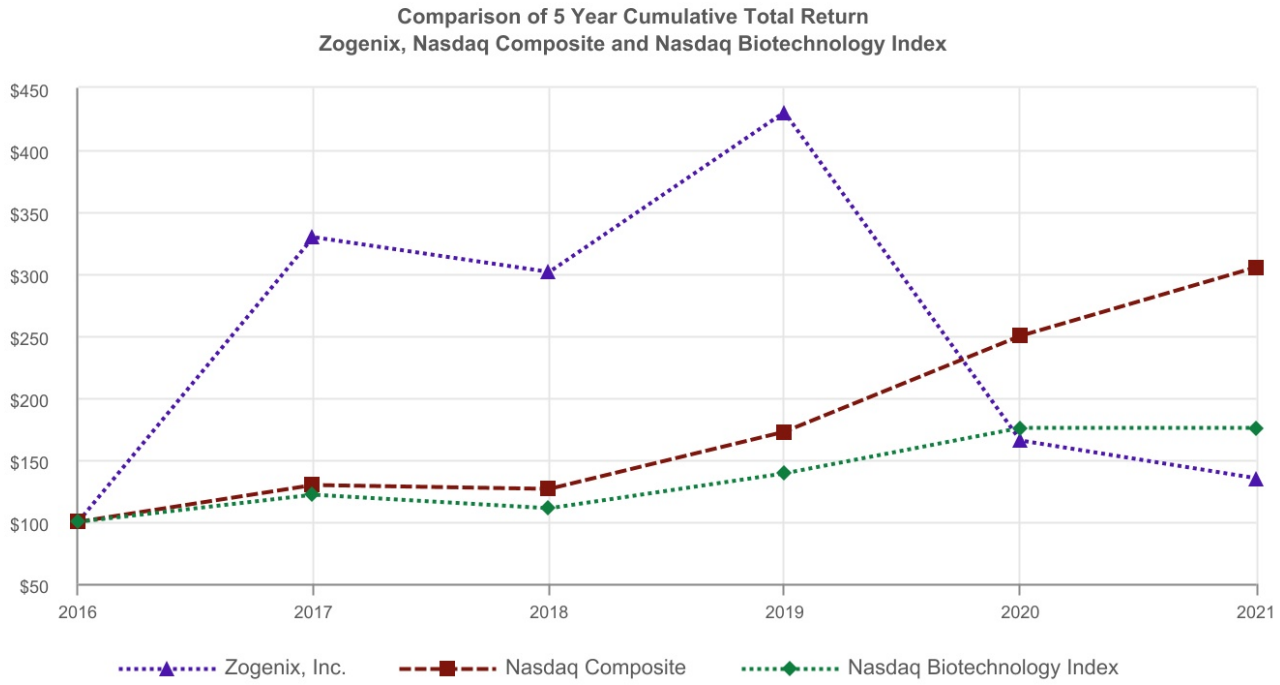
Zogenix common stock is listed on The Nasdaq Global Market under the symbol ZGNX.

Holders of Common Stock

According to the records of our transfer agent, there were nine holders of record of our common stock on February 25, 2022. 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, 2021 to the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes an initial investment of $100 on December 31, 2016, 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.

Recent Sales of Unregistered Securities

None.

Issuer Repurchases of Equity Securities

None.

ITEM 6. RESERVED

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATION

Please read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes included under Part II, Item 8 of 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. Unless otherwise noted or the context otherwise requires, references in this Annual Report on Form 10-K to "we," "us" or "our" refer to Zogenix Inc. and its subsidiaries.

This discussion and analysis generally addresses 2021 and 2020 items and year-over-year comparisons between 2021 and 2020. Discussions of 2019 items and year-over-year comparisons between 2020 and 2019 that are not included in this Annual Report on Form 10-K can be found in Part II, Item 7 of our 2020 Annual Report on Form 10-K filed with the SEC on March 1, 2021.

Overview

We are a global biopharmaceutical company committed to developing and commercializing therapies with the potential to transform the lives of patients and their families living with rare diseases. Our first rare disease therapy, Fintepla (fenfluramine) oral solution has been approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of seizures associated with Dravet syndrome, a rare, severe lifelong epilepsy. We have two additional late-stage development programs underway: Fintepla for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), another rare epilepsy and MT-1621, an investigational therapy for the treatment of TK2 deficiency (TK2d), a rare genetic disease.

We own and control worldwide development and commercialization rights to Fintepla, which was originally obtained in 2014 pursuant to an acquisition of Brabant Pharma, a privately-held U.K.-based pharmaceutical company. In March 2019, we entered into an exclusive distribution agreement with Nippon Shinyaku Co., Ltd. to distribute Fintepla in Japan, if approved for marketing in that country.

Merger Agreement

On January 18, 2022, we entered into a definitive Agreement and Plan of Merger (the "Merger Agreement"), with UCB S.A., a société anonyme formed under the laws of Belgium ("Parent") and Zinc Merger Sub, Inc., a Delaware corporation and an indirect wholly owned subsidiary of Parent ("Purchaser"), pursuant to which, on the terms and subject to the conditions set forth therein, Merger Sub commenced a tender offer (the "Offer") on February 1, 2022 to acquire all of the Company's outstanding shares of common stock, par value $0.001 per share (the "Company Shares"), at a purchase price of (i) $26.00 per Company Share (the "Closing Amount"), net to the seller thereof in cash, subject to reduction for any applicable withholding taxes and without interest, plus (ii) one non-transferrable contingent value right per Company Share representing the right to receive a contingent payment of $2.00 (each, a "CVR", and the Closing Amount plus one CVR, collectively, or any greater amount per Company Share that may be paid pursuant to the Offer, being hereinafter referred to as the "Offer Price"), net to the holder thereof in cash, subject to reduction for any applicable withholding taxes and without interest, upon the achievement of the milestone specified in, and on the other terms and subject to the other conditions set forth in, the CVR Agreement (as defined in the Merger Agreement). Each CVR represents a non-transferable contractual contingent right to receive a cash payment of $2.00, without interest and less any applicable withholding taxes (the "Milestone Payment"), if, and only if, no later than December 31, 2023, the European Commission approves Zogenix's product Fintepla® as an orphan medicinal product for treatment of seizures associated with Lennox-Gastaut syndrome, following an opinion rendered by the Committee for Orphan Medicinal Products of the European Medicines Agency ("EMA") recommending that fenfluramine hydrochloride for the treatment of Lennox-Gastaut syndrome not be removed from the Community Register of Orphan Medicinal Products (the "Milestone").

Completion of the Offer is subject to the satisfaction or waiver of customary conditions, including (i) (i) there having been validly tendered in accordance with the terms of the Offer and not validly withdrawn, as of immediately prior to the expiration of the Offer, a number of Company Shares that, together with the Company Shares then owned by Parent or Merger Sub, represents at least a majority of the Company Shares then outstanding; (ii) the accuracy of the representations and warranties of the Company contained in the Merger Agreement, subject to certain materiality qualifications; (iii) the Company's compliance in all material respects with its covenants and

agreements contained in the Merger Agreement; (iv) the expiration or termination of any waiting period (and any extension thereof) applicable to the Offer or the Merger under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and the receipt of any other clearance, approval or consent applicable to Offer or the Merger (as defined below) under any applicable antitrust law; (v) the absence of a Company Material Adverse Effect (as defined in the Merger Agreement) that is continuing; and (vi) the absence of any law, regulation, order, injunction or ruling issued or enacted by any government authority of competent jurisdiction that would prohibit or make illegal the consummation of the Offer or the Merger, or that would impose certain remedies or restrictions on the ability of Parent to fully own or operate the Company, its businesses or assets.

We expect the Merger to close in the first half of 2022, subject to the regulatory approvals and other customary closing conditions described above and in the Merger Agreement.

Additional information about the Merger and related transactions is set forth in our filings with the Securities and Exchange Commission, or the SEC.

Fintepla for Patients with Rare Epilepsy Disorders

Dravet Syndrome

On June 25, 2020, the FDA granted approval of Fintepla for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older. During the third quarter of 2020, we commercially launched Fintepla through a restricted distribution program, called the Fintepla Risk Evaluation and Mitigation Strategy (REMS) Program. On December 18, 2020, the European Commission (EC) granted marketing authorization for Fintepla for the treatment of seizures associated with Dravet syndrome as an add-on therapy to other anti-epileptic medicines for patients two years of age and older. Fintepla will be available in Europe under a controlled access program requested by the EMA to prevent off-label use for weight management and to confirm that prescribing physicians have been informed of the need for periodic cardiac monitoring in patients taking Fintepla. We initially launched Fintepla for sale in Germany in February 2021 and proceeded with a commercial launch in France and expect to expand into other European markets thereafter. The approval for marketing of Fintepla in the U.S. and in the EU was based on positive safety and efficacy results from two randomized, international, multi-center, placebo-controlled Phase 3 trials (Study 1 and Study 2), as well as data from an interim analysis of a long-term, open-label extension study in 330 Dravet syndrome patients treated up to three years.

In September 2020, we reported positive top-line results from our third Phase 3 trial (Study 3) of Fintepla for the treatment of seizures associated with Dravet syndrome. Study 3 corroborates the substantial impact of Fintepla on convulsive seizure reduction in patients with Dravet syndrome as previously demonstrated in Studies 1 and 2. Study 3 expands the countries where Fintepla has been evaluated to include Japan. On December 12, 2021, the Company submitted a New Drug Application to the Japanese Ministry of Health, Labour & Welfare (MHLW) for the marketing approval of Fintepla for the treatment of epileptic seizures associated with Dravet syndrome in Japan. Fintepla received Orphan Drug Designation from Japan’s Ministry of Health, Labour & Welfare (MHLW) in August 2021.

Lennox-Gastaut Syndrome

In February 2020, we reported positive top-line results from our Phase 3 multicenter, global LGS trial (Study 1601), a double-blind, placebo-controlled study to assess the safety, tolerability and efficacy of Fintepla when added to a patient’s current anti-epileptic regimen. Study 1601 included a total of 263 patients between the ages of 2 and 35 years whose seizures were uncontrolled while on one or more anti-epileptic drugs. The trial met its primary objective of demonstrating that Fintepla at a dose of 0.7 mg/kg/day was superior to placebo in reducing the frequency of drop seizures and demonstrated statistically significant improvements versus placebo in key secondary efficacy measures, including proportion of patients with a clinically meaningful reduction in drop seizure frequency. .

In September 2021, we submitted a supplemental New Drug Application (sNDA) to the FDA for Fintepla for the treatment of seizures associated with LGS. In December 2021, Zogenix announced that the FDA accepted for filing the sNDA, granted our request for Priority Review, and set a Prescription Drug User Fee Act (PDUFA) goal date of March 25, 2022. In December 2021, we submitted a Type II Variation Market Authorization Application to the EMA for Fintepla for the treatment of seizures associated with LGS. If approved, the application would expand the use of Fintepla in the European Union and the United Kingdom beyond patients with Dravet syndrome to include patients with LGS. We plan to make an MAA submission in Japan for LGS in the first quarter of 2023 with an anticipated approval approximately twelve months later.

Fintepla for Other Potential Indications

In addition to Dravet syndrome and LGS, we are evaluating the treatment potential of Fintepla in other serious, treatment-resistant epileptic syndromes.

MT-1621 for Patients with TK2 Deficiency

As a result of our acquisition of Modis in September 2019, we became a party to the Exclusive License Agreement, by and between Modis and Columbia, dated as of September 26, 2016 (the Columbia Agreement), related to MT-1621. MT-1621 is an investigational deoxynucleoside-combination substrate enhancement therapy in development for the treatment of TK2d, a rare, debilitating, and often fatal genetic mitochondrial DNA depletion disease that primarily affects infants and children and for which there are currently no approved therapies.

In April 2020, we held an End-of-Phase 2 meeting with the FDA and in June 2020, we met with the FDA to discuss chemistry, manufacturing, and controls (CMC) for MT1621. In the meetings, the FDA outlined the additional clinical and non-clinical information needed for an NDA submission. In July 2021, we had a Type B Meeting with the FDA where the FDA confirmed the adequacy of the proposed data packages for an NDA submission due to the rare and serious nature of TK2d and the unmet medical need.

Based on this feedback, we are targeting an NDA submission to the FDA for TK2d in the second half of 2022. In addition, we are conducting a Phase 1 pharmacokinetic (PK) study in renal impairment, as recommended by the FDA, to provide dosing recommendations in the setting of impaired renal function and include the results in the NDA submission. The FDA also concurred with our proposed CMC plan for the prospective NDA submission.

In December 2021, we received Scientific Advice feedback from the EMA supportive of our clinical and non-clinical plan to pursue marketing authorization for the treatment of TK2d patients with the age of onset of TK2d younger than 12 years of age. We are targeting an MAA submission after our anticipated NDA submission.

Collaborative Arrangement with Nippon Shinyaku

In March 2019, we entered into an exclusive distribution agreement (Shinyaku Agreement) with Nippon Shinyaku Co., Ltd. (Shinyaku) for the potential commercialization of Fintepla in Japan. We retained responsibility for clinical development programs for Fintepla, including completion of an additional Phase 3 trial (Study 3) to expand the countries to include Japan, amongst others, where Fintepla for the treatment of Dravet syndrome has been evaluated. Upon signing of the agreement, Shinyaku agreed to make upfront payments of $20.0 million. In addition, we are eligible to receive regulatory and sales-based milestone payments of up to $108.5 million. As of December 31, 2021, we have met the criteria to recognize $3.0 million for a regulatory submission milestone related to Dravet syndrome. Once Fintepla is approved for marketing in Japan, if ever, we are obligated to supply product to Shinyaku and will receive a tiered transfer price of up to a high-double digit percentage of the annual net sales of Fintepla in Japan. In September 2020, we reported positive top-line results from Study 3, which corroborates the substantial impact of Fintepla on convulsive seizure reduction in patients with Dravet syndrome as previously demonstrated in Study 1 and Study 2. On December 12, 2021, the Company submitted a New Drug Application to the Japanese Ministry of Health, Labour & Welfare (MHLW) for the marketing approval of Fintepla for the treatment of epileptic seizures associated with Dravet syndrome in Japan..

Tevard Collaboration, Option and License Agreement

In October 2019, we entered into an option agreement with Tevard Biosciences (Tevard), a privately-held company focused on tRNA-based gene therapies. Under the agreement, Tevard granted us an option to license exclusive rights related to a preclinical development program to identify and develop novel tRNA-based gene therapies for Dravet syndrome. During 2020, we extended the option period to exercise our license rights prior to entering into a collaboration, option and license agreement with Tevard. Payments made under the option agreement were nonrefundable, but may be credited against the upfront payment due if we exercise our option on the preclinical development program. Payments made under the option agreement of $2.0 million in 2019 and $5.5 million in 2020 were included in acquired IPR&D expense and related costs in our consolidated statement of operations.

In December 2020, we exercised the option on the Dravet syndrome program and entered into a collaboration, option and license agreement with Tevard (the Tevard Agreement). The financial terms of the Tevard Agreement included an upfront payment of $5.2 million. In connection with the transaction, we also purchased a convertible

promissory note issued by Tevard in the amount of $5.0 million. The note matures in December 2022 and carries interest at 3.5% per year. The note will automatically convert into equity securities issued by Tevard in their next equity financing transaction at a conversion price equal to the price paid per share by other investors of the financing transaction.

In addition to the upfront payments, we have agreed to fund Tevard's early discovery activities under the licensed Dravet syndrome program in accordance with the development plan as determined by the parties to the agreement. Once Tevard completes the early discovery activities for a program, we will be responsible for any potential future development and commercialization activities. Tevard is also eligible to receive additional development, regulatory and commercial-related milestone payments of up to $100.0 million for the Dravet program, as well as tiered royalties on future net sales in the single digits that result from the collaboration. We are also entitled to rights of negotiation and rights of first refusal to potentially obtain licenses to compounds subsequently discovered and developed by Tevard. The agreement, if not terminated sooner, would expire upon the expiration of all applicable royalty terms under the agreement with respect to a licensed program or product; however, we have the unilateral right to terminate the agreement with 180 days advanced notice.

As of December 31, 2021, we do not have any current legal or contractual obligations to provide financing to Tevard and our maximum exposure to future loss is limited to the $5.0 million note receivable, which matures in December 2022. While we have committed to fund the Dravet syndrome development program for Tevard's early discovery activities, our obligation to fund these efforts is contingent upon continued involvement in the program and/or the lack of any adverse events which could cause the discontinuance of the program. Our exposure to future losses is limited as we have the unilateral right to terminate the agreement with 180 days advanced notice.

See the above "Business" section for a more complete discussion of our business.

Business Update Regarding the COVID-19 Pandemic

The full extent to which the ongoing coronavirus disease 2019 (COVID-19 pandemic) will directly or indirectly impact our business continues to evolve and its results on our operations and financial condition, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19, including any related variants, and the actions taken to contain it or treat COVID-19. As a result, we are unable to predict the full impact of the COVID-19 pandemic but it could have a material adverse effect on our business, financial condition, and results of operations.

We are continuing to assess the ongoing impact of COVID-19 on our business operations in an effort to mitigate interruption to our commercialization of Fintepla, clinical programs, research efforts, and other business activities and to ensure the safety and well-being of our employees, partners and patients. COVID-19 infections continue to fluctuate in the U.S. and in many countries worldwide as local surges and new waves of infection continue to be reported, in particular as caused by new variants of the virus that causes COVID-19 and the lack of availability of effective vaccines in certain countries or regions, or failure to utilize available vaccines in other geographies. Although some of the restrictions aimed at minimizing the spread of COVID-19 have been and may from time to time be eased or lifted in the U.S. and other countries from the height of the pandemic, in response to local surges and waves of infection, including those caused by certain variants of the virus, some countries, states, and local governments have maintained or reinstituted these restrictions, or may reinstitute these restrictions from time to time, in response to rising rates of infection. In response to the COVID-19 pandemic, we have implemented precautionary measures to protect the health and safety of our employees, partners, and patients, including providing our employees the flexibility to work remotely from home, as duties permit, and requiring adherence to onsite occupancy limits and appropriate safety measures designed to comply with federal, state, and local guidelines. These safety measures may be eased, lifted, or reinstituted in accordance with updates to such guidelines.

Our ability to successfully commercialize and generate revenue from Fintepla may be directly or indirectly impacted by the COVID-19 pandemic. In addition to our ongoing launch of Fintepla for Dravet syndrome in existing and new markets, we are preparing for a potential product launch of Fintepla for LGS in the U.S., which the FDA granted our supplemental New Drug Application (sNDA) Priority Review with a Prescription Drug User Fee Act (PDUFA) target action date in March 2022. While restrictive safety measures are in place, our sales professionals did not have the same level of in-person interactions with physicians and healthcare providers to conduct educational and promotional activities for Fintepla as they would have absent the COVID-19 pandemic. In response, we have implemented a virtual sales model to supplement traditional means of customer engagement. Although some of these restrictions have been, and may continue to be lifted in certain jurisdictions, the impact of prior and

continued COVID-19 related safety measures, and the potential for re-imposition of restrictions due to local surges and new waves of infection, including those caused by certain variants of the virus, may adversely affect the ability of our sales professionals to effectively market Fintepla, which may have a negative impact on our sales and our market penetration. In addition, the evolving COVID-19 pandemic could directly or indirectly impact the pace of patient enrollment of our Phase 3 study of Fintepla for the treatment of seizures associated with CDKL5 syndrome (CDD), which we initiated in September 2021. To date, we have not experienced any significant interruptions in our ability to supply Fintepla for commercial use in Dravet syndrome or clinical trials for LGS, or MT1621 to our patients currently enrolled in our clinical trials. We currently do not anticipate any interruptions in supply. Any delays in the completion of our clinical trials and any disruption in our supply chain could have a material adverse effect on our business, results of operations and financial condition.

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 management to make judgments, assumptions, and estimates that affect the amounts reported in our consolidated financial statements and accompanying notes. 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.

The significant accounting policies followed, and methods used, in the preparation of our financial statements are detailed in Note 2 to the consolidated financial statements included in this Form 10-K. Due to the material balances of the financial statement elements to which they relate and/or significant judgments, assumptions, and estimates used in the preparation of the consolidated financial statements, we believe the following are critical accounting policies. Actual results could differ from these estimates under different assumptions or conditions and adjustments to such estimates may have a material impact on our financial position and future operating results.

Revenue Recognition

Our revenues consist of product sales of Fintepla and revenues derived from our collaboration arrangement with Nippon Shinyaku Co., Ltd. (Shinyaku).

Net Product Sales

We recognize revenue when control of the promised good or service is transferred to the customer, in an amount that reflects the consideration we expect to be entitled to in exchange for those goods or services. We determine revenue recognition through the following steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when collectability of the consideration to which we are entitled in exchange for the goods or services we transfer to the customer is determined to be probable.

We distribute Fintepla in the U.S. through an arrangement with a specialty distributor who is our customer. The specialty distributor subsequently resells our product through its related specialty pharmacy provider to patients and health care providers. Separately, we have or may enter into payment arrangements with various third-party payers including pharmacy benefit managers, private healthcare insurers and government healthcare programs who provide coverage and reimbursement for our products that have been proscribed to a patient.

Revenue from product sales is recorded at the net sales price (transaction price), which includes estimates of consideration payable to our customer and third-party payers for which reserves are established and that result from government rebates, chargebacks, co-pay assistance, prompt-payment discounts and other allowances that are offered under arrangements between us, our customer, and third-party payers related to the sales of Fintepla. These reserves are classified as either reductions of accounts receivable (if the amounts are payable to our customer) or as refund liabilities within current liabilities (if the amounts are payable to a party other than our customer). Amounts billed or invoiced are included in accounts receivable, net on our consolidated balance sheet. Under our current product sales arrangements, we do not have contract assets (unbilled receivables), as we generally invoice our customer before or at the time of revenue recognition, nor contract liabilities, as we do not receive prepayments from our customers prior to product delivery.

Inputs and assumptions used in our estimates related to our reserves and allowances may fluctuate due to changes in government sponsored programs, payor mix of our customers and the overall economic environment. Historically, actual deductions from sales have not differed significantly from estimated reserves and allowances and we do not expect the differences to be material to our financial position or results of operations.

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, contract manufacturing costs for products that have not obtained regulatory approval, 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, materials used in clinical trials and research and development and costs incurred related to our agreement with Nippon Shinyaku Co., Ltd. We expense 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 recorded as prepaid assets on our consolidated balance sheets until the goods or services are realized or consumed. We classify such prepaid assets as current or non-current assets based on our estimates of the timing of when the goods or services will be realized or consumed.

Our expense accruals for clinical trials are based on estimates of the services received from clinical trial investigational sites, contract research organizations (CROs) and other third-party vendors that support us in our research and development efforts. Payments under some of our contracts with these service providers depend on factors such as the achievement of clinical milestones such as the successful enrollment of certain numbers of patients, site initiation, or completion of a clinical trial. In accruing for these services at each reporting date, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If available, we obtain information regarding unbilled services directly from these service providers. However, we may be required to estimate our accrual based only on information available to us. Once established, accruals are adjusted from time to time, as appropriate, in light of additional information. Amounts ultimately incurred in relation to amounts accrued for these services at a reporting date may be substantially higher or lower than our estimates.

Results of Operations

Revenues

	Year Ended December 31,		
(In thousands)	2021	2020	$ Change
Net product sales	$ 74,740	$ 9,587	$ 65,153
Collaboration revenue	6,950	4,056	2,894
Total revenues	$ 81,690	$ 13,643	$ 68,047

We began to generate product revenue following the approval of Fintepla for Dravet syndrome by the FDA and the EMA in 2020. Prior to the commercial launch of Fintepla in July 2020, our revenues were generated solely from a collaboration agreement with Shinyaku entered into in March 2019.

Net Product Sales

Net product sales increased by $65.2 million during the year ended December 31, 2021, compared to the year ended December 31, 2020, as a result of an entire year of Fintepla sales following commercial launch in the U.S. in the third quarter of 2020, and Germany and France in 2021.

We expect net product sales to increase during 2022 as compared to 2021 as we continue to retain and expand our patient base in existing markets, as well as launch our approved product into additional markets following the country-by-country reimbursement approval process in Europe, including the United Kingdom, Italy and Spain.

Collaboration Revenue

Collaboration revenue increased by $2.9 million during the year ended December 31, 2021, compared to the year ended December 31, 2020, primarily due to the achievement of a $3.0 million regulatory submission milestone for Dravet syndrome under the collaboration arrangement during the fourth quarter of 2021. This resulted in an adjustment in the estimate of the overall transaction price and was recorded on a cumulative catch-up basis, which increased collaboration revenue in the period of adjustment.

As recognition of our collaboration revenue is based on costs incurred to date relative to total estimated costs at completion when measuring progress combined with the uncertainty of when the events underlying various milestones are resolved, we expect our collaboration revenue will fluctuate from period to period.

Cost of Product Sales (Excluding Intangible Asset Amortization)

Cost of product sales (excluding intangible asset amortization) includes the cost of producing and distributing inventories that are related to product revenues during the respective period (including salary-related and stock-based compensation expenses for employees involved with production and distribution, freight and indirect overhead costs) and third-party royalties payable on our net product revenues. Cost of product sales may also include costs related to excess or obsolete inventory adjustment charges, abnormal costs, unabsorbed manufacturing and overhead costs, and manufacturing variances.

For the year ended December 31, 2021, cost of sales primarily consisted of royalties payable on net sales of Fintepla under a license agreement and labeling and packaging costs. Substantially all of the cost of product sold in 2021 were for packaging and labeling as our inventory had a zero-cost basis. Prior to receiving FDA approval for Fintepla, we recorded all manufacturing product costs as research and development expense. We expect our cost of sales for Fintepla to increase as a percentage of net sales in beginning in mid-2022 as we produce and then sell inventory that reflects the full cost of manufacturing.

Research and Development Expense

Research and development (R&D) expense consist of expenses incurred in developing, testing and seeking marketing approval of our product candidates, including: payments made to third-party clinical research organizations (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; commercial quantities of certain product candidates prior to the date we anticipate that such products will receive regulatory approval, personnel related expenses, such as salaries, benefits, travel and other related expenses, including stock-based compensation; and facility, maintenance, depreciation and other related expenses.

For each of our R&D programs, we incur both external and internal costs. External costs include clinical and non-clinical activities performed by CROs, lab services, purchases of product candidate materials and manufacturing development costs. We track external R&D expenses for each of our key development programs. We have not tracked internal costs on a program-by-program basis because our R&D employees and infrastructure resources are utilized across our product candidate development programs.

The table below sets forth components of our research and development expenses for the periods presented.

	Year Ended December 31,		
(In thousands)	2021	2020	$ Change
External costs:			
Fintepla for Dravet syndrome	$ 22,023	$ 32,287	$ (10,264)
Fintepla for LGS	25,013	34,920	(9,907)
MT-1621	23,911	13,703	10,208
Tevard gene-therapy program for Dravet syndrome	3,535	739	2,796
Other[(1)]	3,904	1,942	1,962
Total external costs	78,386	83,591	(5,205)
Internal costs	64,273	54,411	9,862
Total research and development expense	$ 142,659	$ 138,002	$ 4,657

(1) Other external costs include early-phase exploratory research programs.

R&D expenses related to Fintepla for Dravet syndrome decreased by $10.3 million year-over-year primarily due to wind-down of clinical activities, partially offset by costs incurred in conjunction with our Phase 3 clinical trial to support the submission of a New Drug Application to the Japanese Ministry of Health, Labour & Welfare (MHLW) for the marketing approval of Fintepla for Dravet syndrome in Japan, which occurred in the fourth quarter of 2021. R&D expenses related to Fintepla for LGS decreased by $9.9 million year-over-year due to lower program costs incurred for external service providers. In the fourth quarter of 2021, we submitted applications in the U.S. and in the EU for regulatory approvals to market Fintepla for the treatment of seizures associated with LGS. R&D expenses related to MT1621 increased by $10.2 million year-over-year as we continued to advance the MT1621 development program, including work related to chemistry, manufacturing, and controls process requirements. We plan to submit an NDA to the FDA in the second half of 2022. Internal costs for research and development activities increased by $9.9 million year-over-year primarily driven by personnel-related expenses from increased R&D headcount.

Selling, General and Administrative Expense

	Year Ended December 31,		
(In thousands)	**2021**	**2020**	**$ Change**
Selling, general and administrative	$ 148,524	$ 99,574	$ 48,950

Selling, general and administrative expense consists primarily of salaries and related costs for our personnel, including stock-based compensation, market research expenses for our product and product candidates that are in development and marketing expenses to support our commercial launch efforts, executive, finance, accounting, business development and internal support functions, facility-related costs and consulting fees, in each case not otherwise included in research and development expenses.

Selling, general and administrative expense increased by $49.0 million in 2021 compared to 2020. The increase was primarily attributable to a $16.0 million increase in personnel-related costs, which included a $4.9 million increase for stock-based compensation as we build out our specialized and focused commercial teams in support of our Fintepla product launch in the U.S. and in preparation of our product launch in Europe and headcount additions in general and administrative to support our commercial team. In addition, commercial spend related to market research, strategic and logistic planning for our product launch also contributed $12.9 million to the increase. The remainder of the increase was attributable to higher insurance premium costs and an increase in utilization of professional services, as well as infrastructure and facilities-related costs.

Intangible Asset Amortization

Our intangible asset consist of worldwide development, commercialization and related intellectual property rights including patents and licenses for our product, Fintepla, which at the time of our acquisition in October 2014 was classified as an indefinite-lived IPR&D asset. Upon FDA approval of Fintepla in June 2020, this indefinite-lived asset was reclassified to a finite-lived intangible asset subject to amortization.

In July 2020, we commercially launched Fintepla and commenced amortization of this asset on a straight-line basis over its estimated useful life of 13 years. For the year ended December 31, 2021, intangible asset amortization expense was $7.9 million.

Acquired In-Process Research and Development and Related Costs

Acquired IPR&D consists of existing research and development projects at the time of the acquisition. Projects that qualify as IPR&D assets represent those that have not yet reached technological feasibility and have no alternative future use.

For the year ended December 31, 2021, we did not incur acquired IPR&D expense. For the year ended December 31, 2020, acquired IPR&D expense of $10.7 million consisted of non-refundable, option maintenance payments and exercise fees paid to Tevard to acquire license rights under the Dravet syndrome development program.

Change in Fair Value of Contingent Consideration

(In thousands)	Year Ended December 31, 2021	2020
Change in fair value of contingent consideration	$ 1,885	$ 8,600

The contingent consideration liability relates to milestone payments under an existing agreement in connection with our prior acquisition in October 2014. At each reporting period, the estimated fair value of the liability is determined by applying an income approach which utilizes variable inputs, such as the probability of success for achieving regulatory/commercial milestones, anticipated future cash flows, risk-free adjusted discount rates, and nonperformance risk. Any change in the fair value of contingent consideration is recorded within operating expenses.

For the year ended December 31, 2021, the $1.9 million increase in the estimated fair value of our contingent consideration liabilities was primarily attributable to the passage of time. For the year ended December 31, 2020, the $8.6 million increase in the estimated fair value of our contingent consideration liabilities was due to the achievement of milestones based on Fintepla regulatory approvals obtained in the U.S. and in the EU.

Other Income (Expense), Net

(In thousands)	Year Ended December 31, 2021	2020	$ Change
Interest income	$ 659	$ 2,891	$ (2,232)
Interest expense	(15,276)	(3,759)	11,517
Other income	11,406	21,777	(10,371)
Total other income, net	$ (3,211)	$ 20,909	$ (1,086)

Interest income decreased by $2.2 million during the year ended December 31, 2021, compared to the year ended December 31, 2020, as a result of lower average investment balances, which is used to fund our operations. Interest expense increased by $11.5 million during the year ended December 31, 2021, as compared to the year ended December 31, 2020, as our senior convertible notes were outstanding for an entire year. Other income primarily consist of tax election claims made under U.K.'s small and medium-sized enterprises (SMEs) R&D tax relief scheme where we elected to surrender net operating losses that arise from our eligible R&D activities in exchange for a cash payment from the U.K. tax authorities. For the year ended December 31, 2021, we recognized income of $12.4 million related to a tax election claim for the 2019 tax year. For the year ended December 31, 2020, we recognized $19.7 million related to tax election claims for both the 2018 and 2017 tax years.

Income Taxes

For the year ended December 31, 2021, a provision for income taxes of $0.1 million has been recognized related primarily to our subsidiaries located outside of the United States. For the year ended December 31, 2020, income tax benefit of $17.4 million resulted from a change in our valuation allowance balance associated with the completion of our in-process research and development program for Fintepla. Prior to regulatory approval of Fintepla in June 2020, our indefinite-lived asset was not subject to amortization. Upon completion of the IPR&D program, the indefinite-lived intangible asset was reclassified to an intangible asset subject to amortization over its estimated useful life. As a result, future reversals of deferred tax liabilities related to finite-lived intangible assets provided a source of income when assessing the realizability of our U.K. net operating loss carryforwards. We therefore recorded a $17.4 million income tax benefit in 2020 with a corresponding reduction to our valuation allowance on our U.K. deferred tax assets. The income tax benefit included the effects of foreign exchange differences on remeasurement of the deferred tax liability. An immaterial portion of the adjustment for foreign exchange differences was related to prior periods.

Liquidity and Capital Resources

Excluding gains from two discrete business divestitures, we have incurred significant net losses and negative cash flows from operating activities since inception resulting in an accumulated deficit of $1.6 billion as of December 31, 2021. For the years ended December 31, 2021 and 2020, we incurred net losses of $227.4 million and $209.4 million, respectively. We expect to incur operating losses and negative cash flow for additional future periods due to costs associated with the commercialization of Fintepla for Dravet syndrome and pre-commercialization activities

related to Fintepla for LGS in the U.S. and in the EU, the advancement of our clinical programs related to MT-1621 and CDD, and other infrastructure support costs. In addition, excluding amounts accrued for contingent consideration related to our acquisition of Brabant, we may be required to pay $100.0 million and $50.0 million in milestone payments upon regulatory approval of MT-1621 by the FDA and the EMA, respectively, related to our acquisition of Modis. These contingent consideration payments have not be recognized in the consolidated balance sheets as the regulatory approval contingency has not been resolved and the consideration is not yet payable. Historically, we have relied primarily on the proceeds from equity and convertible debt offerings to finance our operations. Our recent financing activities include offerings of common stock and convertible debt.

Underwritten Public Offerings

In March 2020, we completed an underwritten public offering of 9,798,000 shares of our common stock at an offering price of $23.50 per share, including 1,278,000 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares. Net proceeds realized from the offering amounted to approximately $221.7 million, after deducting commissions and other offering costs.

2.75% Convertible Senior Notes Due 2027

In September and October 2020, we issued $230.0 million principal amount of 2.75% convertible senior notes due 2027 in a private offering (collectively, the Convertible Senior Notes or Notes). Total proceeds realized from the sale of the Notes, net of issuance costs of $7.5 million, were $222.5 million. The Notes are governed by an indenture (Indenture), dated as of September 28, 2020, between Zogenix and U.S. Bank National Association, as trustee. Under the Indenture, the Notes are senior, unsecured obligations of Zogenix, are equal in right of payment with its future senior, unsecured indebtedness of Zogenix, and structurally subordinated to all indebtedness and liabilities of its subsidiaries. The principal amount of the Notes was issued at par value and the Notes accrue interest at a rate of 2.75% per year, payable semi-annually in arrears on April 1 and October 1 of each year, beginning on April 1, 2021. The Notes mature on October 1, 2027, unless earlier converted by the holders or redeemed or repurchased by us in accordance with their terms prior to such date. The Indenture contains customary terms and covenants, including certain events of default upon which the Notes may be due and payable immediately, but does not contain any financial covenants. As of December 31, 2021, we were in compliance with all covenants under the Indenture.

Material Cash Requirements

Our primary uses of cash are to fund our operations as we continue to grow our business and discover further indications and uses for our therapies. We will require a significant amount of cash for clinical trials and research and development as we invest in our therapies, the commercialization of our therapies and collaborative arrangements to expand our distribution channels. We expect that our sales and marketing, general and administrative, and research and development expenses will continue to increase as we increase our sales volume, expand our marketing efforts, increase our headcount to drive increased sales of our therapies and continue research and development efforts to further enhance our therapies. Our future funding requirements will depend on many factors, including, but not limited to:

- our ability to successfully market and sell, and the level of demand for, Fintepla;
- delays and cost increases as a result of the COVID-19 pandemic;
- the costs incurred to manage our commercial infrastructure, including our sales and marketing personnel, and costs incurred under our agreements with third parties for warehousing, distribution, cash collection and related commercial activities;
- 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 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, terms and timing of manufacturing for Fintepla and our product candidates;
- 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.

The following table summarizes our cash and cash equivalents and marketable securities:

	December 31,		
(In thousands)	2021	2020	$ Change
Cash and cash equivalents	$ 101,180	$ 166,916	$ (65,736)
Marketable securities	200,548	338,193	(137,645)
Total	$ 301,728	$ 505,109	$ (203,381)

As of December 31, 2021, we had cash, cash equivalents and marketable securities of $301.7 million, compared to $505.1 million as of December 31, 2020. We believe our cash, cash equivalents and marketable securities, together with the cash we expect to generate from product sales and under our collaboration arrangement will be sufficient to meet our anticipated operating requirements for at least the next 12 months following the date of issuance of these consolidated financial statements.

Sources and Uses of Cash

The following table summarizes our cash flow activities:

	Year Ended December 31,	
(In thousands)	2021	2020
Net cash used in operating activities	$ (185,305)	$ (167,531)
Net cash (used in) provided by investing activities	137,395	(165,100)
Net cash provided by financing activities	(17,826)	437,477

Operating Activities

Net cash used in operating activities of $185.7 million in 2021 was primarily attributable to our net loss as we continue to invest in research and development related to our various late-stage development programs, expansion of our infrastructure to support the commercialization of Fintepla and anticipated growth. Non-cash items included stock-based compensation expense of $35.1 million, amortization of debt discount and issuance costs of $8.8 million related to our convertible senior notes and intangible asset amortization of $7.9 million. Net changes in operating assets and liabilities totaled an outflow of $14.3 million principally due to the timing of vendor payments and increases in accounts receivable and inventory as a result of growth in Fintepla product sales.

Net cash used in operating activities of $167.5 million in 2020 was primarily attributable to our net loss and research and development spend related to clinical trials and manufacturing process development for Fintepla. Cash used in operating activities included R&D expenses related to ongoing open-label clinical trials for Fintepla and manufacturing process development for Fintepla and MT1621, commercial preparedness and planning

expenses including additions in headcount to build out our sales force of key account managers and general and administrative costs to support our business objectives.

Investing Activities

Net cash provided by investing activities of $137.4 million in 2021 was primarily attributable to maturities of available-for-sale marketable securities.

Net cash used in investing activities of $165.1 million in 2020 was primarily attributable to net purchases of available-for-sale marketable securities.

Financing Activities

Net cash used in financing activities of $17.8 million in 2021 was primarily attributable to payments of contingent consideration for regulatory and sales-based milestones related to Fintepla, partially offset by net proceeds from the issuance of common stock pursuant to our equity incentive plans.

Net cash provided by financing activities of $437.5 million in 2020 primarily consisted of net proceeds realized from the issuance of our common stock in a public offering, the issuance of convertible debt and proceeds from the sale of common stock under our “at-the-market” program, as well as net proceeds received related to our equity incentive program. In July 2020, we made a $15.0 million milestone payment pursuant to our purchase agreement of Brabant in 2014 upon FDA approval of Fintepla.

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 8, Notes to Consolidated Financial Statements, which is incorporated herein by reference.

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, 2021, we had cash, cash equivalents and marketable securities of $301.7 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 also have an outstanding balance of $230.0 million aggregate principal amount of convertible senior notes that mature in 2027, which has a fixed interest rate of 2.75% per year. We carry these instruments at face value, less unamortized discounts and issuance costs, on our accompanying consolidated balance sheets. Since these instruments bear interest at fixed rates, we have no financial statement risk associated with changes in interest rates. However, the fair value of these instruments fluctuates as interest rate changes and, in the case of our convertible senior notes, when the market price of our common stock fluctuates.

Foreign Exchange Risk

As a result of our U.K. and European 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 December 31, 2021, 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

All financial statement schedules have been omitted, since the required information is not applicable or is not present in amounts sufficient to require submission of the schedule, or because the information required is included in the consolidated financial statements and accompanying notes.

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, 2021 and 2020, 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, 2021, 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, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, 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, 2021, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) and our report dated March 1, 2022 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.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Accrued clinical trial expenses

Description of the Matter

As of December 31, 2021, the Company recorded $13.5 million for accrued clinical trial expenses. As described in Note 2 to the financial statements, the Company's expense accruals for clinical trials are based on estimates of contracted services provided but not yet billed by third-party vendors. When billing terms under such contracts do not coincide with the timing of when the work is performed, management is required to make estimates of outstanding obligations to those third parties at the end of each reporting period. Accrual estimates are based on a number of factors, including management's knowledge of the research and development program activities, invoicing to date, and the provisions in the contract. If possible, the Company obtains information regarding unbilled services directly from these service providers and performs procedures to challenge these estimates based on their internal understanding of the services provided to date.

Auditing accrued clinical trial expenses was complex because of the efforts applied by management to determine the commencement and completion date of vendor tasks, and the cost and extent of work performed during the reporting period for services not yet billed by contracted third-party vendors. Testing the Company's accrued clinical trial expense models also involved increased effort due to the high volume of data used to determine the estimated accrual.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of internal controls over the Company's process for estimating the accrued clinical trial expenses, including controls over management's assessment and measurement of clinical trial progress and related estimates of accrued clinical trial costs, and the completeness and accuracy of underlying data used in the analysis.

We evaluated the estimate of accrued clinical trial expenses. We performed audit procedures that included, among others, direct confirmation of contract terms and conditions with a sample of the Company's third-party vendors. We confirmed progress of contracted clinical activities with third-party vendors and compared such data to the Company's estimates of progress as reflected in their accrual models. We tested the accuracy of the calculations and data utilized, and evaluated the reasonableness of the assumptions used in management's accrual models by vouching actual invoices paid to date, agreeing inputs back to contractual terms and holding discussions with clinical or administrative staff outside of the finance function to corroborate progress and estimated level of expended effort incurred by the Company's third-party vendors.

United Kingdom research and development tax relief scheme

Description of the Matter

As of December 31, 2021, the Company recorded $12.4 million of other income for amounts received under the United Kingdom's ("UK's") small and medium-sized enterprises ("SME") research and development ("R&D") tax relief scheme. As described in Note 18 to the consolidated financial statements, the Company carries out extensive research and development activities that benefit from UK's SME R&D tax relief scheme, whereby an entity can make an election 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. The Company records these amounts as a component of other income, net after an election for tax relief in the form of cash payments has been made for a discrete tax year by submitting the claim, and collectability is deemed probable and reasonably assured.

Auditing the amounts recorded related to the UK's SME R&D tax relief scheme was complex due to the application of foreign tax regulations that allow the Company to claim a cash refundable benefit.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of internal controls over the Company's process for calculating the UK's SME R&D tax relief scheme.

We evaluated other income recorded for the UK's SME R&D tax relief scheme. We performed audit procedures that included, among others, utilizing professionals with specialized skill and knowledge to assist in evaluating the Company's eligibility to participate in the scheme, inspecting the reasonableness of types of qualified the expenses and programs used to determine the claim, and evaluating the reasonableness of the Company's application of relevant foreign tax regulations associated with the UK's SME R&D tax relief scheme. We tested the completeness, accuracy, and relevance of information used in the calculation of the claim. We evaluated the status, results of communications and audits by the UK tax authorities associated with past and current claims made by the Company under the UK's SME R&D tax relief scheme.

/s/ Ernst & Young LLP

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

Redwood City, California

March 1, 2022

ZOGENIX INC.
CONSOLIDATED BALANCE SHEETS

(In thousands, except par value)	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 101,180	$ 166,916
Marketable securities	200,535	338,193
Accounts receivable, net	10,139	3,824
Inventory	5,492	1,026
Prepaid expenses	12,487	7,279
Other current assets	24,735	4,936
Total current assets	354,568	522,174
Property and equipment, net	7,197	8,724
Operating lease right-of-use assets	6,605	7,748
Intangible asset, net	90,673	98,558
Goodwill	6,234	6,234
Other non-current assets	3,212	7,692
Total assets	$ 468,489	$ 651,130
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 21,998	$ 11,945
Accrued and other current liabilities	55,413	54,964
Deferred revenue, current	5,089	5,318
Current portion of operating lease liabilities	1,694	1,688
Current portion of contingent consideration	13,500	8,800
Total current liabilities	97,694	82,715
Deferred revenue, non-current	3,257	5,479
Operating lease liabilities, net of current portion	8,617	10,314
Contingent consideration, net of current portion	21,785	33,600
Convertible debt	158,165	149,353
Total liabilities	289,518	281,461
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000 shares authorized, none issued and outstanding	—	—
Common stock, $0.001 par value; 200,000 and 100,000 shares authorized and 56,095 and 55,736 shares issued and outstanding at December 31, 2021 and 2020, respectively	56	56
Additional paid-in capital	1,731,153	1,694,524
Accumulated other comprehensive loss	15	(71)
Accumulated deficit	(1,552,253)	(1,324,840)
Total stockholders' equity	178,971	369,669
Total liabilities and stockholders' equity	$ 468,489	$ 651,130

See accompanying notes to the consolidated financial statements.

ZOGENIX INC.
CONSOLIDATED STATEMENTS OF OPERATIONS

(In thousands, except per share amounts)	Year Ended December 31, 2021	2020	2019
Revenues:			
Net product sales	$ 74,740	$ 9,587	$ —
Collaboration revenue	6,950	4,056	3,648
Total revenues	81,690	13,643	3,648
Operating costs and expenses:			
Cost of product sales (excluding intangible asset amortization)	4,834	542	—
Research and development	142,659	138,002	115,639
Selling, general and administrative	148,524	99,574	60,792
Intangible asset amortization	7,885	3,942	—
Acquired in-process research and development and related costs	—	10,700	251,438
Change in fair value of contingent consideration	1,885	8,600	5,600
Total operating expenses	305,787	261,360	433,469
Loss from operations	(224,097)	(247,717)	(429,821)
Other income (expense):			
Interest income	659	2,891	9,804
Interest expense	(15,276)	(3,759)	(2)
Other income, net	11,406	21,777	516
Loss from operations before income taxes	(227,308)	(226,808)	(419,503)
Income tax expense (benefit)	105	(17,425)	—
Net loss	$ (227,413)	$ (209,383)	$ (419,503)
Net loss per share, basic and diluted	$ (4.07)	$ (3.90)	$ (9.74)
Weighted average common shares outstanding, basic and diluted	55,880	53,706	43,078

See accompanying notes to the consolidated financial statements.

ZOGENIX INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(In thousands)	Year Ended December 31, 2021	2020	2019
Net loss	$ (227,413)	$ (209,383)	$ (419,5
Other comprehensive income (loss):			
Net unrealized (loss) gains on marketable securities	(202)	(183)	7
Reclassification adjustments for realization of gain on sale of marketable securities included in net loss	—	(7)	(3
Foreign currency translation gain (loss)	288	(260)	
Total other comprehensive income (loss)	86	(450)	3
Comprehensive loss	$ (227,327)	$ (209,833)	$ (419,1

See accompanying notes to the consolidated financial statements.

ZOGENIX INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(In thousands)	Common Stock Shares	Common Stock Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2018	42,078	$ 42	$1,218,710	$ 3	$ (695,954)	$ 522,801
Net loss	—	—	—	—	(419,503)	(419,503)
Other comprehensive income	—	—	—	376	—	376
Issuance of common stock, net of issuance costs	904	1	42,575	—	—	42,576
Issuance of common stock under employee equity plans	712	—	10,182	—	—	10,182
Shares repurchased for tax withholdings related to net share settlement of employee equity awards	(17)	—	(744)	—	—	(744)
Issuance of common stock in connection with asset acquisition	1,595	2	68,122			68,124
Stock-based compensation	—	—	21,247	—	—	21,247
Balance at December 31, 2019	45,272	$ 45	$1,360,092	$ 379	$(1,115,457)	$ 245,059
Net loss	—	—	—	—	(209,383)	(209,383)
Other comprehensive loss	—	—	—	(450)	—	(450)
Issuance of common stock, net of issuance costs	10,000	10	226,566	—	—	226,576
Equity component of convertible debt	—	—	75,333	—	—	75,333
Issuance of common stock under employee equity plans	546	1	5,514	—	—	5,515
Shares repurchased for tax withholdings related to net share settlement of employee equity awards	(82)	—	(2,157)	—	—	(2,157)
Stock-based compensation	—	—	29,176	—	—	29,176
Balance at December 31, 2020	55,736	$ 56	$1,694,524	$ (71)	$(1,324,840)	$ 369,669
Net loss	—	—	—	—	(227,413)	(227,413)
Other comprehensive loss	—	—	—	86	—	86
Issuance of common stock under employee equity plans	466	—	1,962	—	—	1,962
Shares repurchased for tax withholdings related to net share settlement of employee equity awards	(107)	—	(1,788)	—	—	(1,788)
Stock-based compensation	—	—	36,455	—	—	36,455
Balance at December 31, 2021	56,095	$ 56	$1,731,153	$ 15	$(1,552,253)	$ 178,971

See accompanying notes to the consolidated financial statements.

ZOGENIX INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)	Year Ended December 31, 2021	2020	2019
Cash flows from operating activities:			
Net loss	$ (227,413)	$ (209,383)	$ (419,503)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	35,463	29,176	21,247
Depreciation and amortization	9,455	5,465	1,268
Deferred income taxes	—	(17,425)	—
Noncash lease expense	1,143	1,137	1,221
Amortization of debt discount and issuance costs	8,812	2,143	—
Net accretion and amortization of investments in marketable securities	(20)	(570)	(4,887)
Acquired in-process research and development (IPR&D)	—	10,700	251,437
Change in fair value of contingent consideration	1,885	8,600	5,600
Other	(2)	(205)	(471)
Changes in operating assets and liabilities:			
Accounts receivable	(6,315)	(3,824)	—
Inventory	(3,474)	(1,026)	—
Prepaid expenses and other current assets	(25,007)	(575)	7,573
Other assets	4,480	(1,613)	(5,723)
Accounts payable, accrued and other current liabilities	21,330	13,711	5,647
Contingent consideration liability	(1,500)	—	—
Operating lease liability	(1,691)	(1,287)	11,720
Deferred revenue	(2,451)	(2,555)	13,352
Net cash used in operating activities	(185,305)	(167,531)	(111,519)
Cash flows from investing activities:			
Cash paid for IPR&D assets	—	(10,700)	(179,624)
Purchase of Tevard note receivable	—	(5,000)	—
Purchases of marketable securities	(416,155)	(509,335)	(329,641)
Proceeds from maturities of marketable securities	540,133	347,627	415,020
Proceeds from sale of marketable securities	13,500	12,987	176,858
Purchases of property and equipment	(83)	(679)	(9,492)
Net cash provided by (used in) investing activities	137,395	(165,100)	73,121
Cash flows from financing activities:			
Payments for contingent consideration liability	(18,000)	(15,000)	(20,000)
Proceeds from issuance of common stock under equity incentive plans	1,962	5,515	10,182
Payments of tax withholding obligation on vesting restricted stock units	(1,788)	(2,157)	(744)
Net proceeds from issuance of convertible debt	—	223,100	—
Payment of debt issuance costs	—	(557)	—
Proceeds from issuance of common stock, net	—	226,576	42,576
Net cash provided by financing activities	(17,826)	$ 437,477	$ 32,014
Net increase (decrease) in cash and cash equivalents	(65,736)	$ 104,846	$ (6,384)
Cash and cash equivalents at beginning of period	166,916	$ 62,070	$ 68,454
Cash and cash equivalents at end of period	101,180	$ 166,916	$ 62,070

(In thousands)	Year Ended December 31, 2021	2020	2019
Supplemental cash flow disclosure:			
Cash paid for interest	$ 6,378	$ —	$ —
Noncash investing and financing activities:			
Common stock issued as consideration for asset acquisition	$ —	$ —	$ 68,124
Net liabilities assumed in connection with asset acquisition	$ —	$ —	$ 3,688

See accompanying notes to the consolidated financial statements.

ZOGENIX INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Note 1 — Organization and Description of Business

Zogenix Inc., and subsidiaries (also referred to as Zogenix, we, our or us) is a global biopharmaceutical company committed to developing and commercializing therapies with the potential to transform the lives of patients and their families living with rare diseases. Our first rare disease therapy, Fintepla (fenfluramine) oral solution, has been approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of seizures associated with Dravet syndrome, a rare, devastating, severe lifelong epilepsy. Fintepla is also currently under development in Japan. We also have two additional late-stage development programs underway: one for Fintepla for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), and one for MT-1621, an investigational therapy for the treatment of thymidine kinase 2 deficiency (TK2d), a rare genetic disease.

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. We operate as a single operating segment engaged in the research, development and commercialization of pharmaceutical products, and our headquarters are located in Emeryville, California.

Liquidity

As of December 31, 2021, our cash, cash equivalents and marketable securities totaled $301.7 million. Excluding gains from two discrete business divestitures, we have incurred significant net losses and negative cash flows from operating activities since inception resulting in an accumulated deficit of $1.6 billion as of December 31, 2021. We expect to incur operating losses and negative cash flow for additional future periods due to costs associated with the commercialization of Fintepla for Dravet syndrome and pre-commercialization activities related to Fintepla for LGS in the U.S. and in the EU, the advancement of our clinical programs related to MT-1621 and CDD, and other infrastructure support costs. In addition, excluding amounts accrued for contingent consideration related to our acquisition of Brabant, we may be required to pay $100.0 million and $50.0 million in milestone payments upon regulatory approval of MT-1621 by the FDA and the EMA, respectively, related to our acquisition of Modis (See Note 4). These contingent consideration payments have not be recognized in the consolidated balance sheets as the regulatory approval contingency has not been resolved and the consideration is not yet payable. Historically, we have relied primarily on the proceeds from equity and convertible debt offerings to finance our operations. We believe our cash, cash equivalents and marketable securities balances will be sufficient to meet our anticipated operating requirements for at least the next 12 months following the date of issuance of these consolidated financial statements. Until such time, if ever, we can generate a sufficient amount of revenue to finance our cash requirements, we may need to continue to rely on additional financing to achieve our business objectives. However, there is no assurance that such financings could be consummated on acceptable terms or at all. Market volatility resulting from the global novel coronavirus disease (COVID-19) pandemic or other factors could also adversely impact our ability to access capital when and as needed. Failure to raise sufficient capital when needed could require us to significantly delay, scale back or discontinue one or more of our product development programs or commercialization efforts or other aspects of our business plans, and our operating results and financial condition would be adversely affected.

Note 2 — Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The consolidated financial statements and accompanying notes have been prepared in accordance with accounting principles generally accepted in the United States (GAAP). The consolidated financial statements include the accounts of Zogenix Inc. and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Variable Interest Entities

We consolidate a variable interest entity (VIE) if we are the primary beneficiary, defined as the party that has both the power to direct the activities that most significantly impact the VIE’s economic performance and the

obligation to absorb losses of or the right to receive benefits from the VIE that could potentially be significant to the VIE. A variable interest is a contractual, ownership or other interest that changes with changes in the fair value of the VIE's net assets exclusive of variable interests. To determine whether a variable interest we hold could potentially be significant to the VIE, we consider both qualitative and quantitative factors regarding the nature, size and form of our involvement with the VIE. Changes in the economic interests (either by us or third parties) or amendments to the governing documents of the VIE could affect an entity's status as a VIE or the determination of the primary beneficiary. If we are determined to be the primary beneficiary of a VIE, we would include the assets, liabilities, noncontrolling interests and results of activities of the VIE in our consolidated financial statements. The primary beneficiary evaluation is updated continuously.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Revenue Recognition

Our revenues consist of product sales of Fintepla and revenues derived from our collaboration arrangement with Nippon Shinyaku Co., Ltd. (Shinyaku). See Note 3.

Net Product Revenues

We recognize revenue when control of the promised good or service is transferred to the customer, in an amount that reflects the consideration we expect to be entitled to in exchange for those goods or services. We determine revenue recognition through the following steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when collectability of the consideration to which we are entitled in exchange for the goods or services we transfer to the customer is determined to be probable.

We distribute Fintepla in the U.S. through and arrangement with a specialty distributor who is our customer. The specialty distributor subsequently resells our product through its related specialty pharmacy provider to patients and health care providers. Separately, we have or may enter into payment arrangements with various third-party payers including pharmacy benefit managers, private healthcare insurers and government healthcare programs who provide coverage and reimbursement for our products that have been proscribed to a patient.

We distribute Fintepla in Europe (currently in Germany and France) through a third-party logistics provider (3PL) for distribution to pharmacies in those countries. The pharmacies are our customers, who subsequently resell our product directly to patients and health care providers.

Revenue from product sales is recorded at the net sales price (transaction price), which includes estimates of consideration payable to our customer and third-party payers for which reserves are established and that result from government rebates, chargebacks, co-pay assistance, prompt-payment discounts and other allowances that are offered under arrangements between us, our customer, and third-party payers related to the sales of Fintepla. These reserves are classified as either reductions of accounts receivable (if the amounts are payable to our customer) or as refund liabilities within current liabilities (if the amounts are payable to a party other than our customer). Amounts billed or invoiced are included in accounts receivable, net on our consolidated balance sheet. Under our current product sales arrangements, we do not have contract assets (unbilled receivables), as we generally invoice our customer before or at the time of revenue recognition, nor contract liabilities, as we do not receive prepayments from our customers prior to product delivery.

We recognize product revenues when a customer obtains control of our product, which occurs at a point in time and is typically upon delivery to the customer or, in the case of products that are subject to consignment agreements, when the customer takes title of the product from our consigned inventory location for shipment directly to a patient or healthcare provider. In the event the variable consideration is constrained, we include an amount to the extent it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur in a future reporting period. Depending on the type of variable consideration, we use either the most likely method or expected value method to estimate variable consideration related to Fintepla product sales. We do not have any

material constraints on our variable consideration included within the transaction price for Fintepla product sales. The actual amount of consideration ultimately received may differ from our estimates. If actual results in the future vary from estimates, the estimates will be adjusted, which will affect our revenue from net product sales in the period that such variances become known.

Each unit of Fintepla that is ordered by our customers represent a separate performance obligation that is completed when the customer obtains control of our product. We record product revenues, net of variable consideration, any applicable constraint, and consideration payable to parties other the customer at that point in time. We record shipping and handling costs within cost of product sales on our consolidated statements of operations. We classify payments to customers or its affiliates for certain services, to the extent that the services provided are distinct from the sale of our product and we can reasonably estimate its fair value, as selling, general and administrative expenses on our consolidated statements of operations. We have elected to exclude taxes collected from our customers and remitted to governmental authorities from the measurement of the transaction price.

We sell Fintepla to our customer at wholesale acquisition cost, and calculate product revenue from Fintepla sales, net of variable consideration and consideration payable to parties other than our customer. Variable consideration and consideration payable to parties other than the customer consists of estimates related to the following categories:

Trade Discounts and Allowances: We provide customers with discounts for prompt payment and we also pay fees to our exclusive specialty distributor in the U.S. for distribution services rendered that are not distinct from product sales. We expect customers to earn these discounts and fees, and accordingly we deduct these discounts and fees in full from our gross product revenue and accounts receivable at the time we recognize the related revenue.

Government Rebates: Fintepla is eligible for purchase by, or qualifies for reimbursement from, Medicaid and other U.S. and foreign government programs that are eligible for rebates on the price they pay for Fintepla. To determine the appropriate amount to reserve for these rebates, we identify the government-funded health insurer of patients who receive Fintepla as sold by our customers, apply the applicable government discount to these sales, and estimate the portion of total rebates that we anticipate will be claimed.

Other Rebates and Chargebacks: We may contract with various third-party payers for coverage and reimbursement of Fintepla. We estimate the rebates and chargebacks that we expect to be obligated to provide to such third-party payers based upon the terms of the applicable arrangement or negotiations with such third-party payers and our visibility regarding the payer mix.

Patient Assistance Program: We provide financial assistance to eligible patients whose insurance policies have high deductibles or co-payments and deduct our estimate of the amount of such assistance from gross product revenue.

Product Returns: In the U.S., we do not provide contractual return rights to our customer, except in instances where the product is damaged or defective, which we expect to be rare. In Europe, our customers have limited return rights. Because of the pricing of Fintepla and the limited number of patients, the retail pharmacies carry a limited inventory. Based on these factors and the fact that we have not experienced significant product returns to date, management has concluded that product returns will be minimal. In the future, if any of these factors and/or the history of product returns change, an allowance for product returns may be required.

Collaboration Revenue

We analyze our collaboration arrangements to assess whether such arrangements, or transactions between arrangement participants, involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities or are more akin to a vendor-customer relationship. In making this evaluation, we consider whether the activities of the collaboration are considered to be distinct and deemed to be within the scope of the collaborative arrangement guidance and those that are more reflective of a vendor-customer relationship and, therefore, within the scope of the revenue with contracts with customers guidance. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement.

For elements of collaboration arrangements that are not accounted for pursuant to the revenue from contracts with customers guidance, an appropriate recognition method is determined and applied consistently, generally by

analogy to the revenue from contracts with customers guidance. Amounts related to transactions with a counterparty in a collaborative arrangement that is not a customer are presented as collaboration revenue and on a separate line item from revenue recognized from contracts with customers, if any, in our consolidated statements of operations.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the consolidated balance sheets. If the related efforts underlying the deferred revenue is expected to be satisfied within the next twelve months this will be classified in current liabilities. Unconditional rights to receive consideration in advance of performance are recorded as receivables and deferred revenue in the consolidated balance sheets when we have a contractual right to bill and receive the payment, performance is expected to commence shortly and there is less than a year between billing and performance. Amounts recognized for satisfied performance obligations prior to the right to payment becoming unconditional are recorded as contract assets in the consolidated balance sheets. If we expect to have an unconditional right to receive consideration in the next twelve months, this will be classified in current assets. A net contract asset or liability is presented for each contract with a customer.

For arrangements or transactions between arrangement participants determined to be within the scope of the contracts with customers guidance, we perform the following steps to determine the appropriate amount of revenue to be recognized as we fulfill our obligations: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

At contract inception, we assess the goods or services promised in a contract with a customer and identify those distinct goods and services that represent a performance obligation. A promised good or service may not be identified as a performance obligation if it is immaterial in the context of the contract with the customer, if it is not separately identifiable from other promises in the contract (either because it is not capable of being separated or because it is not separable in the context of the contract), or if the performance obligation does not provide the customer with a material right.

We consider the terms of the contract and our customary business practices to determine the transaction price. The transaction price is the amount of consideration to which we expect to be entitled in exchange for transferring promised goods or services to a customer. The consideration promised in a contract with a customer may include fixed amounts, variable amounts, or both. Variable consideration will only be included in the transaction price when it is not considered constrained, which is when it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur.

If it is determined that multiple performance obligations exist, the transaction price is allocated at the inception of the agreement to all identified performance obligations based on the relative stand-alone selling prices unless the transaction price is variable and meets the criteria to be allocated entirely to one or more, but not all, performance obligations in the contract. The relative selling price for each performance obligation is based on observable prices if it is available. If observable prices are not available, we estimate stand-alone selling price for the performance obligation utilizing the estimated cost of the performance obligation with an estimated assumed margin. Once the transaction price has been allocated to a performance obligation using the applicable methodology, it is not subject to reassessment for subsequent changes in stand-alone selling prices.

Revenue is recognized when, or as, we satisfy a performance obligation by transferring a promised good or service to a customer. An asset is transferred when, or as, the customer obtains control of that asset. For performance obligations that are satisfied over time, we recognize revenue using an input or output measure of progress that best depicts our satisfaction of the relevant performance obligation. Revenues from performance obligations associated with a purchase order of Fintepla will be recognized when the customer obtains control of our product, which will occur at a point in time which may be upon shipment or delivery to the customer.

After contract inception, the transaction price is reassessed at every period end and updated for changes such as resolution of uncertain events. Any change in the overall transaction price is allocated to the performance obligations on the same methodology as at contract inception.

Management may be required to exercise judgment in estimating revenue to be recognized. Judgment is required in identifying performance obligations, estimating the transaction price, estimating the stand-alone selling prices of identified performance obligations, which may include forecasted revenue, development timelines,

reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success, and estimating the progress towards satisfaction of performance obligations.

Cost of Product Sales (Excluding Intangible Asset Amortization)

Cost of product sales (excluding intangible asset amortization) includes the cost of producing and distributing inventories that are related to product revenues during the respective period (including salary-related and stock-based compensation expenses for employees involved with production and distribution, freight and indirect overhead costs) and third-party royalties payable on our net product revenues. Cost of product sales may also include costs related to excess or obsolete inventory adjustment charges, abnormal costs, unabsorbed manufacturing and overhead costs, and manufacturing variances.

For the years ended December 31, 2021 and 2020, other than royalties and packaging costs, substantially all of our Fintepla inventory sold had a zero-cost basis as it was manufactured prior to the FDA's approval.

Accounts Receivable, Net

We record accounts receivable, net of certain fees paid to our customer for distribution services rendered to us that are not distinct from sales of product to our customer, prompt payment discounts and chargebacks based on contractual terms. We are also subject to credit risk from our accounts receivable related to our product sales. Accounts receivable are stated net of an allowance that reflects our current estimate of credit losses expected to occur over the life of the receivable. In developing our allowance for expected credit losses, we use assumptions to capture the risk of loss, even if remote, based on a number of factors including existing contractual payment terms, individual customer circumstances, historical payment patterns of our customers, a review of the local economic environment and its potential impact on expected future customer payment patterns.

The payment terms on our trade receivables are relatively short, generally 30 days. As a result, our collection risk is mitigated to a certain extent by the fact that sales are collected in a relatively short period of time, allowing for the ability to reduce exposure on defaults if collection issues are identified. As of December 31, 2021 and 2020, our sole specialty distributor customer in the U.S. accounted for approximately 83% and 100% of our accounts receivable, net. On a quarterly basis, we update our allowance as necessary to reflect expected credit losses over the remaining lives of the accounts receivable for outstanding trade receivables that are past due, have known disputes or have experienced any negative credit events that may result in future collectability issues. We do not currently expect our current or future exposures to credit losses to have a significant impact on us. The estimated allowance for expected credit losses was not material as of December 31, 2021 or 2020, nor were the changes to the allowance during any of the periods presented. However, our customers' ability to pay us on a timely basis, or at all, could be affected by factors specific to their respective businesses and/or by economic conditions, including those related to the COVID-19 pandemic, the extent of which cannot be fully predicted.

Accounts receivable, net, excludes amounts payable to us related to regulatory milestones earned under the Shinyaku Agreement. As of December 31, 2021, we recorded a $3.0 million receivable related to the achievement of a regulatory milestone upon submission of a Japanese new drug application (JNDA) for Dravet syndrome within other current assets on the consolidated balance sheets.

Inventory

Inventory is recorded at the lower of cost or net realizable value, with cost determined on a first-in, first-out basis. Inventory costs include third-party contract manufacturing, third-party packaging services, freight, salaries, wages and stock-based compensation for personnel involved in the manufacturing process, and indirect overhead costs. We periodically review our inventories to identify obsolete, slow moving, excess or otherwise unsaleable items. If obsolete, slow moving, excess or unsaleable items are observed and there are no alternate uses for the inventory, we record a write-down to net realizable value. The determination of net realizable value requires judgment including consideration of many factors, such as estimates of future product demand, product net selling prices, current and future market conditions and potential product obsolescence, among others.

Prior to regulatory approval, we expense costs associated with the manufacture of our product candidates to research and development expense unless we are reasonably certain such costs have future commercial use and net realizable value. Since we consider attaining regulatory approval of a product candidate to be highly uncertain and difficult to predict, we expect only in rare instances will pre-launch inventory be capitalized, if at all.

Acquisitions

We evaluate acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination or asset acquisition by first applying a screen test to determine if substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. If the screen is met, the transaction is accounted for as an asset acquisition. If the screen is not met, further determination is required as to whether or not we have acquired inputs and processes that have the ability to create outputs which would meet the definition of a business. Significant judgment is required in the application of the screen test to determine whether an acquisition is a business combination or an acquisition of assets.

If the transaction is determined not to be a business combination, it is accounted for as an asset acquisition. For asset acquisitions, a cost accumulation model is used to determine the cost of an asset acquisition. Common stock issued as consideration in an asset acquisition is generally measured based on the acquisition date fair value of the equity interests issued. Direct transaction costs are recognized as part of the cost of an asset acquisition. We also evaluate which elements of a transaction should be accounted for as a part of an asset acquisition and which should be accounted for separately. Consideration deposited into escrow accounts are evaluated to determine whether it should be included as part of the cost of an asset acquisition or accounted for as contingent consideration. Amounts held in escrow where we have legal title to such balances but where such accounts are not held in our name, are recorded on a gross basis as an asset with a corresponding liability in our consolidated balance sheet.

The cost of an asset acquisition, including transaction costs, are allocated to identifiable assets acquired and liabilities assumed based on a relative fair value basis. Goodwill is not recognized in an asset acquisition. Any difference between the cost of an asset acquisition and the fair value of the net assets acquired is allocated to the non-monetary identifiable assets based on their relative fair values. Assets acquired as part of an asset acquisition that are considered to be in-process research and development (IPR&D) are immediately expensed unless there is an alternative future use in other research and development projects.

In addition to upfront consideration, our asset acquisitions may also include contingent consideration payments to be made for future milestone events or royalties on net sales of future products. We assess whether such contingent consideration meets the definition of a derivative. Contingent consideration payments in an asset acquisition not required to be accounted for as derivatives are recognized when the contingency is resolved, and the consideration is paid or becomes payable. Contingent consideration payments required to be accounted for as derivatives are recorded at fair value on the date of the acquisition and are subsequently remeasured to fair value at each reporting date. Contingent consideration payments made prior to regulatory approval are expensed as incurred. Contingent consideration payments made subsequent to regulatory approval are capitalized as intangible assets and amortized, subject to impairment assessments.

We classify cash payments related to purchased intangibles in an asset acquisition, including IPR&D assets, as a cash outflow from investing activities because we expect to generate future income and cash flows from these assets if they can be developed into commercially successful products.

If the acquisition is determined to be a business combination, all tangible and intangible assets acquired, including any IPR&D asset, and liabilities assumed, including contingent consideration, are recorded at their fair value. Goodwill is recognized for any difference between the price of acquisition and our fair value determination. In addition, direct transaction costs in connection with business combinations are expensed as incurred, rather than capitalized.

Fair Value of Financial Instruments

Our financial instruments, including cash and cash equivalents, other current assets, promissory note receivable, 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 Note 7 for financial instruments measured or disclosed at fair value for marketable securities, contingent consideration liabilities and our convertible senior notes.

Cash Equivalents and Marketable Securities

We consider 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.

We invest our 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. All of our marketable securities have been accounted for as available-for-sale and carried at fair value. We have classified all of our available-for-sale marketable securities, including those with maturity dates beyond one year, as current assets on the consolidated balance sheets as we may sell these securities at any time for use in current operations even if they have not yet reached maturity. 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 on marketable securities are included in other income (expense). Gains and losses on sales are recorded based on the trade date and determined using the specific identification method.

We periodically assess our available-for-sale marketable securities for impairment. For debt securities in an unrealized loss position, this assessment first takes into account our intent to sell, or whether it is more likely than not that we will be required to sell the security before recovery of its amortized cost basis. If either of these criteria are met, the debt security's amortized cost basis is written down to fair value through interest and other, net. For debt securities in an unrealized loss position that do not meet the aforementioned criteria, we assess whether the decline in fair value has resulted from credit losses or other factors. In making this assessment, we consider the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and any adverse conditions specifically related to the security, among other factors. If this assessment indicates that a credit loss may exist, the present value of cash flows expected to be collected from the security are compared to the amortized cost basis of the security. If the present value of cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for credit losses will be recorded in other income (expense), net, limited by the amount that the fair value is less than the amortized cost basis. Any additional impairment not recorded through an allowance for credit losses is recognized in other comprehensive loss. Changes in the allowance for credit losses are recorded as provision for (or reversal of) credit loss expense. Losses are charged against the allowance when management believes the uncollectability of an available-for-sale security is confirmed or when either of the criteria regarding intent or requirement to sell is met. These changes are recorded in other income (expense), net.

Concentration of Credit Risk

As is common in the pharmaceutical industry for products treating rare diseases, Fintepla is distributed through exclusive arrangements with a specialty distributor in the U.S. and through a third-party logistics (3PL) provider who distributes to pharmacies throughout Europe (currently, in Germany and France). As a result, our accounts receivable balance at December 31, 2021 and 2020 is highly concentrated with our U.S. customer, who accounted for 83% and 100% of the balance, respectively.

In addition, our investments in cash equivalents and marketable securities potentially subject us to concentrations of credit risk. As stated in our investment policy, the primary objective of our investment activities is to preserve principal and maintain a desired level of liquidity to meet working capital needs. Accordingly, our investment portfolio consists of investment-grade rated securities with active secondary or resale markets and is subject to established guidelines relative to diversification and maturities to maintain safety and liquidity. Historically, we have not experienced any material credit losses on our investments, and we believe our exposure to credit risk related to our investing activities are limited. We maintain amounts on deposit with various financial institutions, which may exceed federally insured limits. However, management periodically evaluates the creditworthiness of those institutions, and we have not experienced any losses on such deposits.

Concentration of Supplier Risk

Certain materials and key components that we utilize in our operations are obtained through single suppliers. Since the suppliers of key components and materials must be named in a New Drug Application (NDA) or supplemental NDA (sNDA) 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 our suppliers were interrupted for any reason, we may be unable to supply any of our approved products or product candidates for clinical trials.

Impact of COVID-19 Pandemic

The full extent to which the ongoing coronavirus disease 2019 (COVID-19 pandemic) will directly or indirectly impact our business continues to evolve and its results on our operations and financial condition, will depend on

future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19, including any related variants, and the actions taken to contain it or treat COVID-19.

Our ability to successfully commercialize and generate revenue from Fintepla may be directly or indirectly impacted by the COVID-19 pandemic. In addition to our ongoing launch of Fintepla for Dravet syndrome in existing and new markets, we are preparing for a potential product launch of Fintepla for LGS in the U.S., which the FDA granted our supplemental New Drug Application (sNDA) Priority Review with a Prescription Drug User Fee Act (PDUFA) target action date in March 2022. While restrictive safety measures are in place, our sales professionals did not have the same level of in-person interactions with physicians and healthcare providers to conduct educational and promotional activities for Fintepla as they would have absent the COVID-19 pandemic. In response, we have implemented a virtual sales model to supplement traditional means of customer engagement. Although some of these restrictions have been, and may continue to be lifted in certain jurisdictions, the impact of prior and continued COVID-19 related safety measures, and the potential for re-imposition of restrictions due to local surges and new waves of infection, including those caused by certain variants of the virus, may adversely affect the ability of our sales professionals to effectively market Fintepla, which may have a negative impact on our sales and our market penetration. In addition, the evolving COVID-19 pandemic could directly or indirectly impact the pace of patient enrollment of our Phase 3 study of Fintepla for the treatment of seizures associated with CDKL5 syndrome (CDD), which we initiated in September 2021. To date, we have not experienced any significant interruptions in our ability to supply Fintepla for commercial use in Dravet syndrome or clinical trials for LGS, or MT1621 to our patients currently enrolled in our clinical trials. We currently do not anticipate any interruptions in supply. Any delays in the completion of our clinical trials and any disruption in our supply chain could have a material adverse effect on our business, results of operations and financial condition.

As of December 31, 2021, the COVID-19 pandemic has not impacted the carrying values of our inventory, finite-lived intangible asset, goodwill, long-lived assets and right-of-use assets. Our future assessment of the magnitude and duration of COVID-19, as well as other factors, could result in material impacts to our consolidated financial statements in future reporting periods. Adjustments may be made in subsequent periods to reflect more current estimates and assumptions about matters that are inherently uncertain. Actual results may differ.

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

Upon sale or retirement of the assets, the cost and related accumulated depreciation are removed from the consolidated balance sheet and the resulting gain or loss is recognized in the consolidated statement of operations. Expenditures for maintenance and repairs are expensed as incurred.

Goodwill

Goodwill represents the difference between the purchase price and the estimated fair value of the net assets acquired in a business acquisition. The goodwill balance of $6.2 million at December 31, 2021 and 2020 is directly attributable to our acquisition of Brabant Pharma Limited (Brabant) in 2014 to obtain worldwide development and commercialization rights to Fintepla.

Goodwill is not amortized, but instead is reviewed for impairment at least annually on our assessment date of October 1, or more frequently if events occur or circumstances change that would indicate the carrying amount may be impaired. Goodwill is assigned to, and impairment testing is performed at, the reporting unit level. We determined we have only one reporting unit, which is the same as our operating segment, as well as our reportable segment. Accordingly, our impairment testing is performed at the entity-wide level.

For the year ended December 31, 2021, we performed a quantitative impairment test by comparing the fair value of our net assets with their carrying amounts. As we have a single reporting unit, an appropriate measure of the fair value of our net assets is our market capitalization on the assessment date. Our market capitalization, excluding any potential adjustment for a control premium, exceeded the carrying amount of our net assets as of

October 1, 2021 by a significant amount and we determined our goodwill was not impaired. There were no goodwill impairment charges for all periods presented.

Purchased Intangible Asset

In connection with the acquisition of Brabant, we also recorded an in-process research and development (IPR&D) asset with an estimated fair value of $102.5 million on the acquisition date.

Intangible assets acquired in a business combination related to IPR&D projects are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. In connection with the FDA's approval of Fintepla for marketing in June 2020, we determined the project under development was considered complete and its useful life was no longer indefinite. Prior to the commencement of amortization over its estimated useful life, we performed a final impairment test utilizing a qualitative test and determined there was no impairment. Intangible assets subject to amortization are assessed for impairment as long-lived assets. Finite-lived intangible assets are amortized using the method that best reflects how their economic benefits are utilized or, if a pattern of economic benefits cannot be reliably determined, on a straight-line basis over their estimated useful lives (see Note 9).

Impairment Assessments Related to Long-Lived Assets

Long-lived assets, including finite-lived intangible assets and right-of-use operating lease assets, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets (group) may not be recoverable. Recoverability of assets is determined by comparing the estimated undiscounted net cash flows of the operations related to the assets (asset group) to their carrying amount. If the carrying value of the assets (asset group) exceeds its undiscounted cash flows, we then compare the fair value of the assets (asset group) to their carrying value to determine the impairment loss. The impairment loss will be allocated to the carrying values of the long-lived assets (asset group), but not below their individual fair values.

If we determine that events and circumstances warrant a revision to the remaining period of amortization or depreciation for a specific long-lived asset, its remaining estimated useful life will be revised, and the remaining carrying amount of the long-lived asset will be depreciated or amortized prospectively over the revised remaining estimated useful life. There were no impairment charges or changes to estimated useful lives for long-lived assets (groups) for all periods presented.

Leases

We determine whether the contract is or contains a lease at the inception of the arrangement and if such a lease is classified as a financing lease or operating lease at lease commencement. All of our leases are classified as operating leases. Leases with a term greater than one year are included in operating lease right-of-use assets (ROU asset), current portion of lease liabilities, and lease liabilities, net of current portion in our consolidated balance sheet. If a lease contains an option to renew, the renewal option is included in the calculation of lease liabilities if we are reasonably certain at lease commencement the renewal option will be exercised. Lease liabilities and their corresponding ROU assets are measured at the present value of the remaining lease payments, discounted at an appropriate incremental borrowing rate at lease commencement. Management uses judgment to estimate the appropriate incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Certain adjustments to the ROU asset may be required for items such as initial direct lease costs, lease incentives, scheduled rent escalations and impairment charges if we determine the ROU asset is impaired. Operating lease expense is recognized on a straight-line basis over the lease term.

We do not separate lease components from non-lease components for all existing lease classes. We also do not record leases on our consolidated balance sheets when a lease has a term of one year or less.

Contingent Consideration Related to Business Acquisitions

In connection with the acquisition of Brabant in 2014, we may be required to pay future consideration that is contingent upon the achievement of specified development, regulatory approval and sales-based milestone events for Fintepla. Prior to regulatory approval, we estimate the fair value of contingent consideration liabilities using a

probability-weighted discounted cash flow analysis, which reflects the probability and timing of future payments and a risk-adjusted discount rate.

At each reporting period prior to settlement, we remeasure these liabilities by performing a review of the assumptions discussed above and record an adjustment to reflect any changes in the estimated fair value of our contingent consideration liabilities. Adjustments to the estimated fair value of contingent consideration are included within operating expenses in the consolidated statements of operations. In the absence of any significant changes in key assumptions during a reporting period, the fair value of the contingent consideration liability is expected to increase each period with the recognition of change in fair value of contingent consideration resulting from the passage of time at the applicable discount rate as we approach the payment dates of the contingent consideration. Judgment is used in determining Level 3 inputs and fair value measurements as of a reporting date. Updates to assumptions could have a significant impact on our consolidated results of operations in a reporting period and actual results may differ from estimates. For example, increases in the projected product revenues would decrease the time to payment and bring the contingent consideration liability closer to its undiscounted amount; decreases in these items would have the opposite effect. Increases in the discount rate or to the projected timing of payments would bring the contingent consideration liability further from its undiscounted amount; decreases in these items would have the opposite effect.

Segment Information

Operating segments are defined as components of an enterprise for which discrete financial information is available that is evaluated on a regular basis by our chief operating decision-maker (CODM) in deciding how to allocate resources to an individual segment and in assessing performance of the segment. We operate as a single operating segment engaged in the research, development and commercialization of pharmaceutical products. Our CODM, which is our President/Chief Executive Officer, reviews our operating results on a consolidated basis and manages our operations as a single operating segment. Substantially all of our long-lived assets are located in the U.S.

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 regulatory approval, license fees prior to regulatory approval, professional services, travel costs, dues and subscriptions, depreciation, materials used in clinical trials and research and development and costs incurred related to our agreement with Nippon Shinyaku Co., Ltd. We expense costs relating to the purchase and production of pre-approval inventories as research and development expense in the period incurred until regulatory approval is received. Payments made prior to the receipt of goods or services to be used in research and development are recorded as prepaid assets on our consolidated balance sheets until the goods or services are realized or consumed. We classify such prepaid assets as current or non-current assets based on our estimates of the timing of when the goods or services will be realized or consumed.

Our expense accruals for clinical trials are based on estimates of the services received from clinical trial investigational sites, contract research organizations (CROs) and other third-party vendors that support us in our research and development efforts. Payments under some of our contracts with these service providers depend on factors such as the achievement of clinical milestones such as the successful enrollment of certain numbers of patients, site initiation, or completion of a clinical trial. In accruing for these services at each reporting date, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If available, we obtain information regarding unbilled services directly from these service providers. However, we may be required to estimate our accrual based only on information available to us. Once established, accruals are adjusted from time to time, as appropriate, in light of additional information. Amounts ultimately incurred in relation to amounts accrued for these services at a reporting date may be substantially higher or lower than our estimates.

Advertising Costs

Advertising costs, which include promotional expenses are expensed as incurred and recorded within selling, general and administrative expenses. For the years ended December 31, 2021 and 2020, advertising costs totaled $4.4 million and $1.6 million.

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. We provide 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. We recognize 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 tax position.

U.K.'s Research and Development (R&D) Tax Relief Scheme

We carry out extensive research and development activities that benefit from U.K.'s small and medium-sized enterprises (SME) R&D tax relief scheme, whereby an entity has an option to receive an enhanced U.K. 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 U.K. 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.

Foreign Currency Translation and Transactions

We have certain foreign operations where their functional currency was determined to be their local currency. For these foreign subsidiaries, the local currency of their monetary assets and liabilities are translated to U.S. Dollars at the rates of exchange in effect on the balance sheet date, and local currency revenues and expenses are translated to U.S. Dollars at average rates of exchange in effect during the period. The resulting translation gains or losses are included in our consolidated statements of comprehensive loss as a component of other comprehensive income (loss) and in the consolidated statements of stockholders' equity. We also recognize gains and losses on transactions that are denominated in a currency other than the respective subsidiary's functional currency in other income (expense), net in the consolidated statements of operations.

Other Comprehensive Income (Loss)

Components of other comprehensive income (loss) include changes in fair value of our available-for-sale marketable securities, reclassification adjustments from realization of gain (loss) on sale of marketable securities included in net loss and foreign currency translation adjustments.

Stock-Based Compensation

We recognize 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 expense is recognized on a straight-line basis over the requisite service period. We account for forfeitures as they occur. Stock-based compensation is classified in the accompanying statements of operations based on the function to which the related services are provided. From time to time, we may grant broad-based restricted stock units to employees, including executive officers, that vest upon the satisfaction of both service-based and performance-based vesting conditions. We recognize stock-based compensation over the requisite service period for awards with a performance condition if the performance condition is deemed probable of being met. As a result, our stock-based compensation expense may experience fluctuations, which may impact our reported financial results and period-to-period comparisons of our consolidated statements of operations.

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 represents the estimated length of time over which we expect an option will be outstanding. We used the simplified method, as provided for under the applicable guidance for entities with a limited history of relevant stock option exercise activity, to estimate the expected term.
- Expected volatility—The expected volatility was calculated based on our historical stock prices over the expected term.
- 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 expected term of the option.
- Expected dividend yield—The expected dividend yield was based on our historical practice and anticipated dividends over the expected term of the option.

Valuation of Restricted Stock Units

The fair value of each restricted stock unit was based on our closing stock price on the date of grant.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding during the period, without consideration of common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given our net loss.

Accounting Pronouncements Issued But Not Yet Effective

Account Standard Update (ASU) 2020-06, Debt — *Debt with Conversion and Other Options (subtopic 470-20) and Derivatives and Hedging — Contracts in Entity's Own Equity* (subtopic 815-40) (ASU 2020-06) simplifies the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible debt instruments with cash conversion features. Specifically, ASU 2020-06 removes the existing guidance that we currently follow for our convertible senior notes, which requires entities to account for cash conversion features in equity separately from the host contract. These amendments are expected to result in more freestanding financial instruments qualifying for equity classification and, as a result, not accounted for as derivatives, as well as fewer embedded features requiring separate accounting from the host contract. In addition, ASU 2020-06 eliminates the treasury stock method when calculating diluted earnings per share for convertible instruments that can be settled in whole or in part with equity and requires the use of the if-converted method. Early adoption is permitted, but no earlier than the fiscal year beginning after December 15, 2020. The standard can be applied using a full or modified retrospective approach.

ASU 2020-06 will be effective for us as of January 1, 2022. When effective, we expect the accounting for our convertible senior notes as a single unit of account will: i) increase the carrying value of our convertible notes to be closer to its outstanding principal balance, ii) decrease our interest expense over the expected life of the financial instrument, and iii) result in the debt instrument's effective interest rate to be closer to the stated coupon rate. In addition, the use of the treasury stock method, which allows an entity with a stated policy of settling convertible instruments with a combination of cash and shares to exclude shares issuable upon conversion that it expects to settle with cash when calculating diluted earnings per share, is no longer permitted. Even if we have the intent and ability to settle conversions by paying the conversion value in cash, up to the principal amount being converted and any excess in shares, the adoption of ASU 2020-06 will require that we presume such instruments will be settled by issuance of shares (the "if-converted method"). As a result, our diluted earnings per share under ASU 2020-06 may be lower than if we were able to apply the treasury stock method when calculating the dilutive effect of our senior convertible notes in earnings per share.

We will adopt the new guidance in the annual period beginning January 1, 2022, on a modified retrospective basis. On the date of adoption, we expect to record a net decrease to additional paid-in capital of approximately $75.3 million to remove the equity component separately recorded for the conversion features associated with the convertible debt instruments and equity component associated with the issuance costs, an increase of approximately $65.6 million in the carrying value of our senior convertible notes to reflect the full principal amount of the Notes outstanding net of issuance costs, and a decrease of approximately $9.7 million to accumulated deficit. These preliminary estimates could change as we continue with our implementation efforts. We do not expect an impact to the our statements of operations or cash flows as the result of the adoption of this ASU.

ASU 2021-10, *Government Assistance (Topic 832): Disclosures by Business Entities About Government Assistance*. This ASU provided guidance to increase the transparency of government assistance including the disclosure of i) the types of assistance, ii) an entity's accounting for the assistance, and iii) the effect of the assistance on an entity's financial statements. Under the new guidance, an entity is required to provide the following annual disclosures about transactions with a government that are accounted for by applying a grant or contribution accounting model by analogy: i) information about the nature of the transactions and the related accounting policy used to account for the transactions, ii) the line items on the balance sheet and income statement that are affected by the transactions, and the amounts applicable to each financial statement line item and, iii) significant terms and conditions of the transactions, including commitments and contingencies. This update is effective for us on January 1, 2022, with early adoption permitted. The amendments should be applied either i) prospectively to all transactions within the scope of the amendments that are reflected in financial statements at the date of initial application and new transactions that are entered into after the date of initial application or ii) retrospectively to those transactions. We have not yet adopted this standard, but have described in Note 18, the U.K.'s R&D Tax Relief Scheme from which we benefit.

Note 3 — Revenues

Net Product Sales

We record product sales of Fintepla at the net sales price (transaction price), which includes estimates of consideration payable to our customers and third-party payers for which reserves are established and that result from government rebates, chargebacks, co-pay assistance, prompt-payment discounts and other allowances that are offered under arrangements between us, our customers, and third-party payers.

Fintepla for Dravet syndrome was approved for marketing by the United States Food and Drug Administration (FDA) in the U.S. in June 2020 and by the European Medicine Agency (EMA) in Europe in December 2020. The following table presents our net product sales of Fintepla disaggregated by geographical area:

	Year Ended December 31,	
(In thousands)	2021	2020
United States	$ 65,683	$ 9,587
Europe	9,057	—
Total net product sales	$ 74,740	$ 9,587

The following table summarizes the provisions, and credits/payments, for sales-related deductions.

(In thousands)	Rebates	Trade Discounts, Distributor Fees and Other	Total
Balance at December 31, 2019	$ —	$ —	$ —
Provisions	1,203	380	1,583
Credits/payments	(42)	(251)	(293)
Balance at December 31, 2020	$ 1,161	$ 129	$ 1,290
Provisions	10,096	2,775	12,872
Credits/payments	(6,972)	(2,679)	(9,651)
Balance at December 31, 2021	4,285	225	4,511

Customer Concentration

Our specialty distributor in the U.S. accounted for 88% and 100% of net product revenue for the years ended December 31, 2021 and 2020, respectively.

Collaboration Revenue

In March 2019, we entered into an agreement (Shinyaku Agreement) with Nippon Shinyaku Co., Ltd. (Shinyaku) for the exclusive distribution of Fintepla in Japan for the treatment of Dravet syndrome and LGS. As part

of the Shinyaku Agreement, we are responsible for completing the global clinical development and all regulatory approval activities for Fintepla to support the submission of new drug applications in Japan for Dravet syndrome and LGS. Shinyaku will be responsible for the commercialization activities including the promotion, marketing, sale and distribution of Fintepla in Japan. Upon regulatory approval of Fintepla in Japan, Shinyaku will also act as our exclusive distributor for commercial shipment and distribution of Fintepla in Japan. If we pursue global development of Fintepla for indications other than Dravet syndrome or LGS, Shinyaku has the option to participate in the development for such indications in Japan, subject to cost sharing requirements pursuant to the agreement. Activities under the Shinyaku Agreement will be governed by a joint steering committee (JSC) consisting of three representatives from each party to the agreement. All decisions of the JSC are to be made by a unanimous vote with tie-breaking rights provided to each party for certain matters related to development, regulatory approval and commercialization.

Shinyaku has agreed to support development and regulatory approval of Fintepla in Japan by actively participating in the design of non-clinical, clinical and manufacturing requirements needed for regulatory submission, actively planning and participating in product labeling decisions and discussions with the Japanese Ministry of Health, Labor and Welfare (MHLW) and obtained distribution exclusivity through the payment of $20.0 million. We will be actively running the clinical trials, performing manufacturing validation activities, preparing regulatory filings and holding discussions with MHLW, and negotiating pricing. We and Shinyaku have agreed to proportionally share the Japan specific development costs that may arise outside of the initial development plan and any post-approval clinical study costs in Japan. In addition, we can earn up to $66.0 million from Shinyaku for the achievement of certain regulatory milestones related to the treatment of Dravet syndrome and the treatment of seizures associated with LGS.

After regulatory approval of Fintepla in Japan has been obtained, we have agreed to supply Shinyaku with Fintepla upon receipt of purchase orders at our actual manufacturing cost plus a fixed transfer price mark-up, a fixed percentage of Shinyaku's net sales of Fintepla in Japan for such fiscal year, and a net price mark-up based on a percent of the applicable aggregate sales of Fintepla by Shinyaku for such fiscal year. The net price mark-up percentage increases with Shinyaku’s sales of Fintepla annual net sales in Japan and ranges between mid-twenties and is capped at a low thirties of the aggregate annual net sales for an applicable fiscal year.

In addition, we can earn up to an additional $42.5 million tied to the achievement of certain net sales milestones by Shinyaku through the term of the agreement.

The Shinyaku Agreement expires in September of 2045, unless earlier terminated by either party for a change in control, a material breach, bankruptcy, dissolution, or winding up of such other party. The Shinyaku Agreement may be also terminated by either party: (1) with one year prior written notice to the other party on or after the date of the first commercial sale of a competing generic version of the Fintepla in Japan, (2) if, prior to the launch of the Fintepla in Japan, a party has a good faith concern, based on credible evidence, that such launch is not likely to be possible with commercially reasonable efforts, or (3) if a party believes Fintepla poses a substantial safety concern. We may also terminate the agreement following the second anniversary of the first commercial sale of the Fintepla in Japan if Shinyaku has failed to achieve or maintain certain diligence obligations under the Shinyaku Agreement. Shinyaku may also terminate the agreement if, prior to the launch of the Fintepla in Japan, Shinyaku has a good faith concern that Fintepla will not be commercially viable in Japan.

We concluded that collaborative activities under the Shinyaku Agreement prior to regulatory approval are within the scope of the collaborative arrangements guidance as both parties are active participants and are exposed to significant risks and rewards dependent on the success of commercializing Fintepla in Japan. Shinyaku is not a customer as it does not obtain an output of our development and regulatory approval activities for Fintepla as they were not provided a license to its intellectual property or the ability to manufacture the product, and we do not consider performing development and regulatory approval services to be a part of our ongoing activities.

We considered the revenue from contracts with customers guidance by analogy in determining the unit of account, and the recognition and measurement of such unit of account for collaborative activities under the Shinyaku Agreement and concluded that there are two development programs akin to performance obligations related to collaborative activities for development and regulatory approval efforts for Dravet and LGS. Participation on the JSC was concluded to be both quantitatively and qualitatively immaterial in the context of the Shinyaku Agreement. We are the principal as it relates to the collaborative development and regulatory approval activities primarily because we are responsible for the acceptability of the results of the work of the third-party vendors that are used to assist us in performing such activities. Therefore, such collaboration revenue has been presented on a gross basis in our consolidated statements of operations apart from research and development expenses incurred.

The initial collaboration consideration allocated on a relative standalone selling price basis to each associated development program was determined using the most likely method to consist solely of the fixed consideration payments of $20.0 million. Analogizing to the revenue from contracts with customers variable consideration guidance, all potential regulatory milestone payment consideration will be included in the collaboration consideration if and when it is probable that a significant reversal in the amount of cumulative collaboration consideration recognized will not occur when the uncertainty associated with the variable collaboration consideration is subsequently resolved. As of December 31, 2021, the total transaction price was $23.0 million and consisted of i) the initial $20.0 million fixed consideration and ii) a $3.0 million regulatory submission milestone that was achieved in the fourth quarter of 2021 related to the Dravet syndrome program. The $3.0 million in variable consideration was allocated to the Dravet syndrome program. The remaining variable consideration was determined to be fully constrained, as the achievement of the events tied to these regulatory milestone payments was highly dependent on factors outside of our control.

Collaboration revenue is being recognized over time as the collaborative activities related to each development program are rendered. We determined an input method is a reasonable representative depiction of the performance of the collaborative activities under the Shinyaku Agreement. The method of measuring progress towards completion incorporates actual internal and external costs incurred, relative to total internal and external costs expected to be incurred over an estimated period to satisfy the collaborative activities. The period over which total costs are estimated reflects our estimate of the period over which it will perform the collaborative activities for each development program. Changes in estimates of total internal and external costs expected to be incurred are recognized in the period of change as a cumulative catch-up adjustment to collaboration revenue.

For the years ended December 31, 2021 and 2020, we recognized collaboration revenue of $7.0 million and $4.1 million, respectively. As of December 31, 2021, $8.3 million related to this arrangement was recorded as deferred revenue, which is classified as either current or net of current portion in the accompanying consolidated balance sheets based on the period over which the collaboration revenue is expected to be recognized. We expect to recognize collaboration revenue related to these collaborative activities through early 2024.

We concluded that the supply of Fintepla to Shinyaku will be within the scope of the revenue from contracts with customers guidance if regulatory approval in Japan occurs and when a purchase order is received from Shinyaku. Such activity is considered to be a vendor customer relationship as Shinyaku will be a party that has contracted with an us to obtain goods or services that are an output of our ordinary activities in exchange for consideration and selling approved commercial product to a customer is expected to be part of our ongoing activities. Each purchase order for a shipment of Fintepla will be identified as a separate performance obligation as we did not grant Shinyaku intellectual property rights. The agreed upon price for the supply of Fintepla (cost plus a fixed transfer price mark-up, fixed percentage of aggregate sales of Fintepla by Shinyaku per year, the net price mark-up and sales milestones) to Shinyaku does not represent a material right, and therefore is not a performance obligation, and such pricing on an aggregate basis represents the standalone selling price a distributor would typically pay for such a product in that region or market. There are also no minimum purchase commitments. The transaction price to be allocated to the performance obligation will include the fixed consideration associated with the cost-plus price of Fintepla and variable consideration associated with a fixed percentage of aggregate sales of Fintepla by Shinyaku per year, the net price mark-up and sales milestones subject to the constraint. To date, Shinyaku has not provided us with any purchase orders and thus no revenue has been recognized for the supply of Fintepla.

Note 4 — Acquisitions

Asset Acquisition of Modis

In September 2019, we acquired all of the outstanding equity interests of Modis, a privately-held biopharmaceutical company, to expand our late-stage development pipeline. Modis was formed in May 2016 through a collaboration with academic experts in mitochondrial biology. Modis holds an exclusive worldwide license from Columbia University in New York City (Columbia) to certain intellectual property rights owned or controlled by Columbia to develop and commercialize MT1621. MT-1621 is an investigational deoxynucleoside substrate enhancement therapy (SET) for the treatment of TK2d, an inherited mitochondrial DNA depletion disease that predominantly affects children and is often fatal. Aggregate upfront consideration transferred of approximately $246.5 million consisted of $175.5 million in cash payments made and 1,595,025 unregistered shares of our common stock issued to the outstanding shareholders of Modis as well as employee award holders under the legacy Modis 2017 Stock Plan (Modis Plan). The fair value of common stock issued as acquisition consideration

was $68.1 million on the date the transaction closed. Also included in the aggregate upfront consideration transferred were $3.5 million of transaction costs incurred, reduced by a net working capital adjustment receivable of $0.6 million. Pursuant to the terms of the Modis purchase agreement, certain unvested awards held by employees under the Modis Plan converted into the right to receive a pro-rata share of the purchase consideration at the date of acquisition, with no future service requirement. A component of the total consideration transferred was attributed to the unvested awards with a fair value of $4.9 million and was accounted for as a separate transaction from the asset acquisition. This amount was immediately expensed and included in acquired in-process research and development and related costs in the consolidated statements of operations for the year ended December 31, 2019.

Of the upfront cash consideration, $25.0 million was deposited into an escrow account to fund post-closing net working capital adjustments, and general representations and warranties for a one-year period, which was subsequently released in 2020. In addition, the former shareholders of Modis were eligible to receive milestone payments consisting of $100.0 million upon FDA approval and $50.0 million upon EMA approval of MT-1621, as well as a 5% royalty on any future net sales of specified Modis products. The upfront cash consideration was funded by cash and marketable securities on hand. The shares of our common stock provided as consideration were subsequently registered under our existing shelf registration statement on Form S-3 (No. 333-220759).

We determined substantially all of the fair value of Modis was concentrated in a single IPR&D asset group, which included license rights, clinical trial data, clinical trial development plans, research and development materials, formulations and intellectual property related to MT-1621. Accordingly, the acquired set of assets and activities did not meet the definition of a business. As a result, we accounted for the transaction as an asset acquisition and allocated the remaining upfront consideration transferred to the identifiable tangible and intangible assets acquired and liabilities assumed based on their relative fair values resulting in $244.5 million being assigned to the IPR&D asset associated with MT-1621 and $2.8 million for assumed net liabilities.

As of the acquisition date, Modis had completed a pivotal Phase 2 retrospective treatment clinical trial study (RETRO) of MT-1621 substrate enhancement therapy in patients with TK2d and commenced a Phase 2 prospective, open-label extension clinical trial study of patients with TK2d. As the MT-1621 program had not yet reached technological feasibility and had no alternative future use, the purchased IPR&D asset was expensed immediately subsequent to the acquisition within our consolidated statements of operations. As we had no tax basis in the acquired IPR&D asset, and the acquired IPR&D asset was expensed prior to the measurement of any deferred taxes, no deferred taxes were recognized for the initial differences between the amounts recognized for financial reporting and tax purposes.

The milestone payments due upon FDA or EMA approval and royalty payments on future net sales of MT-1621 products were determined to be contingent consideration and not subject to derivative accounting. Any contingent consideration will be recognized when the contingency is resolved and the consideration becomes payable. As of December 31, 2021 and 2020, no such amounts were deemed to be payable.

The nature of the remaining efforts for completion of the MT-1621 program primarily consist of performing clinical trials and validating contract manufacturing abilities, the cost, length and success of which are extremely difficult to determine. Numerous risks and uncertainties can delay or stop clinical development of a pharmaceutical product prior to the receipt of marketing approval, including, but not limited to, results from clinical trials that do not support continuing development, issues related to manufacturing or intellectual property protection, and other events or circumstances that cause unanticipated delays, technical problems or other difficulties. Given these risks and uncertainties, there can be no assurance that the development of MT-1621 will be successfully completed. If the development of MT-1621 is not successful, in whole or in part, or completed in a timely manner, we may not realize the expected financial benefits from the development of MT-1621.

Note 5 — Strategic License Agreements

Fintepla

Universities of Antwerp and Leuven in Belgium

As a result of our acquisition of Brabant, 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 Agreement), the Universities granted us an exclusive worldwide license to use the data obtained from a study related to low-dose fenfluramine for the treatment of Dravet syndrome or certain related

conditions stemming from infantile epilepsy such as LGS, as well as certain other intellectual property. Under the Universities Agreement, net product sales of Fintepla are subject to royalties in the mid-single-digit percentage, or in the case of a sublicense, a percentage in the mid-twenties of the sub-licensing revenues.

In December 2021, we executed an amendment to the Universities Agreement, which provided for a one-time payment of $7.0 million related to our previous collaboration activities and consideration received to date under the Shinyaku Agreement. The amendment clarified that the Universities' are entitled to 15% of any regulatory or sales-based milestones under the Shinyaku Agreement, if achieved, as well as the method of calculating royalties due for supplying Fintepla, if approved for marketing, to Shinyaku, the exclusive distributor of Fintepla for Japan.

The $7.0 million has been recorded within accrued and other current liabilities in the consolidated balance sheet at December 31, 2021 and included in research and development expense in the consolidated statement of operations for the year ended December 31, 2021 as a cost of developing Fintepla under the Shinyaku Agreement, which has not yet been approved for marketing in Japan. The $7.0 million was subsequently paid in February 2022.

MT-1621

License Agreement with Columbia University

As a result of our acquisition of Modis in September 2019, we became party to the Exclusive License Agreement, by and between Modis and the Trustees of Columbia University in the City of New York, dated as of September 26, 2016, related to MT-1621. We are required to use commercially reasonable efforts to develop and commercialize licensed products worldwide, including to meet certain development and commercialization milestones within specified periods of time. Upon the achievement of certain regulatory and commercial milestones, we are required to pay Columbia University up to $2.9 million and $25.0 million, respectively, as well as tiered royalties on sales for each licensed product, at percentages ranging from the mid-single digits to the high single-digits. The royalty obligations and License Agreement will expire on a country-by-country and product-by-product basis upon the later of (i) 15 years after the first bona fide commercial sale of a licensed product, (ii) the expiration of the last to expire valid patent claim covering a licensed product in a country or (iii) expiration of any regulatory exclusivity covering such licensed product. The License Agreement may be terminated by either by Columbia or by us in the event of an uncured material breach by the other party, or by Columbia in the event we are subject to specified bankruptcy, insolvency or similar circumstances. We can terminate the License Agreement either in its entirety or on a product-by-product and country-by-country basis, upon specified prior written notice to Columbia, provided we are not exploiting licensed products in such countries. No amounts were due or accrued under this agreement at December 31, 2021 or 2020.

Other License Agreement Assumed

We also became party to a license agreement between two other research institutions related to MT-1621 where we may be required to pay up to $3.0 million for research, development and regulatory milestone events and up to $10.0 million for certain sales milestone events. We are also required to pay tiered royalties ranging from low to mid-single digits on net sales of licensed product. No amounts were due or accrued under this agreement at December 31, 2021 or 2020.

Tevard Collaboration, Option and License Agreement

In October 2019, we entered into an option agreement with Tevard Biosciences (Tevard), a privately-held company focused on tRNA-based gene therapies. Under the agreement, Tevard granted us an option to license exclusive rights related to a preclinical development program to identify and develop novel tRNA-based gene therapies for Dravet syndrome. During 2020, we extended the option period to exercise our license rights prior to entering into a collaboration, option and license agreement with Tevard. Payments made under the option agreement were nonrefundable, but may be credited against the upfront payment due if we exercise our option on the preclinical development program. Payments made under the option agreement of $2.0 million in 2019 and $5.5 million in 2020 were included in acquired IPR&D expense and related costs in our consolidated statement of operations.

In December 2020, we exercised the option on the Dravet syndrome program and entered into a collaboration, option and license agreement with Tevard (the Tevard Agreement). The financial terms of the Tevard Agreement included an upfront payment of $5.2 million. In connection with the transaction, we also purchased a convertible promissory note issued by Tevard in the amount of $5.0 million. The note matures in December 2022 and carries

interest at 3.5% per year. The note will automatically convert into equity securities issued by Tevard in their next equity financing transaction at a conversion price equal to the price paid per share by other investors of the financing transaction.

In addition to the upfront payments, we have agreed to fund Tevard's early discovery activities under the licensed Dravet syndrome program in accordance with the development plan as determined by the parties to the agreement. Once Tevard completes the early discovery activities for a program, we will be responsible for any potential future development and commercialization activities. Tevard is also eligible to receive additional development, regulatory and commercial-related milestone payments of up to $100.0 million for the Dravet program, as well as tiered royalties on future net sales in the single digits that result from the collaboration. We are also entitled to rights of negotiation and rights of first refusal to potentially obtain licenses to compounds subsequently discovered and developed by Tevard. The agreement, if not terminated sooner, would expire upon the expiration of all applicable royalty terms under the agreement with respect to a licensed program or product; however, we have the unilateral right to terminate the agreement with 180 days advanced notice

At the inception of the agreement and through December 31, 2021, we determined Tevard is a VIE in which we held variable interests through our licensed Dravet syndrome program and convertible promissory note. We determined that we are not the primary beneficiary of Tevard as we do not have voting control or other forms of power to direct activities that most significantly impact Tevard's economic performance.

In accounting for the Tevard Agreement, we excluded from consideration all prior payments made under the option agreement, which was previously expensed to acquired IPR&D. Upon entering the Tevard Agreement, we made an upfront payment of $10.2 million in exchange for a license to the Dravet syndrome program and the convertible promissory note. The upfront payment was allocated between the acquired IPR&D asset and the convertible promissory note based on their relative fair values of $5.2 million and $5.0 million, respectively. The estimated fair value of the acquired IPR&D asset was determined based on information from discussions with Tevard's management team regarding the potential of the Dravet syndrome program as well as our management team's expectations regarding the timing, future cost and commercial potential for the program. The estimated fair value of the convertible promissory note was determined based on a discounted cash flow analysis, adjusted for credit and market risk, and consideration of the fair value of the embedded conversion feature with a conversion price not more favorable than other investors participating in an equity financing transaction.

The $5.2 million of consideration allocated to the IPR&D asset was determined to have no alternative future use and was immediately charged to acquired IPR&D expense in our consolidated statements of operations and classified as cash used in investing activities on the consolidated statements of cash flows. The $5.0 million of consideration allocated to the convertible promissory note was included in other noncurrent assets on our consolidated balance sheet and carried at amortized costs and classified as cash used in investing activities on the consolidated statements of cash flows. Payments made to fund Tevard's costs incurred under the Dravet syndrome program after the execution of the Tevard Agreement is reflected as research and development expense in our statements of operations. For the years ended December 31, 2021 and 2020, amounts recorded as research and development expense associated with funding the Dravet syndrome program were $3.5 million and $0.7 million, respectively.

At each reporting period, we evaluate the note receivable for current expected credit loss by considering factors such as historical experience, market data, issuer-specific factors, and current economic conditions. As of December 31, 2021, no provision for current expected credit losses was deemed necessary based on the expected timing of an equity financing that would result in the automatic conversion of the note receivable to equity securities of Tevard and their existing cash on hand was sufficient to meet their operating requirements prior to the consummation of a financing transaction.

As of December 31, 2021, we do not have any current legal or contractual obligations to provide financing to Tevard and our maximum exposure to future loss is limited to the $5.0 million note receivable, which matures in December 2022. While we have committed to fund the Dravet syndrome development program for Tevard's early discovery activities, our obligation to fund these efforts is contingent upon continued involvement in the program and/or the lack of any adverse events which could cause the discontinuance of the program. Our exposure to future losses is limited as we have the unilateral right to terminate the agreement with 180 days advanced notice.

Note 6 — Cash and Cash Equivalents, and Marketable Securities

The following table summarizes the amortized cost and fair value of our cash and cash equivalents and marketable securities by major investment category:

	December 31, 2021			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash and cash equivalents:				
Cash	$ 32,852	$ —	$ —	$ 32,852
Money market funds	29,991	—	—	29,991
Commercial paper	35,337	—	—	35,337
Certificates of deposit	3,000	—	—	3,000
Total cash and cash equivalents	101,180	—	—	101,180
Marketable securities:				
Commercial paper	141,718	—	—	141,718
Certificates of deposit	32,253	—	—	32,253
U.S. Government-sponsored enterprises debt securities	6,200	—	—	6,200
Corporate debt securities	20,377	—	(13)	20,364
Total marketable securities	200,548	—	(13)	200,535
Total cash and cash equivalents and marketable securities	$ 301,728	$ —	$ (13)	$ 301,715

As of December 31, 2021, all investments in marketable securities have contractual maturities due within one year. We regularly review our available-for-sale marketable securities in an unrealized loss position and evaluate the current expected credit loss by considering factors such as historical experience, market data, issuer-specific factors, and current economic conditions. As of December 31, 2021, the aggregate difference between the amortized cost and fair value of each security in an unrealized loss position was de minimis. Since any provision for expected credit losses for a security held is limited to the amount the fair value is less than its amortized cost, no allowance for expected credit loss was deemed necessary at December 31, 2021.

(In thousands)	December 31, 2020 Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash and cash equivalents:				
Cash	$ 23,887	$ —	$ —	$ 23,887
Money market funds	80,986	—	—	80,986
Commercial paper	61,043	—	—	61,043
Certificates of deposit	1,000	—	—	1,000
Total cash and cash equivalents	166,916	—	—	166,916
Marketable securities:				
U.S. Treasuries	43,050	1	(1)	43,050
Commercial paper	210,986	—	—	210,986
Certificates of deposit	44,480	—	—	44,480
U.S. Government-sponsored enterprises debt securities	6,200	17	—	6,217
Corporate debt securities	33,288	172	—	33,460
Total marketable securities	338,004	190	(1)	338,193
Total cash and cash equivalents and marketable securities	$ 504,920	$ 190	$ (1)	$ 505,109

See Note 7 for further information regarding the fair value of our financial instruments.

Note 7 — 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, 2021 and 2020:

(In thousands)	December 31, 2021 Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 29,991	$ —	$ —	$ 29,991
Commercial paper	—	35,337	—	35,337
Certificates of deposit	—	3,000	—	3,000
Marketable securities:				
Commercial paper	—	141,718	—	141,718
Certificates of deposit	—	32,253	—	32,253
U.S. Government-sponsored enterprises debt securities	—	6,200	—	6,200
Corporate debt securities	—	20,364	—	20,364
Total assets	$ 29,991	$ 238,872	$ —	$ 268,863
Liabilities:				
Contingent consideration	—	—	$ 35,285	$ 35,285
Total liabilities	$ —	$ —	$ 35,285	$ 35,285

(In thousands)	December 31, 2020 Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 80,986	$ —	$ —	$ 80,986
Commercial paper	—	61,043	—	61,043
Certificates of deposit	—	1,000	—	1,000
Marketable securities:				
U.S. Treasuries	—	43,050	—	43,050
Commercial paper	—	210,986	—	210,986
Certificates of deposit	—	44,480	—	44,480
U.S. Government-sponsored enterprises debt securities	—	6,217	—	6,217
Corporate debt securities	—	33,460	—	33,460
Total assets	$ 80,986	$ 400,236	$ —	$ 481,222
Liabilities:				
Contingent consideration	—	—	$ 42,400	$ 42,400
Total liabilities	$ —	$ —	$ 42,400	$ 42,400

Level 1 and Level 2 Valuation Inputs

Level 1 and Level 2 financial instruments are comprised of investments in money market funds and fixed-income securities. We estimate the fair value of our Level 2 financial instruments 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.

Level 3 Valuation Inputs

Contingent Consideration

Our financial liabilities valued based upon Level 3 inputs are comprised of the contingent consideration arrangement related to the business acquisition of Brabant in October 2014 which included the intellectual property rights for our product, Fintepla (fenfluramine). Under the arrangement, we may be required to pay future consideration that is contingent upon the achievement of specified development, regulatory approval and sales-based milestone events for Fintepla. Prior to regulatory approval, we estimate the fair value of contingent consideration liabilities using a probability-weighted discounted cash flow analysis, which reflects the probability and timing of future payments and a risk-adjusted discount rate. This fair value measurement is based on Level 3 inputs such as the probability and anticipated timelines of achieving milestones related to development, regulatory approvals and product sales goals. The resulting probability-weighted cash flows are discounted at risk-adjusted rates. Following the achievements of regulatory approval milestones and upon commencement of product sales, the fair value measurement is based on projected product sales (based on internal operational budgets and long-range strategic plans), discount rates and projected payment dates.

The following table provides a reconciliation of contingent consideration liabilities measured at fair value on a recurring basis using unobservable inputs (Level 3) for the years ended December 31, 2021 and 2020:

(In thousands)	Contingent Consideration
Balance at December 31, 2019	63,800
Settlements[(1)]	(30,000)
Changes in fair value	8,600
Balance at December 31, 2020	42,400
Settlements[(1)]	(9,000)
Changes in fair value	1,885
Balance at December 31, 2021	$ 35,285

(1) As of December 31, 2021 and 2020, outstanding obligations related to achieved milestones of $4.5 million and $15.0 million, respectively, were no longer contingent. As a result, the amounts have been reclassified from contingent consideration to accounts payable at December 31, 2021 and accrued and other current liabilities at December 31 2020 on the consolidated balance sheets.

Payments of acquisition-related contingent consideration, to the extent they relate to estimated liabilities as of the date of acquisition, are reflected within financing activities in the consolidated statements of cash flows. Payments in excess of acquisition date liabilities are classified within operating activities.

Payments of contingent consideration totaled $15.0 million for the year ended December 31, 2020 were reflected within financing activities. Payments of contingent consideration totaled $19.5 million for the year ended December 31, 2021 and consisted of $18.0 million reflected within financing activities and $1.5 million reflected in operating activities.

As of December 31, 2021, the contingent consideration liabilities was $35.3 million and consisted of Fintepla sales-based milestones with a maximum payout of $36.0 million (undiscounted). Each additional $36.0 million in Fintepla sales triggers a $4.5 million payout for a maximum of 8 remaining sales-based milestone payments.

The following table summarizes the unobservable inputs used in the fair value measurement of our contingent consideration liability as of December 31, 2021.

Fair Value as of December 31, 2021 (in thousands)	Valuation Technique	Unobservable Input	Range	Weighted Average[1]
		Discount rate	0.0% — 2.0%	1.0%
$35,285	Discounted cash flow	Probability of payment	100%	100%
		Projected year of payment	2022 — 2023	2022

(1) Unobservable inputs were weighted by the relative fair value of each sales-based milestone payment.

As of December 31, 2021, we classified $13.5 million of the total contingent consideration liabilities of $35.3 million as current liabilities. The balance sheet classification between current and non-current liabilities was based upon our reasonable expectation as to the timing of settlement of the remaining sales-based milestones.

Convertible Senior Notes

As of December 31, 2021 and 2020, the estimated fair value of our senior convertible notes was approximately $231.2 million and $260.5 million, respectively. When determining the estimated fair value of our senior convertible notes, we utilize a binomial lattice model which incorporates the terms and conditions of the senior convertible notes and market-based risk measurement that are indirectly observable, such as credit risk, which represent Level 2 inputs. The lattice model produces an estimated fair value based on changes in the price of the underlying common stock price over successive periods of time. An estimated yield based on comparable non-convertible debt instruments in the market is used to discount the cash flows.

Note 8 — Other Balance Sheet Details

Inventory

Components of our inventory consists of the following:

	December 31,	
(In thousands)	2021	2020
Raw materials	$ 1,301	$ 391
Work in process	2,387	243
Finished goods	1,804	392
Total	$ 5,492	$ 1,026

Prior to receiving FDA approval for Fintepla, we recorded all manufacturing product costs as research and development expense. As of December 31, 2021 and 2020, no write-downs of inventory were deemed necessary.

Other Current Assets

Other current assets consist of the following:

	December 31,	
(In thousands)	2021	2020
Receivable for U.K. R&D tax relief scheme	$ 12,359	$ —
Note receivable from Tevard	5,000	—
Receivable under collaboration agreement	3,000	1,500
Other	4,376	3,436
Total	$ 24,735	$ 4,936

Property and Equipment, Net

Property and equipment, net consists of the following:

(In thousands)	December 31, 2021	2020
Computer equipment and software	$ 233	$ 429
Leasehold improvements	9,998	9,835
Furniture and fixtures	1,134	1,266
Total	11,365	11,530
Less accumulated depreciation	(4,168)	(2,806)
Property and equipment, net	$ 7,197	$ 8,724

Depreciation expense for the years ended December 31, 2021, 2020 and 2019 was $1.6 million, $1.5 million, and $1.3 million, respectively.

Accrued and Other Current Liabilities

Accrued and other current liabilities consist of the following:

(In thousands)	December 31, 2021	2020
Accrued clinical trial costs	$ 13,537	$ 16,477
Accrued compensation	16,399	10,917
Accrued milestone payment	—	15,000
Accrued license amendment fee	7,000	—
Accrued royalties	4,250	479
Other accrued liabilities	14,227	12,091
Total	$ 55,413	$ 54,964

Note 9 – Intangible Asset

The following table provides details of the carrying amount of our intangible asset:

(In thousands)	December 31, 2021	2020
Finite-lived intangible asset	$ 102,500	$ 102,500
Accumulated amortization	(11,827)	(3,942)
Net carrying value	$ 90,673	$ 98,558

Our intangible asset consists of worldwide development, commercialization and related intellectual property rights including patents and licenses for our product, Fintepla (fenfluramine), which at the time of our acquisition in October 2014 was classified as an indefinite-lived IPR&D asset. Upon FDA approval of Fintepla in June 2020, this indefinite-lived asset was reclassified to a finite-lived intangible asset subject to amortization.

In July 2020, we commercially launched Fintepla and commenced amortization of this asset on a straight-line basis over its estimated useful life. Due to the inherent subjectivity of forecasting the timing in which the cash flows may be generated from this intangible asset over a long-term time horizon, we concluded the pattern of economic benefit cannot be reliably determined. As such, we elected to use the straight-line method of amortization for this intangible asset over 13 years. As of December 31, 2021, the carrying value of the intangible asset will be amortized over its estimated remaining useful life of 11.5 years as follows:

(In thousands)	Amortization Expense
2022	$ 7,885
2023	7,885
2024	7,885
2025	7,885
2026	7,885
Thereafter	51,248
Total	$ 90,673

Note 10 – Convertible Senior Notes

In September and October 2020, we issued $230.0 million principal amount of 2.75% convertible senior notes due 2027 in a private offering (collectively, the Convertible Senior Notes or Notes). Total proceeds realized from the sale of the Notes, net of issuance costs of $7.5 million, were $222.5 million. The Notes are governed by an indenture (the Indenture), dated as of September 28, 2020, between Zogenix and U.S. Bank National Association, as trustee. Under the Indenture, the Notes are senior, unsecured obligations of Zogenix, are equal in right of payment with its future senior, unsecured indebtedness of Zogenix, and structurally subordinated to all indebtedness and liabilities of its subsidiaries. The principal amount of the Notes was issued at par value and the Notes accrue interest at a rate of 2.75% per year, payable semi-annually in arrears on April 1 and October 1 of each year, beginning on April 1, 2021. The Notes mature on October 1, 2027, unless earlier converted by the holders or redeemed or repurchased by us in accordance with their terms prior to such date. The Indenture contains customary terms and covenants, including certain events of default upon which the Notes may be due and payable immediately, but does not contain any financial covenants.

The Notes are convertible, subject to certain conditions described below, into shares of our common stock at an initial conversion rate of 41.1794 shares per $1,000 principal amount of the Notes, which represents an initial conversion price of approximately $24.28 per share, subject to adjustments upon the occurrence of certain events. Certain corporate events described in the Indenture may increase the conversion rate for holders who elect to convert their Notes in connection with such corporate event should they occur. We also may choose to repurchase outstanding Notes through open-market transactions, including through Rule 10b5-1 trading plan to facilitate open-market repurchases, or otherwise, from time to time.

Holders may convert the Notes in multiples of $1,000 principal amount at any time prior to October 1, 2027, but only in the following circumstances:

- during any calendar quarter ending after December 31, 2020, if our closing stock price exceeds 130% of the conversion price on each of at least 20 trading days of the last 30 consecutive trading days of the immediately preceding calendar quarter;
- during the five consecutive business day period after any 10 consecutive trading day period in which the Notes' trading price is less than 98% of the product of our closing stock price times the conversion rate; or
- the occurrence of certain corporate events, such as a change of control, merger, default or liquidation.

In addition, holders may also convert their Notes at their option at any time beginning on July 1, 2027 until the close of business on the second scheduled trading day immediately before the maturity date for the Notes, without regard to the foregoing circumstances.

Upon conversion, we will pay or deliver, as the case may be, cash, shares of our common stock or a combination thereof at our election.

We may not redeem the Notes prior to October 7, 2024. On or after October 7, 2024, the Notes are redeemable for cash, in whole or in part (subject to minimum redemption amounts), at our option at any time, and from time to time, before the 40th scheduled trading day immediately before October 1, 2027, at a cash redemption price equal to 100% of the principal amount of the Notes to be redeemed, plus accrued and unpaid interest, if any, but only if our closing stock price exceeds 130% of the conversion price on (1) each of at least 20 trading days, whether or not consecutive, during the 30 consecutive trading days ending on, and including, the trading day immediately before the date we send the related redemption notice; and (2) the trading day immediately before the

date we send such notice. In addition, calling any note for redemption will constitute a make-whole fundamental change with respect to that Note, in which case the conversion rate applicable to the conversion of that Note will be increased in certain circumstances if it is converted after it is called for redemption.

The Indenture contains representations and warranties by us, indemnification provisions in favor of the lenders and customary affirmative and negative covenants related to timing filings and reporting, and events of default. As of December 31, 2021, we were in compliance with all covenants under the Indenture.

In accounting for the issuance of the Notes, we performed an assessment of all embedded features of the debt instrument to determine if (i) such features should be bifurcated and separately accounted for, and (ii) if bifurcation requirements are met, whether such features should be classified and accounted for as equity or liability instruments. If the embedded feature meets the requirements to be bifurcated and accounted for as a liability, the fair value of the embedded feature is measured initially, included as a liability on the consolidated balance sheets and re-measured to fair value at each reporting period.

We determined the embedded conversion feature in the Notes is not required to be separately accounted for as a derivative liability instrument because it is considered to be indexed to our common stock. However, since the Notes may be settled with a combination of cash and shares, at our election, we are required to separate the Notes into debt and equity components. The value assigned to the debt component is the estimated fair value, as of the issuance date, of a similar debt instrument issued by us without the conversion feature. The difference between the full principal amount of the Notes and this estimated fair value was recorded as a debt discount on the Notes, with a corresponding offset to additional paid-in capital (the equity component). In addition, debt issuance costs associated with the Notes were allocated to the debt and equity components in proportion to the allocation of the full principal amount to those components.

At issuance, the debt component of the Notes was estimated to have a fair value of $152.1 million based on contractual cash flows discounted at our estimated non-convertible debt borrowing rate of 9.7%. Our determination of an appropriate discount rate was based on a yield curve derived from then-recent publicly-traded bond offerings with a similar term for companies with similar credit ratings to us (Level 2 inputs). As a result, the equity component of $77.9 million, which represents the difference between the proceeds from the issuance of the Notes and the fair value of the debt component, was recognized as a debt discount. In addition, debt issuance costs of $7.5 million related to the issuance of the Notes were comprised of $4.9 million attributable to the debt component, and recorded as debt discount, with the remaining $2.5 million attributable to the equity component and netted with the equity component discussed above resulting in $75.3 million recorded to additional paid-in capital within stockholders' equity on the consolidated balance sheet. The debt discount and issuance costs of $82.8 million are being amortized as interest expense over the expected term of the Notes of seven years using the effective interest rate of 9.9%. For the year ended December 31, 2021, the effective interest rate on the liability component of the Notes remained unchanged from the date of issuance. The unamortized debt discount and issuance costs of $71.8 million as of December 31, 2021 will be amortized over the estimated remaining term of approximately 5.8 years. In addition, the equity component continues to meet the conditions for equity classification.

During the fourth quarter of 2021, the closing price of our common stock did not exceed 130% of the applicable conversion price of the Notes on at least 20 of the last 30 consecutive trading days of the quarter; furthermore, no other conditions allowing holders of the Notes to convert were met as of December 31, 2021. Therefore, the Notes are not convertible for the first quarter of 2022 and are classified as long-term debt. If the closing price conditions are met in a future quarter, the Notes will be convertible at the holders' option during the immediately following quarter. Based on the closing price of our common stock of $16.25 per share on December 31, 2021, the if-converted value of the Notes was less than the outstanding principal balance.

In January 2022, we entered into a definitive agreement and plan of merger with UCB S.A. (See Note 19). The contemplated transaction represents a specified corporate event under the Indenture. Upon closing of the transaction, if at all, each holder of Notes will be entitled to convert such holder's Notes into the right to receive merger consideration in respect of each share into which the Notes would have been convertible pursuant to the applicable conversion rate under the Indenture, including any make-whole adjustment in connection with the contemplated transaction as may be applicable under the Indenture.

The following table provides information on the Notes balance:

(In thousands)	December 31, 2021	2020
Liability component		
Principal amount of Notes	$ 230,000	$ 230,000
Less: Unamortized debt discount and issuance costs	(71,835)	(80,647)
Net carrying amount	$ 158,165	$ 149,353
Equity component — net carrying value	$ 75,333	$ 75,333

Interest expense related to the Notes was included in other income (expense), net on the consolidated statements of operations as follows:

(In thousands)	Year Ended December 31, 2021	2020
Contractual coupon interest	$ 8,811	$ 1,600
Amortization of debt discount and issuance costs	6,359	2,143
Total interest expense	$ 15,170	$ 3,743

Note 11 — Leases

We have noncancelable operating leases consisting of administrative and research and development office space for our headquarters in Emeryville, California and our U.K. subsidiary in Maidenhead, United Kingdom. The leases will expire in May 2027 and February 2025, respectively. We also maintain limited office space in Ireland, Germany, Italy and Japan. Our Emeryville lease includes a renewal option for an additional five years, which is not included in the operating lease liabilities as we determined renewal was not reasonably assured at lease inception under the legacy lease standard. The operating lease liabilities also included a lease related to the former headquarters of Modis in Oakland, California until its expiration in July 2021.

We do not have any material finance leases or service contracts with lease arrangements. Our lease agreements do not contain any material residual value guarantees or material restrictive covenants.

The components of lease expense were as follows:

(In thousands)	Year Ended December 31, 2021	2020	2019
Components of lease costs:			
Operating lease cost	$ 1,799	$ 1,989	$ 2,045
Short-term lease cost	438	444	851
Sublease income	—	(115)	(580)
Total lease expense	$ 2,237	$ 2,318	$ 2,316

Supplemental cash flow information related to operating leases was as follows:

(In thousands)	Year Ended December 31, 2021	2020	2019
Cash used in operating activities:			
Cash paid for amounts included in the measurement of lease liabilities	$ 2,330	$ 2,178	$ 1,842
Noncash investing activities:			
Right-of-use lease assets obtained in exchange for new lease liabilities	—	1,156	354

Supplemental balance sheet information related to leases was as follows:

(In thousands)	December 31, 2021	2020
Right-of-use assets	$ 6,605	$ 7,748
Current portion of operating lease liabilities	1,694	1,688
Operating lease liabilities, net of current portion	8,617	10,314
Total operating lease liabilities	$ 10,311	$ 12,002
Weighted average remaining lease term (in years)	5.2	6.0
Weighted average discount rate, weighted based on the remaining balance of lease payments	6.2 %	6.2 %

The following table reconciles the undiscounted future lease payments under noncancelable operating leases with terms of more than one year to the total operating lease liabilities recognized on the consolidated balance sheet as of December 31, 2021 (in thousands):

Years Ending December 31:	Operating Leases
2022	$ 2,261
2023	2,318
2024	2,326
2025	2,070
2026	2,132
2027	899
Total lease payments	12,006
Less: imputed interest	(1,695)
Total operating lease liabilities	$ 10,311

Note 12 — Commitments and Contingencies

Litigation

In July 2020, we received a letter, notifying us that Apotex Inc. and Apotex Corp. (collectively, "Apotex") submitted to FDA an abbreviated new drug application ("ANDA") for a generic version of 2.2 mg base/ml Fintepla (fenfluramine hydrochloride) that included "Paragraph IV" certifications (pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV)) with respect to two of our patents covering Fintepla. These patents are listed in FDA's list of Approved Drug Products with Therapeutic Equivalence Evaluations, commonly referred to as the Orange Book, for Fintepla. The letter included a statement setting forth the basis for Apotex's opinion that these patents are invalid and/or will not be infringed by the manufacture, use or sale of Apotex's fenfluramine hydrochloride oral solution, 2.2 mg base/ml product. In August 2021, we filed a complaint against Apotex Inc. and Apotex Corp. for infringement based on these Paragraph IV certifications. In October 2021, we received a letter notifying us that Apotex had amended its ANDA and submitted additional Paragraph IV certifications with respect two additional Orange Book-listed patents covering Fintepla. The letter included a statement setting forth the basis for Apotex's opinion that these two additional patents are also invalid and/or will not be infringed by the manufacture, use or sale of Apotex's fenfluramine hydrochloride oral solution, 2.2 mg base/ml product. In October 2021, we filed a second complaint against Apotex Inc. and Apotex Corp. for infringement based on these additional paragraph IV certifications. These cases have since been consolidated.

In August 2021, we received a letter notifying us that Lupin Limited ("Lupin") submitted to FDA an abbreviated new drug application ("ANDA") for a generic version of 2.2 mg base/ml Fintepla (fenfluramine hydrochloride) that contains "Paragraph IV" certifications. These patents are listed in FDA's list of Approved Drug Products with Therapeutic Equivalence Evaluations, commonly referred to as the Orange Book, for Fintepla. The letter included a statement setting forth the basis for Apotex's opinion that these patents are invalid and/or will not be infringed by the

manufacture, use or sale of Lupin's fenfluramine hydrochloride oral solution, 2.2 mg base/ml product. In October 2021, we filed a complaint against Lupin for patent infringement under the Hatch-Waxman Act in the United States District Court for the District of Delaware.

Fintepla has Orphan Drug exclusivity, which prevents FDA from approving an ANDA referencing Fintepla until June 2027. We intend to vigorously enforce our intellectual property rights relating to Fintepla. We cannot predict the ultimate outcome of these actions, and we may spend significant resources enforcing and defending these patents. If we are unsuccessful, some or all of our claims in the patents may be narrowed or invalidated and the patent protection for our products could be shortened, allowing for the sale of generic versions of these products earlier than their patent expiration, which could have a significant negative effect on our revenues and results of operations.

Merger-Related Litigation

Subsequent to year end and following the announcement of the execution of the Agreement and Plan of Merger, dated January 18, 2022, by and among UCB S.A., Zinc Merger Sub, Inc. and Zogenix, Inc. (see Note 19 — Subsequent Event), several complaints related to the merger have been filed. The complaints named as defendants include Zogenix and members of our board of directors as well in one complaint, UCB S.A. and Zinc Merger Sub, Inc. as defendants.

The Complaints generally allege that the defendants violated Section 14(d), 14(e) and 20(a) of the Securities Exchange Act of 1934, as well as Rules 14a-9 and 14d-9 promulgated thereunder. Specifically, one or more of the Complaints allege that the Schedule 14D-9 (as amended or supplemented from time to time), the "Schedule 14D-9" filed on February 1, 2022 with the SEC by Zogenix fails to disclose material information and/or materially misrepresents information concerning the sales process leading up to the merger, potential conflicts of interest of BofA Securities and Zogenix insiders, our financial projections, the financial analyses of BofA Securities, and the financial analyses of SVB Leerink. The complaint in the Finuliar Action also asserts state law claims against the members of our board of directors alleging that they breached their fiduciary duty of candor/disclosure by causing or permitting the Schedule 14D-9 to be filed. The relief sought in one or more of the Complaints includes enjoining the consummation of the merger, enjoining defendants from filing any amendment to the Schedule 14D-9 unless certain allegedly material information is included, directing defendants to disseminate an amended Schedule 14D-9 that does not contain any untrue statements of material fact and that states all material facts required in it or necessary to make the statements therein not misleading, declaring that defendants violated Sections 14(d), 14(e), and 20(a) of the Exchange Act and Rules 14a-9 and 14d-9 promulgated thereunder, rescinding, to the extent already consummated, the merger and awarding rescissory damages, directing defendants to account for all alleged damages suffered as a result of defendants' alleged wrongdoing, awarding the plaintiffs their respective costs and disbursements, and granting other and further equitable relief as the Court may deem just and proper.

We cannot currently predict the ultimate outcome of such claims or estimate a range of loss.

Indemnification Agreements

In the ordinary course of business, we may provide indemnification of varying scope and terms to vendors, lessors, customers and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. These indemnities include indemnities to our directors and officers to the maximum extent permitted under applicable Delaware law. The maximum potential amount of future payments that we could be required to make under these indemnification agreements is, in many cases, unlimited. We have not incurred any material costs as a result of such indemnifications and is not currently aware of any indemnification claims.

Unconditional Purchase Obligations

We have supply agreements for the manufacture of active pharmaceutical ingredient (API) used in Fintepla and procurement of raw materials (other than the API) used to formulate, fill, test and release an oral solution of Fintepla. As of December 31, 2021, annual minimum purchase commitments under these supply agreements were not material.

In addition, we enter into contracts in the normal course of business with CROs for preclinical studies and clinical trials and contract manufacturing organizations for the manufacture of drug materials. The contracts are cancellable, with varying provisions regarding termination. If a contract with a specific vendor were to be cancelled,

we would only be obligated for costs of products or services that have been incurred by the vendor prior the effective date of cancellation, plus applicable cancellation fees.

Note 13 — Stockholders' Equity

Preferred Stock

We have 10.0 million shares of preferred stock authorized for issuance, par value of $0.001 per share. As of December 31, 2021 and 2020, no shares of preferred stock were issued and outstanding.

Common Stock

In May 2021, our stockholders approved and we filed an amendment to our Fifth Amended and Restated Certificate of Incorporation, as amended, to increase the total number of authorized shares of common stock from 100.0 million to 200.0 million. Each holder of our common stock, par value of $0.001 per share, is entitled to one vote for each share of such stock held. As of December 31, 2021 and 2020, there were 56.1 million and 55.7 million shares of common stock issued and outstanding.

The following table presents common stock reserved for future issuance for the following financial instruments:

	December 31,	
(In thousands)	2021	2020
Outstanding stock options and stock unit awards	7,790	5,703
Warrants to purchase common stock	—	28
Reserved for future grants under employee equity plans	6,914	3,899
Reserved for issuance upon conversion of convertible senior notes	12,313	12,313
Total	27,017	21,943

At December 31, 2021, we had approximately 116.9 million shares of authorized and unreserved common stock available for issuance.

Sale of Common Stock

At-the-Market Offerings

We have an at-the-market sales agreement (the ATM Sales Agreement) with Cantor Fitzgerald & Co. (Cantor) pursuant to which Cantor agreed to act as a sales agent in connection with sales of our common stock from time to time pursuant to an effective registration statement.

In December 2017, we filed a prospectus supplement to our automatic "shelf" registration statement on Form S-3 registering the offering, issuance and sale of up to $75.0 million in gross aggregate proceeds of common stock under the ATM Sales Agreement. For the year ended December 31, 2019, we sold approximately 0.9 million shares of common stock resulting in net proceeds of approximately $42.6 million, after deducting commissions and other offering costs.

In June 2020, we filed a prospectus supplement to our automatic "shelf" registration statement on Form S-3 registering the offering, issuance and sale of up to $200.0 million in gross aggregate proceeds of our common stock under the ATM Sales Agreement. During 2020, we sold approximately 0.2 million shares of common stock and realized net proceeds of approximately $4.9 million, after deducting commissions and other offering costs.

Underwritten Public Offerings

In March 2020, we completed an underwritten public offering of 9.8 million shares of our common stock at an offering price of $23.50 per share, including 1.3 million shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares. Net proceeds realized from the offering amounted to approximately $221.7 million, after deducting commissions and other offering costs.

Accumulated Other Comprehensive Income

A summary of changes in the balances of each component of accumulated other comprehensive loss, net of tax, follows:

(In thousands)	Net Unrealized Gains (Losses) on Marketable Securities	Foreign Currency Translation Adjustments	Accumulated Other Comprehensive Income
Balance at December 31, 2018	3	—	3
Amounts arising during the period	702	—	702
Reclassification adjustments	(326)	—	(326)
Balance at December 31, 2019	379	—	379
Amounts arising during the period	(197)	(260)	(457)
Reclassification adjustments	7	—	7
Balance at December 31, 2020	$ 189	$ (260)	$ (71)
Amounts arising during the period	(202)	288	86
Balance at December 31, 2021	$ (13)	$ 28	$ 15

Note 14 — Stock-Based Compensation

We have various equity incentive plans under which we grant employees and non-employee directors stock options, time-based restricted stock units (RSUs) and performance-based stock units (PSUs). Options granted generally have a contractual term of ten years and have a per share exercise price equal to the closing price of our common stock on the date of grant. Options and RSUs typically vest over a four-year period from the date of grant. We also grant broad-based PSUs to employees, including executive officers, that vest upon the satisfaction of both time-based and performance-based vesting conditions. The following is a description of our various equity incentive plans.

Summary of Stock-Based Compensation Plans

2010 Plan

The 2010 Equity Incentive Award Plan (2010 Plan) was adopted by our board of directors and became effective in November 2010. The 2010 Plan was amended and restated in each of June 2012, May 2019 and May 2021. The May 2019 amendment was approved by our stockholders at our 2019 Annual Meeting of Stockholders and provided for an increase to the aggregate number of shares authorized for issuance under the plan from 7,500,000 to 11,500,000. In addition, the expiration date of the plan was extended to March 2029. The May 2021 amendment was approved by our stockholders at our 2021 Annual Meeting of Stockholders and provided for an increase to the aggregate number of shares authorized for issuance under the plan to 16,000,000 shares. In addition, the expiration date of the plan was extended to May 2031.

The 2010 Plan provides for the issuance of incentive and non-statutory stock options, restricted shares, performance shares, stock appreciation rights, RSUs, PSUs and other stock-based incentives to officers, employees and others.

2013 and 2021 Inducement Plans

In December 2013 and May 2021, our board of directors adopted the 2013 Employment Inducement Equity Incentive Award Plan (2013 Inducement Plan) and the 2021 Employment Inducement Equity Incentive Award Plan (2021 Inducement Plan), respectively. Both inducement plans are non-shareholder approved stock plans adopted pursuant to the “inducement exception” provided under Nasdaq listing rules. The inducement plans are used exclusively for the issuance of non-statutory stock options and restricted stock units to certain new hires who satisfy the requirements to be granted inducement grants under Nasdaq rules as an inducement material to the individual’s entry into employment with us. The terms of both inducement plans are substantially similar to the terms of our 2010 Plan. The 2013 Inducement Plan was adopted in December 2013 and initially reserved 337,500 shares of common stock for issuance, which was subsequently increased to 637,500 shares in May 2018. In connection with seeking stockholder approval of the amended and restated 2010 Plan in May 2019, we agreed not to make further awards under the 2013 Inducement Plan. The 2021 Inducement Plan was adopted in May 2021 and initially reserved 1,000,000 shares of common stock for issuance.

Employee Stock Purchase Plan

In November 2010, our board of directors adopted an Employee Stock Purchase Plan (ESPP), which allows employees to purchase shares of our common stock during specified offering periods at a discount to the fair market value at the time of purchase. In May 2020, our shareholders approved an amendment and restatement of the ESPP, which provided for an increase to the aggregate number of shares authorized for issuance from 375,000 to 875,000 shares and to eliminate the annual evergreen feature, which automatically added 31,250 shares to the aggregate shares authorized for issuance on January 1 of each year under the plan. In addition, the expiration date of the ESPP was modified from October 2020 to the date that all shares authorized have been issued.

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 1st and December 1st of a calendar year.

Common stock may be purchased under the ESPP at a price equal to 85% of the fair market value of our common 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 our 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 a preceding offering period with a 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 5,000 shares. In addition, the Internal Revenue Code (IRC) limits purchases under an ESPP to $25,000 worth of stock in any one calendar year, valued as of the first day of an offering period.

As of December 31, 2021, 6,528,510 common shares were available for future equity award grants under the 2010 Plan and 2021 Inducement Plan and 385,515 common shares were available for issuance under the ESPP.

Stock-Based Compensation Plan Activity

The following sections summarize activity under our stock-based compensation plans.

Stock Options

The following table summarizes our stock option activity for the year ended December 31, 2021:

	Shares (in thousands)	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2020	5,311	$ 29.12		
Granted	1,833	17.79		
Exercised	(58)	10.08		
Canceled	(401)	28.71		
Outstanding at December 31, 2021	6,685	$ 26.20	6.9	$ 7,926
Exercisable at December 31, 2021	4,101	$ 27.00	5.7	$ 7,232

The total intrinsic value of options exercised for the years ended December 31, 2021, 2020 and 2019 was $0.4 million, $5.1 million and $22.4 million, respectively.

Stock Unit Awards

The following table summarizes our stock unit awards activity for the year ended December 31, 2021:

	RSUs		PSUs	
	Shares (in thousands)	Weighted Average Grant Date Fair Value	Shares (in thousands)	Weighted Average Grant Date Fair Value
Nonvested at December 31, 2020	393	$ 37.68	—	$ —
Granted	616	17.66	494	19.53
Vested	(144)	39.98	(152)	19.85
Canceled	(61)	25.24	(42)	19.99
Nonvested at December 31, 2021	804	$ 22.85	300	$ 19.30

The total intrinsic value of stock unit awards vested for the years ended December 31, 2021, 2020 and 2019 was $5.0 million, $5.7 million and $1.9 million, respectively.

ESPP

Employees purchased 112,337 shares, 51,745 shares and 28,146 shares under our ESPP for the years ended December 31, 2021, 2020 and 2019, respectively.

Valuation of Equity Awards

We use the Black-Scholes option-pricing model for determining the estimated fair value and stock-based compensation related to stock options. A summary of the assumptions used to estimate the fair values of stock option grants for the years presented is as follows:

	Year Ended December 31,		
	2021	2020	2019
Risk free interest rate	0.5% to 1.4%	0.3% to 1.8%	1.4% to 2.6%
Expected term	5.3 to 6.1 years	5.3 to 6.1 years	5.3 to 6.1 years
Expected volatility	70.0% to 73.7%	73.2% to 76.7%	73.5% to 82.3%
Expected dividend yield	—%	—%	—%
Weighted-average fair value of option on grant date	$11.36	$17.86	$32.64

The fair value of RSUs and PSUs are based on the closing price of our common stock on the date of grant. The fair value of ESPP awards issued was not material for all periods presented.

Stock-Based Compensation Expense Allocation

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

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Research and development	12,962	12,139	8,293
Selling, general and administrative	22,501	17,037	12,954
Total	$ 35,463	$ 29,176	$ 21,247

Stock-based compensation of $1.0 million was capitalized into inventory for the year ended December 31, 2021.

As of December 31, 2021, there was approximately $54.4 million of total unrecognized compensation costs related to outstanding equity awards scheduled to be recognized over a weighted average period of 2.6 years.

Note 15 – Net Loss Per Share

Basic net loss per share is calculated by dividing net loss by the weighted average number of shares outstanding for the period. Diluted net loss per share is calculated by dividing net loss by the weighted average number of shares of common stock and potential dilutive common stock equivalents outstanding during the period if the effect is dilutive. Our potentially dilutive shares of common stock include outstanding stock options, RSUs, PSUs, warrants to purchase common stock and rights under our Notes.

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

	Year Ended December 31,		
	2021	2020	2019
Numerator			
Net loss	$ (227,413)	$ (209,383)	$ (419,503)
Denominator			
Weighted average common shares outstanding, basic and diluted	55,880	53,706	43,078
Net loss per share, basic and diluted	$ (4.07)	$ (3.90)	$ (9.74)

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

	Year Ended December 31,		
(In thousands)	2021	2020	2019
Shares subject to outstanding stock options	6,242	4,966	4,085
Shares subject to outstanding RSUs and PSUs	1,051	464	382
Shares subject to outstanding warrants to purchase common stock	15	28	28
Shares issuable upon conversion of Notes	9,471	4,415	—
Total	16,779	9,873	4,495

Note 16 — Employee Benefit Plans

We maintain defined contribution retirement plans for our employees. We established a 401(k) Plan for our U.S. employees and a defined benefit pension plan for our U.K. employees by which participants may defer taxation on a portion of their earnings, subject to a maximum amount under each applicable plan. We may make discretionary matching contributions to the plans on behalf of participants in any plan year. Any discretionary matching contributions made on behalf of participants become immediately vested and non-forfeitable to the participant. Total expense recognized by us for discretionary matching contributions made in 2021, 2020 and 2019 was $2.5 million, $1.2 million, and $0.5 million, respectively.

Note 17 — Income Taxes

For financial reporting purposes, the components of loss from continuing operations before income taxes are presented in the following table.

	Year Ended December 31,		
(In thousands)	2021	2020	2019
United States	$ (193,176)	$ (170,812)	$ (325,769)
Foreign	(34,132)	(55,996)	(93,734)
Total	$ (227,308)	$ (226,808)	$ (419,503)

The following table summarizes carryforwards of net operating losses and tax credits as of December 31, 2021.

(in millions)	Amount
Federal net operating losses	$ 669.2
State net operating losses	427.7
Foreign net operating losses	289.2
Federal research and development credits	6.4
State research and development credits	4.2
Orphan drug research and development credits	2.0

At December 31, 2021, our federal, state, and foreign (primarily related to the U.K.) net operating loss carryforwards, including the acquired net operating losses from our acquisition of Modis, were approximately $669.2 million, $427.7 million and $289.2 million, respectively, which may be subject to limitations as described below. If not utilized, a significant portion of our federal net operating loss carryforwards incurred prior to 2018 will begin to expire in 2029 and the state net operating loss carryforwards incurred prior to 2018 will begin to expire in 2022. 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. However, the deductibility of such federal net operating losses is limited to 80% of taxable income. As of December 31, 2021, of the $669.2 million in total federal net operating loss carryforwards, $414.7 million do not expire. It is uncertain if and to what extent various states will conform to the Tax Act. In the U.K., our net operating loss carryforwards do not expire, but the use of net operating loss carryforwards in relation to U.K. taxable income incurred on or after April 1, 2017 will be limited each year to £5.0 million plus an incremental 50% of U.K. taxable income, subject to a regulatory established allowance per group.

In addition, we have federal and California research and development income tax credit carryforwards of approximately $6.4 million and $4.2 million. If not utilized, the federal research and development income tax credit carryforwards will begin to expire in 2031. The California research and development income tax credit carryforwards do not expire and can be carried forward indefinitely. As of December 31, 2021, we had federal orphan drug tax credit carryforwards of $2.0 million, which begin to expire in 2036. 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 we file tax returns. We are currently not under audit by any tax jurisdiction.

As of December 31, 2021, we have experienced at least three ownership changes. The first ownership change occurred in August 2006 and resulted in a reduction to our net operating loss carryforwards of $1.9 million. We had a second ownership change in September 2011 which resulted in reductions to our federal net operating loss carryforwards of $121.1 million, research and development income tax credits of $3.0 million, and California net operating loss carryforwards of $53.3 million. We 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. We recently completed an evaluation of the potential effect of Section 382 on our ability to utilize our net operating losses, including those acquired from our acquisition of Modis. Any operating losses and other tax attributes generated by us subsequent to January 2014, including those acquired from our acquisition of Modis, are currently not subject to any IRC Section 382 limitations. Pursuant to the IRC, the use of our net operating loss and research and development income tax credit carryforwards may be limited in the event of a future cumulative change in ownership of more than 50% within a three-year period.

A reconciliation of income tax provision to amounts computed by applying the statutory federal income tax rate to loss from continuing operations before income taxes is shown as follows (in thousands):

	December 31,		
	2021	2020	2019
Income tax at federal statutory rate	$ (47,735)	$ (47,630)	$ (88,096)
State taxes, net of federal benefit	(5,803)	(4,316)	(65)
Non-deductible acquired IPR&D charge and other expenses[(1)]	—	—	52,044
Change in valuation allowance	54,799	40,039	21,155
Impact of foreign rate change on deferred taxes	(12,405)	(2,950)	1,887
Other permanent differences	2,117	3,993	4,101
State tax rate benefit	164	(1,346)	(18)
Foreign rate differential	393	752	1,883
Stock-based compensation	2,484	1,180	(2,674)
Net operating losses surrendered under U.K.'s R&D tax relief scheme	—	—	9,349
State apportionment adjustments	482	(2,673)	48
Impact of foreign exchange rate differences	5,679	(4,532)	—
Credits and other	(70)	58	386
Income tax expense (benefit)	$ 105	$ (17,425)	$ —

(1) Represents amounts attributable to our asset acquisition of Modis. See Note 4 for additional information.

The significant components of deferred tax assets (liabilities) are as follows:

	December 31,	
(In thousands)	2021	2020
Deferred tax assets:		
Federal, state and foreign net operating loss carryforwards	$ 237,708	$ 186,963
Capitalized research and development	666	486
Accrued expenses	5,895	2,498
Research and development credits	5,343	5,343
Amortization	2,718	2,949
Lease liability	2,291	2,534
Stock-based compensation	10,212	7,878
Other, net	2,523	2,690
Total deferred tax assets	267,356	211,341
Less: valuation allowance	(231,335)	(176,594)
Total deferred tax assets, net of valuation allowance	$ 36,021	$ 34,747
Deferred tax liabilities:		
Operating lease right-of-use asset	$ (1,423)	$ (1,585)
IPR&D	(18,573)	(15,857)
Discount on Notes	(16,025)	(17,305)
Total deferred tax liabilities	(36,021)	(34,747)
Total net deferred tax liabilities	$ —	$ —

For the year ended December 31, 2021, a provision for income taxes of $0.1 million has been recognized related primarily to our subsidiaries located outside of the United States. For the year ended December 31, 2020, income tax benefit of $17.4 million resulted from a change in our valuation allowance balance associated with the completion of our in-process research and development program for Fintepla. Prior to regulatory approval of Fintepla in June 2020, our indefinite-lived asset was not subject to amortization. Upon completion of the IPR&D program, the indefinite-lived intangible asset was reclassified to an intangible asset subject to amortization over its estimated useful life. As a result, future reversals of deferred tax liabilities related to finite-lived intangible assets provided a source of income when assessing the realizability of our U.K. net operating loss carryforwards. We therefore recorded a $17.4 million income tax benefit in 2020 with a corresponding reduction to our valuation allowance on our U.K. deferred tax assets. The income tax benefit included the effects of foreign exchange

differences on remeasurement of the deferred tax liability. An immaterial portion of the adjustment for foreign exchange differences was related to prior periods.

As of December 31, 2021 and 2020, we have established a full valuation allowance against our U.S. and foreign deferred tax assets that are in excess of our reversing taxable temporary differences in those jurisdictions as we determined it is more likely than not that the tax benefit will not be realized.

The increase in valuation allowance of $54.7 million during 2021 was primarily attributable to tax benefits generated from current period net operating losses. The increase in valuation allowance of $25.1 million during 2020 was primarily attributable to tax benefits generated from net operating losses, offset by the impact of tax benefits from intangibles that became subject to amortization for financial statement purposes discussed above.

We recognize 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 our unrecognized tax benefits (in thousands):

	December 31,		
	2021	2020	2019
Beginning balance of unrecognized tax benefits	$ 3,638	$ 3,541	$ 1,487
Gross increases based on tax positions related to current year	—	—	1,495
Gross increases based on tax positions related to prior years		97	559
Gross decreases based on tax positions related to prior years	—	—	—
Settlements with taxing authorities	—	—	—
Expiration of statute of limitations	—	—	—
Ending balance of unrecognized tax benefits	$ 3,638	$ 3,638	$ 3,541

As at December 31, 2021 and 2020, there were no unrecognized tax benefits that, if recognized, would affect our effective tax rate as any tax benefit would increase a deferred tax asset, which is currently offset by a full valuation allowance.

We record interest and, if applicable, penalties related to income tax matters as a component of income tax expense. No interest or penalties have been recorded for all periods presented. We do not expect any significant increases or decreases to our unrecognized tax benefits in the next twelve months.

Note 18 — U.K.'s R&D Tax Relief Scheme

We conduct extensive research and development activities that benefit from U.K.'s small and medium-sized enterprises (SMEs) R&D tax relief scheme. Under this tax relief scheme, a SME can make an election (i) to receive an enhanced U.K. tax deduction on its eligible R&D activities or, when an SME entity is in a net operating loss position, or (ii) to surrender net operating losses that arise from its eligible R&D activities in exchange for a cash payment from the U.K. tax authorities. There is two-year window after the end of a tax year to seek relief under this scheme. 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 us 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 by submitting a claim for a discrete tax year and collectability is deemed probable and reasonably assured.

In December 2019, we elected to surrender net operating losses by submitting claims to receive cash payments of $9.9 million and $9.8 million related to our 2017 and 2018 tax years, respectively. For the year ended December 31, 2020, we recognized income and collected cash of $19.7 million upon approval of our submitted claims by the U.K. tax authorities as a component of other income, net on the consolidated statement of operations. In December 2021, we submitted a claim for $12.4 million related to eligible R&D activities incurred in our 2019 tax year and the amount was recognized as other income for the year ended December 31, 2021. As of December 31, 2021, a $12.4 million receivable was recorded within other current assets on the consolidated balance sheets. For our 2020 tax year, we have not yet decided whether to seek tax relief by surrendering some of our losses for a tax credit cash rebate claim or electing to receive enhanced U.K. tax deductions on our eligible R&D activities.

Note 19 — Subsequent Event

On January 18, 2022, we entered into a definitive agreement and plan of merger (the Merger Agreement) with UCB S.A., a société anonyme formed under the laws of Belgium (UCB) and its subsidiary, Zinc Merger Sub, Inc., a Delaware corporation (Purchaser) pursuant to which, among other things, Purchaser will be merged with and into Zogenix (the Merger), with Zogenix surviving the Merger as a wholly-owned subsidiary of UCB, subject to the terms and conditions of the Merger Agreement. Under the terms of the Merger Agreement, and upon the terms and subject to the conditions thereof, Purchaser commenced a tender offer to purchase all of the outstanding common shares of Zogenix for (i) $26.00 per share in cash, without interest and less any applicable tax withholding, plus (ii) one non-transferrable contingent value right per common share representing the right to receive a contingent payment of $2.00 in cash, without interest and less any applicable tax withholding, which amount will become payable, if at all, if a specified milestone is achieved on or prior to December 31, 2023. The boards of directors of both Zogenix and UCB have unanimously approved the transaction.

The obligation of UCB and Purchaser to consummate the tender offer is subject to the tender of a majority of our outstanding common shares in the Offer and other customary conditions. If these conditions are satisfied and the tender offer closes, Purchaser will acquire any remaining shares through a merger pursuant to section 251(h) of the Delaware General Corporate Law. The completion of the Merger is subject to customary conditions, including, among others, the expiration or termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, the absence of any order or law that has the effect of enjoining or otherwise prohibiting the completion of the Merger, each party's representations and warranties being true and correct as of the closing, generally to a "Material Adverse Effect" standard. The Merger Agreement provides for a termination fee of $59.0 million payable by us under certain circumstances, including if we terminate the Merger Agreement to accept a superior proposal and enter into a definitive written agreement with respect to such proposal.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the timelines specified in the 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, 2021 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, 2021, 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, 2021, which is included below.

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, 2021, 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, 2021, 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, 2021 and 2020, 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, 2021, and the related notes and our report dated March 1, 2022 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
March 1, 2022

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTION THAT PREVENTS INSPECTIONS

Not applicable.

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 2022 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, 2021, 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 AND 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 ACCOUNTANT 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.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

We have filed the following documents as part of this Annual Report on Form 10-K:

(1) Consolidated Financial Statements

(2) Financial Statement Schedules

All financial statement schedules have been omitted, since the required information is not applicable or is not present in amounts sufficient to require submission of the schedule, or because the information required is included in the consolidated financial statements and accompanying notes included in this Form 10-K.

(3) Exhibits

The exhibits required by Item 601 of Regulation S-K are listed below.

EXHIBIT INDEX

Exhibit No.	Description	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit No.	
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	
2.2*	Agreement and Plan of Merger, dated August 23, 2019, by and among Zogenix, Inc., Xena Merger Sub, Inc., Modis Therapeutics, Inc. and Shareholder Representative Services, LLC, as the shareholders' representative	8-K	001-34962	August 26, 2019	2.1	
2.3	Agreement and Plan of Merger, dated January 18, 2022, by and among UCB S.A., Zinc Merger Sub, Inc. and Zogenix, Inc.	8-K	001-34962	January 19, 2022	2.1	
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	Certificate of Amendment of Fifth Amended and Restated Certificate of Incorporation	10-Q	001-34962	August 6, 2019	3.4	
3.5	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	Indenture, dated as of September 28, 2020, between Zogenix, Inc. and U.S. Bank National Association, as trustee	8-K	001-34962	September 28, 2020	4.1	
4.3	Form of Global Note representing the 2.75% Convertible Senior Notes due 2027	8-K	001-34962	September 28, 2020	4.1	
4.4	Description of Registered Securities	10-K	001-34962	March 2, 2020	4.3	
10.1	Form of Director and Executive Officer Indemnification Agreement	S-1/A	333-169210	October 27, 2010	10.1	
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, as amended through May 22, 2019	8-K	001-34962	May 22, 2019	10.1	
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#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2010 Equity Incentive Award Plan	10-K	001-34962	March 2, 2020	10.6	
10.7#	Employment Inducement Equity Incentive Award Plan and form of stock option agreement thereunder	8-K	001-34962	December 5, 2013	10.1	

Exhibit No.	Description	Incorporated by Reference				File Herev
		Form	File Number	Date of Filing	Exhibit No.	
10.8#	Annual Incentive Plan	10-Q	001-34962	May 11, 2015	10.3	
10.9#	Independent Director Compensation Policy as amended and restated effective May 27, 2021	10-Q	001-34962	August 5, 2021	10.1	
10.10#	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	
10.11#	Employment Agreement, dated June 29, 2015, by and between the Registrant and Gail M. Farfel, Ph.D.	10-Q	001-34962	August 10, 2015	10.5	
10.12#	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	
10.13#	Employment Agreement dated January 16, 2017, by and between the Registrant and Michael P. Smith	10-Q	001-34962	May 4, 2017	10.2	
10.14#	Employment Agreement dated July 2, 2018, by and between the Registrant and Ashish Sagrolikar	10-Q	001-34962	November 8, 2018	10.1	
10.15#	Employment Agreement dated April 20, 2020, by and between the Registrant and Shawnte M. Mitchell	10-Q	001-34962	August 6, 2020	10.1	
10.16#	Amendment to Employment Agreement, dated July 2, 2018, by and between the Registrant and Ashish Sagrolikar	10-Q	001-34962	November 8, 2021	10.1	
10.17#	Second Amendment to Employment Agreement, dated July 2, 2018, by and between the Registrant and Ashish	10-Q	001-34962	November 8, 2021	10.2	
10.18#	Third Amendment to Employment Agreement, dated July 2, 2018, by and between the Registrant and Ashish	10-Q	001-34962	November 8, 2021	10.3	
10.19†	Collaboration and License Agreement dated as of October 23, 2014 by and among The Katholieke Universiteit Leuven, University Hospital Antwerp and Brabant Pharma Limited	10-Q	001-34962	November 6, 2014	10.5	
10.20	Lease Agreement, dated October 1, 2018, by and between the Registrant and Emery Station West, LLC	10-K	001-34962	February 28, 2019	10.21	
10.21	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	
10.22+	Manufacturing and Supply Agreement dated January 31, 2019 by and between Zogenix International Limited and Aptuit (Oxford) Limited	10-Q	001-34962	May 9, 2019	10.1	
10.23+	Distributorship Agreement dated March 18, 2019 by and between the Registrant and Nippon Shinyaku Company, Ltd.	10-Q	001-34962	May 9, 2019	10.2	

Exhibit No.	Description	Incorporated by Reference				File Herev
		Form	File Number	Date of Filing	Exhibit No.	
10.24+	Exclusive License Agreement by and between the Trustees of Columbia University and Modis Therapeutics, Inc. (as successor-in-interest to Meves Pharmaceuticals, LLC), dated September 26, 2016	10-Q	001-34962	November 7, 2019	10.1	
10.25+	Amendment No. 1 to Exclusive License Agreement by and between the Trustees of Columbia University and Modis Therapeutics, Inc., dated December 5, 2019	10-K	001-34962	March 2, 2020	10.22	
10.26	Supply Agreement, by and between the Registrant and Penn Pharmaceutical Services Limited, trading as PCI Pharma Services, dated July 17, 2019	10-Q	001-34962	November 7, 2019	10.2	
10.27+	Collaboration, Option and License Agreement by and between Tevard Biosciences, Inc. and Zogenix, Inc.	10-K	001-34962	March 1, 2021	10.24	
21.1	Subsidiaries of the Registrant					X
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 Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)					X
32.1‡	Certification of Chief Executive Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)					
32.2‡	Certification of Chief Financial Officer pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002 (18 U.S.C. §1350, as adopted)					
101	Inline XBRL Document Set for the consolidated financial statements and accompanying notes in Part II, Item 8, “Financial Statements” of this Annual Report on Form 10-K.					X
104	Inline XBRL for the cover page of this Annual Report on Form 10-K, included in the Exhibit 101 Inline XBRL Document Set.					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

* Confidential portions of this Exhibit were redacted pursuant to Item 601(b)(2) of Regulation S-K and Zogenix Inc. agrees to furnish supplementally to the Securities and Exchange Commission a copy of any redacted information or omitted schedule and/or exhibit upon request.

+ Confidential portions of this Exhibit were redacted pursuant to Item 601(b)(10) of Regulation S-K and Zogenix Inc. agrees to furnish supplementally to the Securities and Exchange Commission a copy of any redacted information or omitted schedule and/or exhibit upon request.

# Indicates management contract or compensatory plan.

‡ Furnished herewith.

ITEM 16. FORM 10-K SUMMARY

None.

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.

March 1, 2022

By: /s/ STEPHEN J. FARR, PH.D.

Stephen J. Farr, Ph.D.

President and Chief Executive Officer

March 1, 2022

By: /s/ MICHAEL P. SMITH

Michael P. Smith

Executive Vice President, Chief Financial Officer and Treasurer

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.

Name	Title	Date
/s/ STEPHEN J. FARR, PH.D. **Stephen J. Farr, Ph.D.**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 1, 2022
/s/ MICHAEL P. SMITH **Michael P. Smith**	Executive Vice President, Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	March 1, 2022
/s/ CAM L. GARNER **Cam L. Garner**	Chairman of the Board	March 1, 2022
/s/ LOUIS C. BOCK **Louis C. Bock**	Director	March 1, 2022
/s/ JAMES B. BREITMEYER, M.D., PH.D. **James B. Breitmeyer, M.D., Ph.D**	Director	March 1, 2022
/s/ ERLE T. MAST **Erle T. Mast**	Director	March 1, 2022
/s/ CAROLINE M. LOEWY **Caroline M. Loewy**	Director	March 1, 2022
/s/ MARY E. STUTTS **Mary E. Stutts**	Director	March 1, 2022
/s/ RENEE TANNENBAUM, PHARM.D. **Renee Tannenbaum, Pharm.D.**	Director	March 1, 2022
/s/ DENELLE J. WAYNICK **Denelle J. Waynick**	Director	March 1, 2022
/s/ MARK WIGGINS **Mark Wiggins**	Director	March 1, 2022