PTC THERAPEUTICS™

2024 ANNUAL REPORT

Introduction

PTC is a global biopharmaceutical company that discovers, develops and commercializes clinically differentiated medicines that provide benefits to children and adults living with rare disorders. Our ability to innovate to identify new therapies and to globally commercialize products is the foundation that drives investment in a robust and diversified pipeline of transformative medicines. The company's strategy is to leverage its strong scientific expertise and global commercial infrastructure to deliver transformative therapies for patients who have little to no treatment options.

Our Science

Our research efforts are focused on two scientific platforms - Splicing and Inflammation and Ferroptosis - where PTC has unique expertise to discover and advance innovative therapies to the clinic. We have a robust development portfolio with a number of potentially promising therapies for rare neurologic and metabolic diseases including phenylketonuria (PKU), Friedreich's ataxia (FA) and Huntington's Disease (HD).

Our Commitment

We are committed to children and adults living with serious diseases of high unmet need. We work hard to provide resources and support to patients and their families throughout their rare disorder journey through compassionate collaboration, throughout the drug development process. We strive to ensure we deeply understand a patient's disease journey and involve them every step of the way – from early research and development to clinical trials, to commercialization and support programs.

Our People

Our focus on excellence begins with developing and retaining a global workforce that is equipped to lead in their fields. By adapting new ways of working, driving execution excellence, and staying true to our patient-focused mission we further strengthen our patient-centric, compliant and innovative culture. Our commitment to patients drives us to think differently about solutions and to work collaboratively as One PTC.

A Message to Our Shareholders

As we began 2024, I shared our ambitious plans to position PTC for future success. I am proud to say that 2024 was a year of outstanding execution across every part of the company.

We achieved all planned clinical and regulatory milestones on time, including the submission of four approval applications to the U.S. Food and Drug Administration (FDA), all of which were accepted for review, including: Kebilidi™ (eladocagene exuparvovec-tneq) for AADC deficiency which was approved in November 2024 and is the first-ever direct-to-brain administered gene therapy approved by FDA; sepiapterin for phenylketonuria (PKU) which has a regulatory action date of July 29, 2025; Translarna™ (ataluren) for nonsense mutation Duchenne muscular dystrophy (nmDMD); and vatiquinone for Friedreich's ataxia (FA) which was accepted with priority review and has a regulatory action date of Aug. 19, 2025. In addition to the U.S. filings, we submitted marketing applications for sepiapterin in key markets globally including the European Union (EU), Brazil, and Japan.

We also had an outstanding year of commercial performance, exceeding revenue guidance despite significant headwinds for our global Duchenne muscular dystrophy business. This commercial performance is a testament to our commercial teams' ability to effectively execute around the globe, even in genericized and competitive markets.

2024 was a year of outstanding execution across every part of the company

Through our revenue performance, effective management of operating expenses and the rapid and robust monetization of the priority review voucher received with the FDA approval of Kebilidi, we ended 2024 with over $1.1 billion in cash. In addition, following the closing of the Novartis PTC518 transaction in January 2025, we received an additional $1.0 billion. This strong cash position provides us with the resources to support our planned commercial launches, continue to invest in our innovative R&D platforms and engage in business development activities to complement our existing commercial and R&D portfolios. We now have the potential to be cashflow breakeven without the need to raise additional capital.

In 2025, we are planning for another year of execution and success. There are a number of potential important value-creating milestones ahead, including the potential global launch of sepiapterin, expected data readout from the PIVOT-HD Phase 2 study of PTC518 in Huntington's Disease (HD) patients, and a number of additional scheduled regulatory decisions in the U.S. and outside the U.S.

The global launch of sepiapterin will be PTC's first-ever global launch. There remains a significant unmet need for PKU patients as the vast majority of patients are not well controlled by available therapies. The data collected to date demonstrate that sepiapterin can provide meaningful benefit to the full range of PKU patients. Data from ongoing studies

were recently highlighted at the 2025 American College of Medical Genetics and Genomics (ACMG) Annual Clinical Genetics Meeting. Over 97% of subjects participating in the phenylalanine (Phe) tolerance protocol of the APHENITY open-label extension study demonstrated the ability to liberalize their diet while on sepiapterin treatment with two-thirds able to reach the recommended daily allowance for protein for an individual without PKU while maintaining control of blood Phe levels. In addition, a genetic variant analysis of subjects participating in the APHENITY study demonstrates that over 70% had a Genotype-Phenotype Value (GPV) consistent with classical PKU. These data provide further evidence of the potential meaningful benefits of sepiapterin treatment, including significant diet liberalization. With approximately 58,000 addressable PKU patients worldwide, including approximately 17,000 PKU patients in the U.S. with the majority not on medical treatments, our experienced commercial team and global commercial infrastructure, we believe sepiapterin has the potential to exceed $1.0 billion in revenue in the U.S. alone.

The U.S. commercial team is also preparing for the potential launch of vatiquinone. There are an estimated 6,000 patients living with FA in the U.S. with approximately one-third of whom are children with no approved treatment option. Patients are typically treated at a small number of specialty centers and community neurology settings where PTC has established relationships. We have the potential opportunity to introduce vatiquinone as the first and only therapy for children with FA as well as provide a potential treatment option for adults living with FA. Vatiquinone's well-differentiated mechanism of action with long-term safety and efficacy can provide an important treatment option for these patients suffering from this devastating rare neurological disease.

We had many exciting developments in 2024 for our PTC518 HD program. In June, we shared the interim results from the PIVOT-HD study on the first approximately 30 patients who completed 12 months of treatment. All key objectives were met: dose-dependent and durable lowering of mutant Huntingtin protein in blood and demonstrated dose-dependent lowering of cerebrospinal fluid mutant Huntingtin protein levels in line with what was recorded peripherally. In addition, we demonstrated dose-dependent benefits on several clinical scales, including the total motor scale and the composite Unified Huntington's Disease Rating Scale (cUHDRS), and importantly, PTC518 was shown to be safe and well-tolerated.

In December 2024, we announced a collaboration with Novartis for the development and commercialization of PTC518. As part of the agreement, PTC received $1.0 billion upfront and has the potential to achieve up to $1.9 billion in development, regulatory, and sales milestones. In addition, PTC maintains a 40% U.S. profit share and will receive double-digit geared royalties on ex-U.S. sales. Following the completion of the placebo-controlled portion of the PIVOT-HD study, Novartis will assume all development, manufacturing and commercialization responsibilities for PTC518, including the Phase 3 trial.

In the second quarter of 2025, we will share 12–month results from all enrolled subjects in the PIVOT-HD study, as well as longer term data from the subjects on whom we have previously shared 12–month results. Our team will continue to work with the Novartis team on the next steps in the PTC518 development program as we look to bring the first-ever disease modifying therapy to individuals with HD.

In 2025, we will continue to advance the next generation of innovative PTC products through our focused research and development activities. We have two research platforms that leverage our highly differentiated scientific expertise: splicing and inflammation and ferroptosis.

The PTC teams responsible for the successful discovery and development of our spinal muscular atrophy (SMA) and HD programs pioneered the field of splicing therapies and are well-positioned to continue to lead it. Over the past decade, we have made a number of key learnings that have expanded the set of potential druggable splicing targets and allowed us to streamline key steps in the preclinical development process. One recent advance is PTSeek™. PTSeek is a proprietary screening engine that allows for rapid and reliable identification of potential hits for specific splicing targets. Through this process, we have significantly accelerated preclinical timelines and have a number of active splicing programs targeting both central nervous system (CNS) and non-CNS indications that we plan to bring forward in 2025.

We have also made significant progress on our inflammation and ferroptosis platform. This platform focuses on targets that are key to the inflammatory and oxidative stress pathways known to underpin many diseases. We have several active programs targeting both CNS and non-CNS indications that we will advance in 2025, including a Phase 2–ready DHODH inhibitor for neuroinflammatory conditions. In addition, we have an NLRP3 program that we will move towards IND-enabling studies, as well as preclinical programs targeting alpha synuclein and Nrf2 activation.

Our teams' ability to effectively execute on our mission of delivering innovative therapies to children and adults living with disorders of high unmet need is made possible by our unwavering passion and commitment to the patients we proudly serve.

We entered 2024 with an ambitious agenda to position PTC for future success. With the many outstanding achievements of 2024 and our demonstrated ability to effectively execute across every part of the business we accomplished this goal and look forward to a successful 2025 and beyond.

Outstanding 2024 Revenue Performance Driven by Inline Products

translarna™ ataluren

Emflaza® (deflazacort)
6 mg | 18 mg | 30 mg | 36 mg tablets
22.75 mg/mL oral suspension

Upstaza™ (eladocagene exuparvovec)

Tegsedi® (inotersen) injection 284 mg/1.5 mL

waylivra® (volanesorsen) injection 285 mg/1.5 mL

Evrysdi® risdiplam

2024 Total Revenue

$807M

Strong Cash Position Enables Future Revenue Growth and R&D Innovation

Reach Cashflow Breakeven Without Additional Capital

Support Commercial Launches and Innovative R&D Programs

Fund BD Activities to Complement Product Portfolio

Research Platforms Provide Continuous Source of Innovative Therapies

Splicing

Validated Splicing Platform Provides Source of Innovative and Valuable Therapies

PTC has pioneered discovery and development of oral splicing therapies

PTSeek™

Platform innovations such as PTSeek™ accelerate discovery of novel splicing therapies

Multiple active CNS programs advancing towards clinic

Additional early-stage programs targeting non-CNS indications

Inflammation & Ferroptosis

Inflammation & Ferroptosis Programs Targeting CNS and Non-CNS Disorders

Focused on novel targets key to inflammation and oxidative stress

Active programs targeting CNS and non-CNS disorders

Phase 2 ready DHODH inhibitor program for neuroinflammation indications

NLRP3 inhibitor program

Preclinical program targeting alpha synuclein for Parkinson's disease

Preclinical program targeting nrf2 activation for both CNS and peripheral indications

Four U.S. Regulatory Approval Applications Submitted in 2024

AADC deficiency gene therapy – KEBILIDI™	*Approved*
Sepiapterin phenylketonuria NDA	*Accepted*
Translarna nmDuchenne Muscular Dystrophy NDA	*Accepted*
Vatiquinone Friedreich's ataxia NDA	*Accepted*

Execution in 2024 Provided a Foundation for Success

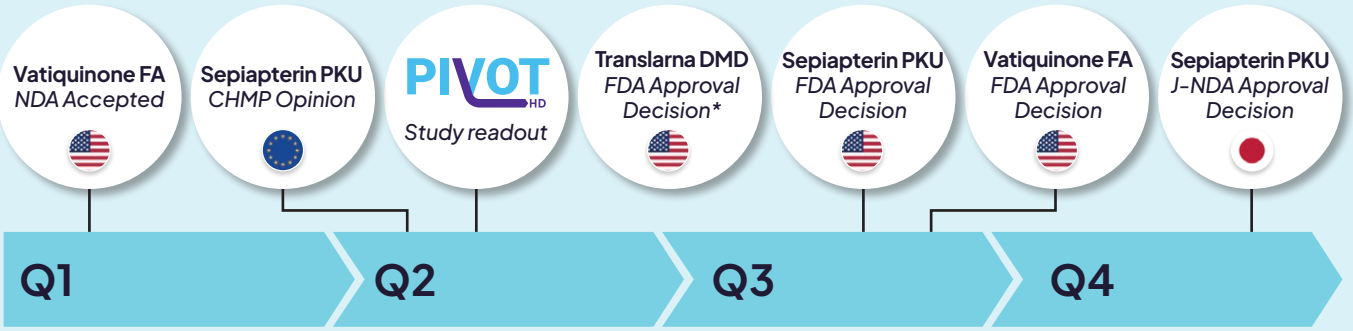
All Development Milestones Achieved

Outstanding Revenue Performance

Strong Cash Position

Advanced Programs from Innovative Scientific Platforms

Numerous Potential Value-Creating Milestones Expected in 2025



* No action date provided

FORM **10K**

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended: December 31, 2024

or

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

Commission file number: 001-35969

PTC THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**04-3416587**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
500 Warren Corporate Center Drive **Warren, NJ**	**07059**
(Address of principal executive offices)	(Zip Code)

(908) 222-7000

(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol (s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	PTCT	Nasdaq Global Select 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 Section 15(d) of the 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 the 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 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☑

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

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

The aggregate market value of the Common Stock held by non-affiliates of the registrant, based upon the last sale price of the Common Stock reported on the Nasdaq Global Select Market on June 28, 2024, the last business day of the registrant's most recently completed second fiscal quarter, was $1,733,690,074. For purposes of this calculation, shares of Common Stock held by directors and officers have been treated as shares held by affiliates.

As of February 25, 2025, the registrant had 78,869,368 shares of Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2025 Annual Meeting of Shareholders which is expected to be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2024.

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PTC Therapeutics, Inc.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the outcome of pricing, coverage and reimbursement negotiations with third-party payors for our products or product candidates that we commercialize or may commercialize in the future;
- expectations with respect to sepiapterin for the treatment of phenylketonuria, including any regulatory submissions and potential approvals, commercialization, and the potential achievement of regulatory and sales milestones and contingent payments that we may be obligated to make
- our ability to maintain our marketing authorization of Translarna for the treatment of nonsense mutation Duchenne muscular dystrophy, or nmDMD, in Brazil, Russia, the European Economic Area, or the EEA, and other regions, including whether the European Commission adopts the negative opinion from the Committee for Medicinal Products for Human Use, or CHMP, for the conditional marketing authorization for Translarna in the EEA, or our ability to identify other potential mechanisms by which we may provide Translarna to nmDMD patients in the EEA;
- our ability to use the clinical data from our international drug registry study and real-world evidence concerning Translarna's benefits to support a continued marketing authorization for Translarna for the treatment of nmDMD in the EEA;
- our ability to use the results of Study 041, a randomized, 18-month, placebo-controlled clinical trial of Translarna for the treatment of nmDMD followed by an 18-month open-label extension, and from our international drug registry study to support a marketing approval for Translarna for the treatment of nmDMD in the United States;
- whether investigators agree with our interpretation of the results of clinical trials and the totality of clinical data from our trials of Translarna;
- expectations with respect to our license and collaboration agreement with Novartis Pharmaceuticals Corporation, including our right to receive any development, regulatory and sales milestones, and profit sharing and royalty payments from Novartis;
- expectations with respect to vatiquinone for the treatment of Friedreich's ataxia, including any regulatory submissions and potential approvals, commercialization, and the potential achievement of regulatory and sales milestones and contingent payments that we may be obligated to make;
- expectations with respect to Upstaza/Kebilidi, including commercialization, manufacturing capabilities, and the potential achievement of sales milestones and contingent payments that we may be obligated to make;
- our expectations with respect to the commercial status of Evrysdi® (risdiplam) and our program directed against spinal muscular atrophy in collaboration with F. Hoffmann La Roche Ltd and Hoffmann La Roche Inc. and the Spinal Muscular Atrophy Foundation and our estimates regarding future revenues from sales-based royalty payments or the achievement of milestones in that program;
- our expectations and the potential financial impact and benefits related to our Collaboration and License Agreement with a subsidiary of Ionis Pharmaceuticals, Inc., including the commercialization of Tegsedi and

Waylivra, and our expectations with respect to royalty payments by us based on our potential achievement of certain net sales thresholds;

- the timing and scope of our commercialization of our products and product candidates;
- our estimates regarding the potential market opportunity for our products or product candidates, including the size of eligible patient populations and our ability to identify such patients;
- our ability to obtain additional and maintain existing reimbursed named patient and cohort early access programs for our products on adequate terms, or at all;
- our estimates regarding expenses, future revenues, third-party discounts and rebates, capital requirements and needs for additional financing, including our ability to maintain the level of our expenses consistent with our internal budgets and forecasts and to secure additional funds on favorable terms or at all;
- our ability to realize the anticipated benefits of our acquisitions or other strategic transactions, including the possibility that the expected impact of benefits from the acquisitions or strategic transactions will not be realized or will not be realized within the expected time period, significant transaction costs, the integration of operations and employees into our business, our ability to obtain marketing approval of our product candidates we acquired from the acquisitions or other strategic transactions and unknown liabilities;
- the rate and degree of market acceptance and clinical utility of any of our products or product candidates;
- the ability and willingness of patients and healthcare professionals to access our products and product candidates through alternative means if pricing and reimbursement negotiations in the applicable territory do not have a positive outcome;
- the timing of, and our ability to obtain additional marketing authorizations for our products and product candidates;
- the ability of our products and our product candidates to meet existing or future regulatory standards;
- the potential receipt of revenues from future sales of our products or product candidates;
- the expected impact of our loss of market exclusivity for Emflaza® (deflazacort) for the treatment of Duchenne muscular dystrophy in the United States under the Orphan Drug Act of 1983;
- our sales, marketing and distribution capabilities and strategy, including the ability of our third-party manufacturers to manufacture and deliver our products and product candidates in clinically and commercially sufficient quantities and the ability of distributors to process orders in a timely manner and satisfy their other obligations to us;
- our ability to establish and maintain arrangements for the manufacture of our products and product candidates that are sufficient to meet clinical trial and commercial launch requirements;
- our ability to complete any post-marketing requirements imposed by regulatory agencies with respect to our products;
- our expectations with respect to the potential financial impact and benefits of our leased biologics manufacturing facility and our ability to satisfy our obligations under the terms of the lease agreement for such facility;
- our ability to satisfy our obligations under the indenture governing our 1.50% convertible senior notes due September 15, 2026;
- our regulatory submissions, including with respect to timing and outcome of regulatory review;

- the timing and conduct of our ongoing, planned and potential future clinical trials and studies for sepiapterin and our splicing and inflammation and ferroptosis programs as well as studies in our products for maintaining authorizations, label extensions and additional indications, including the timing of initiation, enrollment and completion of the trials and the period during which the results of the trials will become available;

- our plans to advance our earlier stage programs and pursue research and development of other product candidates, including our splicing and inflammation and ferroptosis programs;

- whether we may pursue business development opportunities, including potential collaborations, alliances, and acquisition or licensing of assets and our ability to successfully develop or commercialize any assets to which we may gain rights pursuant to such business development opportunities;

- the potential advantages of our products and any product candidate;

- our intellectual property position;

- the impact of government laws and regulations;

- the impact of litigation that has been or may be brought against us or of litigation that we are pursuing against others; and

- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly under the heading "Summary of Risk Factors" and the risk factors detailed further in Part I, Item 1A. Risk Factors that we believe could cause actual results or events to differ materially from the forward-looking statements that we make.

Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to 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. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

In this Annual Report on Form 10-K, unless otherwise stated or the context otherwise requires, references to "PTC," "PTC Therapeutics," "we," "us," "our," "the Company," and similar references refer to PTC Therapeutics, Inc. and, where appropriate, its subsidiaries. The trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

All website addresses given in this Annual Report on Form 10-K are for information only and are not intended to be an active link or to incorporate any website information into this document.

SUMMARY OF RISK FACTORS

Below is a summary of the principal risk factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks and uncertainties that we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found in Item 1A. Risk Factors, of this Annual Report on Form 10-K, and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the Securities Exchange Commission, before making an investment decision regarding our common stock. The forward-looking statements discussed above are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Summary of Risk Factors

- We may be unable to continue to execute our commercial strategy for our products, fail to obtain renewal of, or satisfy the conditions of our marketing authorization for our products;
- Delays or failures in obtaining regulatory approval would materially impair our commercialization capabilities;
- We may be unable to continue to commercialize Translarna for nmDMD in the EEA if the EC adopts the negative opinion issued by the CHMP for the renewal of the existing conditional authorization for Translarna.
- We may not qualify for certain specialized pathways to develop our product candidates or to seek approval;
- We or our collaborators may experience any of a number of possible unforeseen events in connection with clinical trials related to our products and product candidates;
- Subgroup, retrospective, post-hoc, and certain statistical analyses may not be reliable and typically will not form the basis for regulatory approval;
- We may experience delays or difficulties in the enrollment of patients in our clinical trials;
- We may identify serious adverse side effects during the development or further development of any product or product candidate;
- Our products and product candidates may be difficult to manufacture;
- Our products and product candidates may fail to achieve market acceptance in the medical community;
- We may be unable to establish or maintain sales, marketing and distribution capabilities or enter into agreements with third parties to market, sell and distribute our products or product candidates;
- A substantial portion of our commercial sales currently occurs in territories outside of the United States which subjects us to additional business risks and laws and regulations, including those governing export restrictions and economic sanctions;
- We face substantial competition;
- Our products or product candidates may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives;
- There may be future changes in legal and regulatory requirements that may materially impact our results of operations;
- We have incurred significant losses since our inception and expect to continue to incur significant operating expenses for the foreseeable future. We may need additional funding and we may never generate profits from operations or maintain profitability;
- We may engage in strategic transactions to acquire assets, businesses, or rights to products, product candidates or technologies or from collaborations or make investments in other companies or technologies that could harm our business and dilute our stockholders' ownership;
- Raising additional capital may dilute our stockholders' ownership, restrict our operations or require us to relinquish rights to our technologies or product candidates;
- We may not be able to comply with applicable laws and regulations for our products or product candidates;
- We may not be able to obtain orphan drug exclusivity for our products or product candidates in either the United States or the EU;
- All pharmaceutical products for which marketing authorization has been granted are subject to extensive and rigorous regulation;

- Failure to obtain and maintain acceptable pricing and reimbursement terms for our products would delay our commercialization efforts;
- Legislative and regulatory changes affecting the pharmaceutical industry or the healthcare system more broadly may negatively affect our business;
- We may fail to properly allocate our resources;
- We contract with third parties for the manufacture and distribution of our products and certain of our product candidates and these third parties may encounter issues that affect our business;
- We rely on third parties to conduct our preclinical and clinical trials and other essential services;
- We currently depend, and expect to continue to depend, on collaborations with third parties for the development and commercialization of some of our products and product candidates;
- Our business and operations would suffer in the event of computer system failures, cyber-attacks or a deficiency in our, or our collaborators' or third-party vendors', cyber-security;
- We may be subject to product liability and other civil lawsuits;
- We may be unable to retain our key executives;
- We may be unable to obtain or maintain patent protection for our technology and products;
- We may become involved in lawsuits to protect or enforce our intellectual property or in connection with allegations that we are infringing on third-party intellectual property rights;
- Without patent protection, our marketed products may face generic competition;
- We may not obtain or maintain adequate trademark protection for our brand names;
- Our rights to develop and commercialize Upstaza/Kebilidi are subject, in part, to the terms and conditions of licenses granted to us by others;
- We may not have sufficient cash flow from our business to make payments on our debt; and
- The price of our common stock may be volatile and fluctuate substantially.

PART I

Item 1. Business

Overview

We are a global biopharmaceutical company that discovers, develops and commercializes clinically differentiated medicines that provide benefits to children and adults living with rare disorders. Our ability to innovate to identify new therapies and to globally commercialize products is the foundation that drives investment in a robust and diversified pipeline of transformative medicines. Our mission is to provide access to best-in-class treatments for patients who have little to no treatment options. Our strategy is to leverage our strong scientific and clinical expertise and global commercial infrastructure to bring therapies to patients. We believe that this allows us to maximize value for all of our stakeholders.

Our Pipeline

We have a diversified therapeutic portfolio that includes several commercial products and product candidates in various stages of development, including discovery, research and clinical stages, focused on the development of new treatments for multiple therapeutic areas for rare diseases relating to neurology and metabolism. The disclosure below summarizes the status of our significant clinical-stage programs and commercial products as of the date of this report, including those with our strategic partners:

- ***Global Commercial Footprint***
  - ***Global DMD Franchise –*** We have two products, Translarna™ (ataluren) and Emflaza® (deflazacort), for the treatment of Duchenne muscular dystrophy, or DMD, a rare, life-threatening disorder. Translarna currently has conditional marketing authorization in the European Economic Area, or EEA, for the treatment of nonsense mutation Duchenne muscular dystrophy, or nmDMD, in ambulatory patients aged two years and older. In January 2024, the Committee of Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, issued a negative opinion for the renewal of the conditional marketing authorization following a re-examination procedure. In May 2024, the European Commission, or EC, decided not to adopt the CHMP's negative opinion for the renewal of the conditional marketing authorization of Translarna and returned such opinion to the CHMP for re-evaluation. In June 2024, following the EC's request for re-review, the CHMP issued a negative opinion on the renewal of the conditional marketing authorization of Translarna for the treatment of nmDMD. On October 18, 2024, the CHMP maintained its negative opinion for the renewal of the conditional marketing authorization following the requested reexamination procedure. In accordance with EMA regulations, the EC has 67 days from the date of issuance to adopt the opinion. At this time, the EC has not yet adopted the negative opinion. If the EC adopts the negative opinion, Translarna would no longer have marketing authorization in the member states of the EEA. The marketing authorization for Translarna remains in effect, pending the EC's potential adoption of the negative opinion. We are exploring other potential mechanisms by which we may provide Translarna to nmDMD patients in the EEA if the negative opinion is adopted by the EC. Translarna also has marketing authorization in Russia for the treatment of nmDMD in patients aged two years and older, and in Brazil for the treatment of nmDMD in ambulatory patients two years and older and for continued treatment of patients that become non-ambulatory, as well as in various other countries as described below. Emflaza is approved in the United States for the treatment of DMD in patients two years and older.

- ***Upstaza™ (eladocagene exuparvovec) / Kebilidi™ (eladocagene exuparvovec-tneq)*** – Upstaza, a gene therapy for the treatment of Aromatic L-Amino Decarboxylase, or AADC, deficiency, a rare central nervous system, or CNS, disorder is approved for the treatment of AADC deficiency for patients 18 months and older within the EEA and the United Kingdom. In November 2024, the U.S. Food and Drug Administration, or FDA, granted accelerated approval for this gene therapy for the treatment of AADC deficiency in the United States. This gene therapy is marketed with the brand name Kebilidi in the United States.
- ***Tegsedi® (inotersen) and Waylivra® (volanesorsen)*** **–** We hold the rights for the commercialization of Tegsedi and Waylivra for the treatment of rare diseases in countries in Latin America and the Caribbean pursuant to our Collaboration and License Agreement with a subsidiary of Ionis Pharmaceuticals, Inc., or Ionis. Tegsedi has received marketing authorization in the United States, European Union, or EU, and Brazil for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis, or hATTR amyloidosis. Waylivra is approved in Brazil for the treatment of familial chylomicronemia syndrome, or FCS, and familial partial lipodystrophy, or FPL.
- ***Evrysdi® (risdiplam)*** **–** Evrysdi, a treatment for spinal muscular atrophy, or SMA, was approved by the FDA for the treatment of SMA in adults and children of all ages and by the EC for the treatment of 5q SMA in patients of all ages with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies. Evrysdi has also received marketing authorization for the treatment of SMA in over 100 countries. Evrysdi is a product of our SMA program and our collaboration with F. Hoffman-La Roche Ltd. and Hoffman-La Roche Inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or SMA Foundation.

- ***Diversified Development Pipeline***
  - ***Sepiapterin*** **–** Sepiapterin is our product candidate for the treatment of phenylketonuria, or PKU. In May 2023, we announced that the primary endpoint was achieved in our registration-directed Phase 3 trial for sepiapterin for phenylketonuria, or PKU. In March 2024, we submitted a marketing authorization application, or MAA, to the EMA for sepiapterin for the treatment of PKU in the EEA, which was validated and accepted for review by the EMA in May 2024. We expect an opinion from the CHMP in the second quarter of 2025. In July 2024, we submitted a new drug application, or NDA, to the FDA for sepiapterin for the treatment of pediatric and adult patients with PKU, including the full spectrum of ages and disease subtypes, in the United States. In September 2024, the FDA accepted for filing the NDA, with a target regulatory action date of July 29, 2025. We also made regulatory submissions for sepiapterin for the treatment of PKU in Brazil in the third quarter of 2024 and in Japan in the fourth quarter of 2024, with a regulatory decision in Japan expected in the fourth quarter of 2025.
  - ***Splicing Platform*** **–** In addition to our SMA program, our splicing platform also includes PTC518, which is being developed for the treatment of Huntington's disease, or HD. We initiated a Phase 2 study of PTC518 for the treatment of HD in the first quarter of 2022, which consists of an initial 12-week placebo-controlled phase focused on safety, pharmacology and pharmacodynamic effects followed by a nine-month placebo-controlled phase focused on PTC518 biomarker effect. In June 2023, we announced interim data from the 12-week placebo-controlled phase of the Phase 2 study of PTC518. In June 2024, we announced interim results from the full Phase 2 study of PTC518. In September 2024, the FDA granted Fast Track designation to the PTC518 program for the treatment of HD. In December 2024, we held a Type C meeting with the FDA to discuss whether huntingtin protein lowering could be considered a surrogate endpoint for accelerated approval of PTC518. The FDA was aligned on the scientific rationale and asked to see additional data supportive of an association between huntingtin protein lowering and changes in clinical outcome scores. We expect to provide results from the Phase 2 study of PTC518 for the treatment of HD in the second quarter of 2025. In November 2024, we entered into a License and Collaboration Agreement with Novartis Pharmaceuticals Corporation, or Novartis, relating to our PTC518 program, or the Novartis Agreement. Pursuant to the Novartis Agreement, we will continue to conduct the ongoing Phase 2A Clinical Trial and the ongoing open label extension, or OLE, Clinical Trial pursuant to its existing development plan, with the goal of transitioning the ongoing OLE Clinical Trial to Novartis within 12 months after the effective date of the Novartis Agreement. Novartis will be responsible for all other development of licensed compounds and licensed products and the manufacture and commercialization of licensed compounds and licensed products worldwide.

- ***Inflammation and Ferroptosis Platform*** – The most advanced molecule in our inflammation and ferroptosis platform is vatiquinone. We announced topline results from a registration-directed Phase 3 trial of vatiquinone in children and young adults with Friedreich's ataxia, or FA, called MOVE-FA, in May 2023. While the trial did not meet its primary endpoint, vatiquinone treatment did demonstrate significant benefit on key disease subscales, including the upright stability subscale, as well as on other disease relevant endpoints. In the first quarter of 2024, we met with the FDA, who expressed willingness to review an NDA for vatiquinone for the treatment of FA, based on the MOVE-FA trial as well as data from the ongoing OLE study following the MOVE-FA trial, potentially allowing for the submission of an NDA in late 2024. In October 2024, we announced that the pre-specified endpoint for two different FA long-term extension studies was met, with statistically significant evidence of durable treatment benefit on disease progression. In December 2024, we submitted an NDA to the FDA for vatiquinone for the treatment of children and adults living with FA. In February 2025, the FDA accepted for filing the NDA and granted priority review with a target regulatory action date of August 19, 2025.

- ***Pre-clinical Pipeline***
  - We continue to invest in our pre-clinical product pipeline by committing resources to research and development programs to provide access to best-in-class treatments for patients who have an unmet medical need. Our pre-clinical efforts are focused on two scientific platforms: splicing and inflammation and ferroptosis, two areas of science where PTC has significant expertise.

Global Commercial Footprint

Global DMD Franchise

Duchenne muscular dystrophy (DMD)

Muscular dystrophies are genetic disorders involving progressive muscle wasting and weakness. DMD is the most common and one of the most severe types of muscular dystrophy. DMD occurs when a mutation in the dystrophin gene prevents the cell from making a functional dystrophin protein. Dystrophin is a muscle membrane associated protein and is critical to the structural and membrane stability of muscle fibers in skeletal, diaphragm and heart muscle. The absence of normally functioning dystrophin results in muscle fragility, such that muscle injury occurs when muscles contract or stretch during normal use. As muscle damage progresses, connective tissue and fat replace muscle fibers, resulting in inexorable muscle weakness.

Because the dystrophin gene is located on the X chromosome, DMD occurs primarily in young boys, although approximately 10% of female carriers show some disease symptoms. DMD is rare, and estimates of occurrence include approximately 1 in every 3,500 live male births, according to the National Organization for Rare Diseases and approximately 1 in every 5,000 live male births according to Ryder (2017) in the European Journal of Human Genetics. We estimate that there are between approximately 10,000 to 15,000 DMD patients in the United States. Several different types of mutation in the dystrophin gene can result in DMD, including deletion, duplication and nonsense mutations. A test known as multiplex ligation-dependent probe amplification (MLPA) can detect large deletions and duplications, which account for approximately 75% of all mutations. However, gene sequencing is required to identify small mutations such as nonsense mutations. We estimate that nonsense mutations account for approximately 13% of cases of DMD. Without treatment, patients with DMD typically lose walking ability by their early teens, require ventilation support in their late teens, and eventually experience premature death due to heart and lung failure. Even with medical care, most people with DMD die from cardiac or respiratory failure before or during their 30s.

Marketing authorization matters

Translarna for the treatment of nonsense mutation Duchenne muscular dystrophy

European Economic Area

We received marketing authorization from the EC in August 2014 for Translarna for the treatment of nmDMD in ambulatory patients aged five years and older in the member states of the EEA, subject to annual renewal and other conditions. In July 2018, the EC approved a label-extension request to our marketing authorization for Translarna in the EEA to include patients from two to up to five years of age. In July 2020, the EC approved the removal of the statement "efficacy has not been demonstrated in non-ambulatory patients" from the indication statement for Translarna.

The marketing authorization is subject to annual review and renewal by the EC following reassessment by the EMA of the benefit-risk balance of continued authorization, which we refer to as the annual EMA reassessment. In September 2022, we submitted a Type II variation to the EMA to support conversion of the conditional marketing authorization for Translarna to a standard marketing authorization, which included a report on the placebo-controlled trial of Study 041 and data from the open-label extension as further described below. In February 2023, we also submitted an annual marketing authorization renewal request to the EMA. In September 2023, the CHMP gave a negative opinion on the conversion of the conditional marketing authorization to full marketing authorization of Translarna for the treatment of nmDMD and a negative opinion on the renewal of the existing conditional marketing authorization of Translarna for the treatment of nmDMD. In January 2024, the CHMP issued a negative opinion for the renewal of the conditional marketing authorization following a re-examination procedure. In May 2024, the EC decided not to adopt the CHMP's negative opinion for the renewal of the conditional marketing authorization of Translarna and returned such opinion to the CHMP for re-evaluation. In June 2024, following the EC's request for re-review, the CHMP issued a negative opinion on the renewal of the conditional marketing authorization of Translarna for the treatment of nmDMD. In October 2024, the CHMP maintained its negative opinion for the renewal of the conditional marketing authorization following the requested reexamination procedure. In accordance with EMA regulations, the EC has 67 days from the date of issuance to adopt the opinion. At this time, the EC has not yet adopted the negative opinion. If the EC adopts the negative opinion, Translarna would no longer have marketing authorization in the member states of the EEA. The marketing authorization for Translarna remains in effect, pending the EC's potential adoption of the negative opinion. We are exploring other potential mechanisms by which we may provide Translarna to nmDMD patients in the EEA if the negative opinion is adopted by the EC.

Marketing authorization is required in order for us to engage in any EEA-wide commercialization of Translarna in the EEA, which allows us to participate in pricing and reimbursement negotiations, on a country-by-country basis with each country in the EEA. Individual countries in the EEA have the ability to make Translarna available under early access programs, or EAP programs, or through similar styled programs. There is substantial risk that if the EC adopts the CHMP's negative opinion or we are otherwise unable to renew our EEA marketing authorization during any annual renewal cycle or we are unable to identify other potential mechanisms in which we may provide Translarna to nmDMD patients in the EEA should the CHMP's negative opinion be adopted by the EC or our product label is materially restricted, we would lose all, or a significant portion of, our ability to generate revenue from sales of Translarna in the EEA and other territories. For more information regarding the risks associated with a potential EC adoption of the CHMP's negative opinion on Translarna's marketing authorization, see Item 1A. Risk Factors, "*We may be unable to continue to commercialize Translarna for nmDMD in the EEA if the EC adopts the negative opinion issued by the CHMP for the renewal of the existing conditional authorization for Translarna.*"

See "Item 1. Business-Commercial Matters-Market Access Considerations" and "Item 1A. Risk Factors-Risks Related to the Development and Commercialization of our Products and our Product Candidates" and "-Risks Related to Regulatory Approval of our Product and our Product Candidates" for further information regarding the marketing authorization in the EEA, the market access process and related risks.

As the marketing authorization holder, we are obligated to monitor the use of Translarna for nmDMD to detect, assess and take required action with respect to information that could impact the safety profile of Translarna and to report this information, through pharmacovigilance submissions, to the EMA. Following its assessment of these submissions, the

EMA can recommend to the EC actions ranging from the continued maintenance of the marketing authorization to its withdrawal.

United States

Translarna is an investigational new drug in the United States. During the first quarter of 2017, we filed an NDA for Translarna for the treatment of nmDMD over protest with the FDA. In October 2017, the Office of Drug Evaluation I of the FDA issued a Complete Response Letter, or CRL, for the NDA, stating that it was unable to approve the application in its current form. In response, we filed a formal dispute resolution request with the Office of New Drugs of the FDA. In February 2018, the Office of New Drugs of the FDA denied our appeal of the CRL. In its response, the Office of New Drugs recommended a possible path forward for our ataluren NDA submission based on the accelerated approval pathway. This would involve a re-submission of an NDA containing the current data on effectiveness and safety of ataluren with new data to be generated on dystrophin production in nmDMD patients' muscles. We followed the FDA's recommendation and collected, using newer technologies via procedures and methods that we designed, such dystrophin data in a new study, Study 045, and announced the results of Study 045 in February 2021. Study 045 did not meet its pre-specified primary endpoint. In June 2022, we announced top-line results from the placebo-controlled trial of Study 041, which was our 18 months, placebo-controlled trial, followed by an 18 months open label extension, of Translarna in the treatment of ambulatory patients with nmDMD aged five years or older. Following this announcement, we submitted a meeting request to the FDA to gain clarity on the regulatory pathway for a potential re-submission of an NDA for Translarna. The FDA provided initial written feedback that Study 041 does not provide substantial evidence of effectiveness to support NDA re-submission. We held a Type C meeting with the FDA in the fourth quarter of 2023 to discuss the totality of Translarna data. Based on feedback from the FDA, we re-submitted the NDA in July 2024, based on the results from Study 041 and from our international drug registry study for nmDMD patients receiving Translarna. In October 2024, the FDA accepted for review the resubmission of the NDA for Translarna for the treatment of nmDMD. As this was an NDA resubmission following a CRL to the NDA which was filed over protest in 2016, the FDA is not obligated to follow the review timelines under Prescription Drug User Free Act, or PDUFA, guidelines and an action date has not been provided.

See "Item 1. Business-Government Regulation-The new drug and biologic approval process" below for further discussion with respect to the NDA process. See "Item 1. Business-Translarna (ataluren)" and "Item 1A. Risk Factors-Risks Related to the Development and Commercialization of our Products and our Product Candidates" and "-Risks Related to Regulatory Approval of our Products and our Product Candidates" for further detail regarding the results of our completed trials and studies of Translarna for the treatment of nmDMD, our regulatory strategy in the United States, our history with submissions to the FDA and the related risks to our business.

Other Territories

Translarna received marketing authorization for the treatment of nmDMD in Israel and South Korea in 2015, Chile in 2018, Brazil in 2019 and Russia in 2020, in addition to approvals from other countries, and these licenses are currently active. Many territories outside of the EEA, including Israel, South Korea and Chile, reference and depend on the determinations by the EMA when considering the grant of a marketing authorization. It is possible that we would not be able to maintain our marketing authorizations in these regions in the event the EMA decides not to renew or otherwise modifies or withdraws our marketing authorization in the EEA. In addition, Translarna is authorized in the United Kingdom and is undergoing a national assessment. The marketing authorization for Translarna in Brazil and Russia are subject to renewal every five years. We have been pursuing and expect to continue to pursue marketing authorizations for Translarna for the treatment of nmDMD in other regions.

Emflaza for the treatment of Duchenne muscular dystrophy in the United States

Emflaza, both in tablet and suspension form, received approval from the FDA in February 2017 as a treatment for DMD in patients five years of age and older in the United States. In June 2019, the FDA approved our label expansion request for Emflaza for patients two to five years of age. We estimate that there are between approximately 10,000 and 15,000 DMD patients in the United States.

Emflaza received a seven-year marketing exclusivity period in the United States for its approved indications, commencing on the date of FDA approval, under the provisions of the Orphan Drug Act of 1983, or the Orphan Drug Act. We have previously relied on this exclusivity period to commercialize Emflaza in the United States. Emflaza's seven-year period of orphan drug exclusivity related to the treatment of DMD in patients five years and older expired in February 2024. We expect the expiration of this orphan drug exclusivity to have a significant negative impact on Emflaza net product revenue. Emflaza's orphan drug exclusivity related to the treatment of DMD in patients two years of age to less than five expires in June 2026. See "Item 1. Business-Government Regulation" for further discussion with respect to marketing protection we rely on.

Upstaza / Kebilidi

Upstaza/Kebilidi is an adeno-associated virus, or AAV, gene therapy for the treatment of AADC deficiency, a rare CNS disorder arising from reductions in the enzyme AADC that results from mutations in the dopa decarboxylase gene. In July 2022, the EC approved Upstaza for the treatment of AADC deficiency for patients 18 months and older within the EEA. In November 2022, the Medicines and Healthcare Products Regulatory Agency approved Upstaza for the treatment of AADC deficiency for patients 18 months and older within the United Kingdom. On November 13, 2024, the FDA granted accelerated approval of our gene therapy for the treatment of children and adults with AADC deficiency, which is marketed with the brand name Kebilidi in the United States. We are obligated to complete certain post-marketing requirements in connection with the FDA's approval, including clinical safety studies.

AADC is the enzyme responsible for the conversion of L-dopa to dopamine. Dopamine is a key neurotransmitter that acts within the striatum (caudate and putamen), a component of the brain's deep grey matter, to modulate output of neurons that project to the motor and premotor cortices of the brain that plan and execute normal motor function. Dopamine is required in the brain for humans to develop and maintain proper motor function.

AADC deficiency is a monogenic disorder of neurotransmitter synthesis that manifests in young children and most commonly results in profound developmental delay, often seen as complete arrest of motor development. AADC deficiency generally causes the inability to develop motor control, resulting in breathing, feeding, and swallowing problems, frequent hospitalizations, and the need for life-long care. On average, patients with AADC deficiency die in the first decade of life due to profound motor dysfunction and secondary complications such as choking, hypoxia, and pneumonia. Currently, no treatment options are available for the underlying cause of the disorder, and care is limited to palliative options with significant burden on caregivers.

The prevalence of AADC deficiency has been estimated to be approximately 5,000 patients worldwide, with a live-birth incidence of up to 1 in 40,000 worldwide. While several diagnostic tests for AADC deficiency are available, we believe the condition remains largely undiagnosed or misdiagnosed and may be confused with cerebral palsy.

Patients are treated with Upstaza/Kebilidi during a single procedure in which the gene therapy is administered directly to the region of the brain, called the putamen, where dopamine is made and released. The targeted micro-dosing approach administering small amounts of gene therapy directly to focal regions of affected cells in the putamen has the benefit of keeping the supply requirements for materials low, improving access of the therapeutic gene to key cells, potentially limiting immune and complement-mediated responses and reducing the risk of off-target uptake and excretion of the gene therapy by the liver and kidneys.

Upstaza and Kebilidi for the treatment of AADC deficiency has orphan drug designation in the EU and United States, respectively. Due to its orphan medicinal product designation by the EMA, we rely on a ten-year exclusive marketing period for Upstaza in the EEA, which may potentially be extended for two additional years if we receive approval for a pediatric exclusivity incentive. Kebilidi has a twelve-year exclusive marketing period in the United States for the approved indication, commencing on the date of FDA approval, under the provisions of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as well as a concurrent seven-year exclusive marketing period, under the provisions of the Orphan Drug Act. We rely on the twelve-year BPCIA regulatory exclusivity and concurrent seven-year Orphan Drug Act exclusivity to commercialize Kebilidi in the United States, which we expect to expire in November 2036 and November 2031, respectively.

See “Item 1. Business-Government Regulation-The new drug and biologic approval process” below for further discussion with respect to the Biologics License Application, or BLA, process.

Tegsedi and Waylivra

In August 2018 we entered into a Collaboration and License Agreement with Akcea Therapeutics, Inc., or Akcea, a subsidiary of Ionis for the commercialization by us of Tegsedi, Waylivra and products containing those compounds in countries in Latin America and the Caribbean, or the PTC Territory. See “Item 1. Business-Our Collaborations, License Agreements and Funding Arrangements-Tegsedi and Waylivra” below for further discussion with respect to this collaboration and license agreement.

Tegsedi

Tegsedi, a product of Ionis’ proprietary antisense technology, is an antisense oligonucleotide, or ASO, inhibitor of human transthyretin, or TTR, production. Tegsedi is the world’s first RNA-targeted therapeutic to treat patients with hereditary transthyretin amyloidosis, or hATTR amyloidosis. In October 2019, it received marketing authorization from ANVISA, the Brazilian health regulatory authority, for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hATTR amyloidosis in Brazil. Our marketing authorization for Tegsedi in Brazil is subject to renewal every five years. It has also received marketing authorization in the United States and EU for the same indication.

hATTR amyloidosis is a progressive, systemic and fatal inherited disease caused by the abnormal formation of the TTR protein and aggregation of TTR amyloid deposits in various tissues and organs throughout the body, including in peripheral nerves, heart, intestinal tract, eyes, kidneys, central nervous system, thyroid and bone marrow. The progressive accumulation of TTR amyloid deposits in these tissues and organs leads to sensory, motor and autonomic dysfunction often having debilitating effects on multiple aspects of a patient’s life. Patients with hATTR amyloidosis often present with a mixed phenotype and experience overlapping symptoms of polyneuropathy and cardiomyopathy.

Ultimately, hATTR amyloidosis generally results in death within three to fifteen years of symptom onset. Therapeutic options for the treatment of patients with hATTR amyloidosis are limited and there are currently no disease-modifying drugs approved for the disease. There are an estimated 50,000 patients with hATTR amyloidosis worldwide, including approximately 6,000 patients with polyneuropathic hATTR amyloidosis in Latin America.

Waylivra

Waylivra is an ASO that has received marketing authorization in the EU for the treatment of FCS, subject to certain conditions. The United States and EU regulatory agencies have granted orphan drug designation to Waylivra for the treatment of FCS. In connection with the marketing approval for Waylivra in the EU, the EC is requiring Akcea to provide results of a study based on a registry of patients to investigate how blood checks and adjustments to frequency of injections are carried out in practice and how well they work to prevent thrombocytopenia and bleeding in FCS patients taking Waylivra. In August 2021, ANVISA approved Waylivra as the first treatment for FCS in Brazil. Our marketing authorization for Waylivra in Brazil is subject to renewal every five years.

FCS is an ultra-rare disease caused by impaired function of the enzyme lipoprotein lipase, or LPL, and characterized by severe hypertriglyceridemia (>880mg/dL) and a risk of unpredictable and potentially fatal acute pancreatitis. Because of limited LPL function, people with FCS cannot break down chylomicrons, lipoprotein particles that are 90% triglycerides. In addition to pancreatitis, FCS patients are at risk of chronic complications due to permanent organ damage. They can experience daily symptoms including abdominal pain, generalized fatigue and impaired cognitions that affect their ability to work. People with FCS also report major emotional and psychosocial effects including anxiety, social withdrawal, depression and brain fog. There is no effective therapy for FCS currently available.

Additionally, we received approval of Waylivra for the treatment of FPL in Brazil in December 2022. FPL is a rare genetic metabolic disease characterized by selective, progressive loss of body fat (adipose tissue) from various areas of the body leading to ectopic fat deposition in liver and muscle and development of insulin resistance, diabetes, dyslipidemia and fatty liver disease. Individuals with FPL often have reduced subcutaneous fat in the arms and legs and the head and trunk

regions may or may not have loss of fat. Conversely, affected individuals may also have excess subcutaneous fat accumulation in other areas of the body, especially the neck, face and intra-abdominal regions.

Evrysdi

Evrysdi was approved by the FDA in August 2020 for the treatment of SMA in adults and children two months and older and by the EC in March 2021 for the treatment of 5q SMA in patients two months and older with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies. Evrysdi has also received marketing authorization for the treatment of SMA in over 100 countries. In May 2022, the FDA approved a label expansion for Evrysdi to include infants under two months old with SMA. In August 2023, the EC approved an extension of the Evrysdi marketing authorization to include infants under two months old in the EU. Evrysdi is a product of our SMA program and our collaboration with Roche and the SMA Foundation. For additional information, see "Item 1. Business – Our Collaborations, License Agreements and Funding Arrangements – Roche and the SMA Foundation."

SMA is a genetic neuromuscular disease characterized by muscle wasting and weakness. The disease generally manifests early in life. SMA is caused by mutation or deletion of the Survival of Motor Neuron 1, or SMN1, gene that encodes the survival of motor neuron, or SMN, protein. The SMN protein is critical to the health and survival of the nerve cells in the spinal cord responsible for muscle contraction. A second gene, Survival of Motor Neuron 2, or SMN2, is very similar to SMN1, contains a T nucleotide at position 6 in exon 7 and produces low, insufficient levels of functional SMN protein due to alternative splicing of exon 7. According to the SMA Foundation, SMA is the leading genetic cause of death in infants and toddlers. Approximately 1 in 10,000 children is born with the disease. We estimate that there are between 20,000 to 30,000 children and adults living with SMA in the United States, Europe and Japan.

Diversified Development Pipeline

Our pipeline includes a number of programs at various stages of development including sepiapterin, PTC518 and other programs from our splicing and inflammation and ferroptosis platforms. Additionally, we have ongoing clinical studies of our current commercial product for maintaining authorizations and enabling additional authorizations.

Sepiapterin

Sepiapterin is a precursor to intracellular tetrahydrobiopterin, which is a critical enzymatic cofactor involved in metabolism and synthesis of numerous metabolic products. Sepiapterin has been pursued as a possible treatment for orphan metabolic diseases associated with defects in the tetrahydrobiopterin biochemical pathways, including PKU. PKU is an inborn error of metabolism caused predominantly by mutations in the phenylalanine hydroxylase gene resulting in toxic buildup of the amino acid phenylalanine, or Phe, in the brain, and, if left untreated, severe and irreversible disabilities such as permanent intellectual disability, seizures, delayed development, behavioral problems and possibly psychiatric disorders can occur. We believe that there are approximately 58,000 PKU patients globally. In May 2023, we announced that the primary endpoint was achieved in our registration-directed Phase 3 trial for sepiapterin for PKU. The primary endpoint of the study was the achievement of statistically-significant reduction in blood Phe level. The primary analysis population included those patients who have a greater than 30% reduction in blood Phe levels during the Part 1 run-in phase of the trial. Sepiapterin demonstrated Phe level reduction of approximately 63% in the overall primary analysis population and Phe level reduction of approximately 69% in the subset for classical PKU patients. Additionally, sepiapterin was well tolerated with no serious adverse events. Following the placebo-controlled study, patients were eligible to enroll in a long-term open-label study, which is still ongoing and will evaluate long-term safety, durability and Phe tolerance. In March 2024, we submitted an MAA to the EMA for sepiapterin for the treatment of PKU in the EEA, which was validated and accepted for review by the EMA in May 2024. We expect an opinion from the CHMP in the second quarter of 2025. In July 2024, we submitted an NDA to the FDA for sepiapterin for the treatment of pediatric and adult patients with PKU, including the full spectrum of ages and disease subtypes, in the United States. In September 2024, the FDA accepted for filing the NDA, with a target regulatory action date of July 29, 2025. We also made regulatory submissions for sepiapterin for the treatment of PKU in Brazil in the third quarter of 2024, and in Japan in the fourth quarter of 2024, with a regulatory decision in Japan expected in the fourth quarter of 2025.

Splicing Platform

Our splicing platform focuses on the development of innovative therapies for diseases of unmet medical need that may be ameliorated through the regulation of pre-mRNA splicing.

In addition to Evrysdi and our SMA program, our splicing platform also includes PTC518, which is being developed for the treatment of HD. HD is a neurodegenerative and progressive brain disorder caused by a toxic gain-of-function triplet repeat expansion in the huntingtin gene resulting in uncontrolled movements and cognitive loss. There are currently no disease-modifying therapies approved to delay the onset or slow the progression of HD. We believe that there are approximately 135,000 HD patients globally. PTC518 is an orally bioavailable molecule with broad central nervous system and systemic distribution that has been designed to reduce huntingtin protein expression with high selectivity and specificity. We announced the results from our Phase 1 study of PTC518 in healthy volunteers in September 2021 demonstrating dose-dependent lowering of huntingtin messenger ribonucleic acid and protein levels, that PTC518 efficiently crosses blood brain barrier at significant levels and that PTC518 was well tolerated. We initiated a Phase 2 study of PTC518 for the treatment of HD in the first quarter of 2022, which consists of an initial 12-week placebo-controlled phase focused on safety, pharmacology and pharmacodynamic effects followed by a nine-month placebo-controlled phase focused on PTC518 biomarker effect. In June 2023, we announced interim data from the 12-week placebo-controlled phase of the Phase 2 study of PTC518. The study demonstrated dose-dependent lowering of huntingtin, or HTT, protein levels in peripheral blood cells, reaching an approximate mean 30% reduction in mutant HTT levels at the 10mg dose level. In addition, PTC518 exposure in the cerebrospinal fluid was consistent with or higher than plasma unbound drug levels. Furthermore, PTC518 was well tolerated with no treatment-related serious adverse events. In June 2024, we announced interim results from the full Phase 2 study of PTC518. At month 12, PTC518 treatment demonstrated durable dose-dependent lowering of mutant HTT, or mHTT, protein in the blood and dose-dependent lowering of mHTT protein in the cerebrospinal fluid in the interim cohort of stage 2 patients. In addition, favorable trends were demonstrated on several relevant HD clinical assessments. Furthermore, following 12 months of treatment, PTC518 continued to be well tolerated. In September 2024, the FDA granted Fast Track designation to the PTC518 program for the treatment of HD. In December 2024, we held a Type C meeting with the FDA to discuss whether huntingtin protein lowering could be considered a surrogate endpoint for accelerated approval of PTC518. The FDA was aligned on the scientific rationale and asked to see additional data supportive of an association between huntingtin protein lowering and changes in clinical outcome scores. We expect to provide results from the Phase 2 study of PTC518 for the treatment of HD in the second quarter of 2025.

In November 2024, we entered into the Novartis Agreement, relating to our PTC518 HD program which included related molecules. This transaction closed in January 2025. Pursuant to the Novartis Agreement, we will continue to conduct the ongoing Phase 2A Clinical Trial and the ongoing OLE Clinical Trial pursuant to its existing development plan, with the goal of transitioning the ongoing OLE Clinical Trial to Novartis within 12 months after the effective date of the Novartis Agreement. Novartis will be responsible for all other development of licensed compounds and licensed products and the manufacture and commercialization of licensed compounds and licensed products worldwide. For additional information, see "Item 1. Business – Our Collaborations, License Agreements and Funding Arrangements – Novartis Pharmaceuticals Corporation."

Inflammation and Ferroptosis Platform

Our inflammation and ferroptosis platform consists of small molecule compounds that target oxidoreductase enzymes that regulate oxidative stress and inflammatory pathways central to the pathology of a number of CNS diseases. Oxidation-reduction, or redox, reactions are an essential component of the generation and regulation of energy in living systems. These reactions are regulated through a set of enzymes known as oxidoreductase enzymes that uniquely require the transfer of an electron, or a redox chemical reaction, to affect their biological activity.

One of the advanced molecules in our inflammation and ferroptosis platform is vatiquinone. Vatiquinone is a small molecule orally bioavailable compound that has been in development for inherited mitochondrial diseases and related genetic disorders of oxidative stress. Vatiquinone targets 15-lipoxygenase, or 15-LO, a key regulator of oxidative stress, lipid-based neuro-inflammation, alpha-synuclein oxidation and aggregation and cell death. We are developing vatiquinone for the treatment of FA. FA is a rare and life-shortening neurodegenerative disease caused by a single defect in the FXN

gene which causes reduced production of the frataxin protein. We believe that there are approximately 25,000 FA patients globally, including approximately 6,000 in the United States, of which approximately one-third are pediatric. Vatiquinone has previously been studied in FA patients in a Phase 2 trial that included a six-month placebo-controlled phase followed by an 18-month open label extension. In this trial, long-term vatiquinone treatment (18-24 months) was associated with an improvement in overall disease severity and neurological function relative to natural history. Vatiquinone has been generally well-tolerated in the clinic.

We announced topline results from our MOVE-FA trial, a registration-directed Phase 3 trial of vatiquinone in children and young adults with FA, in May 2023. While the trial did not meet its primary endpoint of statistically significant change in modified Friedreich Ataxia Rating Scale, or mFARS, score at 72 weeks in the primary analysis population, vatiquinone treatment did demonstrate significant benefit on key disease subscales and secondary endpoints. In addition, in the population of subjects that completed the study protocol, significance was reached in the mFARS endpoint and several secondary endpoints, including the upright stability subscale. Furthermore, vatiquinone was well tolerated. In the first quarter of 2024, we met with the FDA, who expressed willingness to review an NDA for vatiquinone for the treatment of FA based on the MOVE-FA trial as well as data from the ongoing open label extension study following the MOVE-FA trial. In October 2024, we announced that the pre-specified endpoint for two different FA long-term extension studies was met, with statistically significant evidence of durable treatment benefit on disease progression. In December 2024, we submitted an NDA to the FDA for vatiquinone for the treatment of children and adults living with FA. In February 2025, the FDA accepted for filing the NDA and granted priority review with a target regulatory action date of August 19, 2025.

In November 2024, we announced that the global Phase 2 placebo-controlled CardinALS study of utreloxastat for the treatment of amyotrophic lateral sclerosis, or ALS, did not meet its primary endpoint of slowing disease progression on the composite ALSFRS-R and mortality analysis. Due to the lack of efficacy and biomarker signal, further development of utreloxastat for the treatment of ALS is not planned at this time.

Translarna (ataluren)

We discovered Translarna by applying our technologies to identify molecules that promote or enhance the suppression of nonsense mutations. Nonsense mutations are implicated in a variety of genetic disorders. Nonsense mutations create a premature stop signal in the translation of the genetic code contained in mRNA and prevent the production of full-length, functional proteins. Based on our research, we believe that Translarna interacts with the ribosome, which is the component of the cell that decodes the mRNA molecule and manufactures proteins, to enable the ribosome to read through premature nonsense stop signals on mRNA and allow the cell to produce a full-length, functional protein. As a result, we believe that Translarna has the potential to be an important therapy for genetic disorders which are the result of a nonsense mutation. Genetic tests are available for many genetic disorders, including those noted above, to determine if the underlying cause is a nonsense mutation. Translarna has been generally well-tolerated in all of our clinical trials, which have enrolled over 1,000 individuals to date.

Planned and ongoing clinical development of Translarna in nonsense mutation Duchenne muscular dystrophy

Observational study, data collection, and open label, extension trials of Translarna for treatment of nmDMD

We are undertaking a multi-center, observational post-approval study of patients receiving Translarna on a commercial basis, or Study 025o, as required by the Pharmacovigilance Risk Assessment Committee of the EMA and in collaboration with TREAT-NMD and the Cooperative International Neuromuscular Research Group. During the study we will gather data on the safety, effectiveness, and prescription patterns of Translarna in routine clinical practice. We have successfully enrolled more than 300 patients in Study 025o and we expect to follow their progress over five years.

An open label, extension trial, Study 016, involving patients who participated in ACT DMD is also ongoing, across multiple sites in the United States and Canada with patients on commercial supply. We ended the two open label extension trials involving patients who had participated in our prior trials for nmDMD and have transitioned U.S. and Canadian patients from these trials to Study 016 while other patients have transitioned to commercial supply via commercial pathways or EAP programs.

Completed clinical trials of Translarna in nonsense mutation Duchenne muscular dystrophy

Phase 2 pediatric study

As part of our pediatric development commitments under our marketing authorization in the EEA and to support the potential expansion of the Translarna label to younger patients with nmDMD, we initiated a Phase 2 pediatric clinical study to evaluate the safety and pharmacokinetics of Translarna in patients two to five years of age. The study, initiated in June 2016, included a four-week screening period, a four-week study period, and a 48-week extension period for patients who complete the four-week study period (52 weeks total treatment). In July 2018, the EMA approved a label-extension request to our marketing authorization for Translarna in the EEA to include patients from two to up to five years of age, based on data from this study.

Phase 3 clinical trial of Translarna for nmDMD (ACT DMD)

In October 2015, we announced results from ACT DMD, also referred to as Study 020, our Phase 3, double-blind, placebo-controlled, 48-week clinical trial to evaluate the safety and efficacy of Translarna in patients with nmDMD. ACT DMD involved 228 patients at 53 sites across 18 countries.

In the overall intent-to-treat, or ITT, study population, the primary endpoint of change from baseline at week 48 in the 6MWT, showed a 15 meter benefit in favor of Translarna, which did not meet statistical significance.

A summary of the safety and efficacy results from ACT DMD is outlined below.

Safety and tolerability. The results of ACT DMD confirmed the favorable safety profile of Translarna seen in our 48-week, 174-patient Phase 2b double-blind, placebo-controlled clinical trial evaluating the long-term safety and efficacy of Translarna in patients with nmDMD completed in 2009, or the Phase 2b trial.

Translarna was generally well tolerated at both dose levels in our Phase 2b clinical trial. There were no study discontinuations due to adverse events. Most treatment-emergent adverse events were mild or moderate in severity. Investigators' attributions of drug-related adverse effects were generally similar across the placebo and Translarna arms. The most common adverse events in this trial were vomiting (46.6% overall), headache (29.3%), diarrhea (24.1%), nasopharyngitis (20.7%), fever (19.0%), cough (19.0%) and upper abdominal pain (17.8%). These events were generally balanced across treatment arms and are typical of pediatric illnesses. Adverse events with at least a 10% incidence in any treatment arm that were seen with increased frequency from the placebo group to the Translarna 40 mg dose group to the Translarna 80 mg dose group were nausea (12.3% for placebo, 14.0% for the Translarna 40 mg group and 16.7% for the Translarna 80 mg group), abdominal pain (7.0% for placebo, 12.3% for the Translarna 40 mg group and 16.7% for the Translarna 80 mg group), pain in extremity (10.5% for placebo, 12.3% for the Translarna 40 mg group and 13.3% for the Translarna 80 mg group), flatulence (7.0% for placebo, 8.8% for the Translarna 40 mg group and 11.7% for the Translarna 80 mg group) and nasal congestion (7.0% for placebo, 8.8% for the Translarna 40 mg group and 10.0% for the Translarna 80 mg group). There were no serious adverse events observed during the trial that were considered possibly or probably related to Translarna. Determination of relatedness of the serious adverse event to Translarna was made by the trial investigator, based on his or her judgment.

Translarna was generally well tolerated in ACT DMD. There were two study discontinuations due to adverse events, including one in the Translarna arm (constipation) and one in the placebo arm (disease progression). Most treatment-emergent adverse events were mild or moderate in severity. The most common adverse events in this trial were vomiting (20.4% overall), nasopharyngitis (20.0%), headache (18.3%), and fall (17.8%). These events were generally balanced across treatment arms and are typical of pediatric illnesses and/or patients with DMD. Adverse events with at least a 10% incidence in either treatment arm that were seen with increased frequency from the placebo group to the Translarna 40 mg dose group were vomiting (18.3% for placebo, 23.6% for the Translarna 40 mg group), nasopharyngitis (19.1% for placebo, 20.9% for the Translarna 40 mg group), fall (17.4% for placebo, 18.3% for the Translarna 40 mg group), cough (11.3% for placebo, 16.5% for the Translarna 40 mg group) diarrhea (8.7% for placebo, 17.4% for the Translarna 40 mg group), and pyrexia (10.4% for placebo, 13.9% for the Translarna 40 mg group). An overview of adverse events in this trial is shown in the table below.

Overview of treatment-emergent adverse events in Phase 3 clinical trial (as-treated population)

Parameter	Placebo N=115	Translarna 40 mg group N=115	All patients N=230
Patients with ≥1 adverse event	101 (87.8)%	103 (89.6)%	204 (88.7)%
Adverse events by severity			
Grade 1 (mild)	54 (47.0)%	61 (53.0)%	115 (50.0)%
Grade 2 (moderate)	37 (32.2)%	35 (30.4)%	72 (31.3)%
Grade 3 (severe)	9 (7.8)%	7 (6.1)%	16 (7.0)%
Grade 4 (life-threatening)	—	—	—
Adverse events by relatedness			
Unrelated	47 (40.9)%	44 (38.3)%	91 (39.6)%
Unlikely	30 (26.1)%	20 (17.4)%	50 (21.7)%
Possible	18 (15.7)%	27 (23.5)%	45 (19.6)%
Probable	6 (5.2)%	12 (10.4)%	18 (7.8)%
Discontinuations due to adverse events	1 (0.9)%	1 (0.9)%	2 (0.9)%
Serious adverse events	4 (3.5)%	4 (3.5)%	8 (3.5)%
Deaths	—	—	—

There were no serious adverse events observed during the trial that were considered possibly or probably related to Translarna. Determination of relatedness of the serious adverse event to Translarna was made by the trial investigator, based on his or her judgment.

Intent to Treat (ITT) Population. The primary efficacy endpoint in ACT DMD was change in 6-minute walk distance, or 6MWD, from baseline to week 48. In the ITT population, a 15 meter benefit (p=0.213) was observed in the primary endpoint which did not meet statistical significance.

Secondary endpoints in the trial included the proportion of patients with at least 10% worsening in 6MWD at week 48 of the trial compared to baseline, or 10% 6MWD worsening, and change in timed function tests of time to run/walk 10 meters, climb four stairs and descend four stairs. The hazard ratio for Translarna versus placebo was 0.75 (p=0.160) for 10% 6MWD worsening. Benefits trended in favor of Translarna over placebo in the timed function tests in the ITT population, including observed results in time to run/walk 10 meters (1.2 seconds; p=0.117), time to climb four stairs (1.8 seconds; p=0.058), and time to descend four stairs (1.8 seconds; p=0.012).

Additional endpoints included the North Start Ambulatory Assessment, or NSAA, test, a functional scale designed for boys affected by DMD, and the Pediatric Outcomes Data Collection Instrument, or PODCI, a validated tool for measuring quality of life in pediatric patients with orthopedic conditions. These additional endpoints favored Translarna in the ITT population but did not meet statistical significance.

Pre-Specified Analyses. The statistical analysis plan submitted to the FDA for ACT DMD set forth pre-specified analyses of efficacy to be conducted, including subgroups of patients with baseline 6MWD less than 350 meters and patients with baseline 6MWD of greater than or equal to 300 and less than 400 meters, which we refer to as our key subgroups.

The pre-specification of our key subgroups was scientifically justified based upon knowledge of the biology and natural history of the disease and the evolving understanding of the of the six minute walk test as used to assess DMD patients. We considered the pre-specified less than 350 meter baseline 6MWD population as a key subgroup based on the knowledge that 350 meters represents a transition point for patients towards a more rapid decline in walking ability as supported by analysis from our Phase 2b trial. Furthermore, we considered the pre-specified 300 to 400 meter baseline 6MWD population as a key subgroup based on an increasing understanding of the sensitivity limitations of the six minute walk test as an endpoint in 48-week studies. Natural history data suggest that the 6MWT may not be the optimal tool to demonstrate efficacy in patients with either a baseline 6MWD of less than 300 meters, as these patients have significant muscle loss as monitored by magnetic resonance spectroscopy and are at high risk for losing ambulation regardless of

treatment, or in high walking patients, such as those with a baseline 6MWD at or greater than 400 meters, as these patients are likely to remain stable over a 48 week testing period.

By defining these key subgroups, we thereby also defined corresponding subgroups of patients with baseline 6MWD greater than or equal to 350 meters, greater than or equal to 400 meters, and less than 300 meters. We also pre-specified a meta-analysis of the combined results from ACT DMD and the Phase 2b ambulatory decline phase patients.

Pre-specified sub-group analysis. We saw strong evidence of clinical benefit in the pre-specified subgroup of patients with baseline 6MWD between 300 and 400 meters. Specifically, we observed a benefit in Translarna-treated patients of 47 meters (nominal p=0.007) in the 6MWT in this subgroup. This was consistent with an observed benefit of 49 meters (nominal p=0.026) in our Phase 2b clinical trial in the 300 to 400 meters baseline 6MWD population. We also saw clinically meaningful benefit for Translarna over placebo in each of the timed function tests, including observed results in time to run/walk 10 meters (2.1 seconds; nominal p=0.066), time to climb four stairs (3.6 seconds; nominal p=0.003), and time to descend four stairs (4.3 seconds; nominal p<0.001). The hazard ratio for Translarna versus placebo was 0.79 (nominal p=0.418) for 10% 6MWD worsening. In addition, a benefit of 4.5 points over placebo (nominal p=0.041) was observed in the NSAA test, which we believe is clinically meaningful. We believe that the benefits observed in this key pre-specified subgroup support the use of the 6MWT in the patients with a walking ability in the 300 to 400 meters range and the understanding that the reliability of the 6MWT over a 48 week period was limited at both the lower and upper ends of our 6MWD enrollment range.

In the pre-specified subgroup of patients with baseline 6MWD less than 350 meters, we observed a benefit of 24 meters (nominal p=0.210) in favor of Translarna in the 6MWT. An analysis of the results from our Phase 2b clinical trial in the less than 350 meters baseline 6MWD population, defined post-hoc, demonstrated a 68 meter benefit in the 6MWT (nominal p=0.006). In the timed function tests for the subgroup of ACT DMD patients with baseline 6MWD less than 350 meters, we observed benefits for Translarna over placebo in time to run/walk 10 meters (2.3 seconds; nominal p=0.033), time to climb four stairs (4.2 seconds; nominal p=0.019) and time to descend four stairs (4.0 seconds; nominal p=0.007).

Typically, a trial result is statistically significant if the chance of it occurring when the treatment is like placebo is less than one in 20, resulting in a p-value of less than 0.05. A nominal p-value is the result of one particular comparison when more than one comparison is possible, such as when two active treatments are compared to placebo or when two or more subgroups are analyzed.

As described above, we believe the 6MWT lacks sensitivity to detect a clinical effect in patients with baseline less than 300 meters in a 48-week trial. However, the timed function tests trended in favor of patients treated with Translarna with a baseline 6MWD below 300 meters, including observed benefit over placebo in time to run/walk 10 meters (2.5 seconds; nominal p=0.066), time to climb four stairs (2.4 seconds; nominal p=0.790), and time to descend four stairs (2.1 seconds; nominal p=0.595). We believe the positive trends in this population reflect that short muscle burst activity tests may be a better clinical measure for patients that are at a more advanced stage of disease progression. Consistent with the natural history of ambulatory DMD patients with 6MWD greater than 400 meters, which indicates stability in walking ability over a 48 week period, we observed no meaningful difference in 6MWT between patient groups. Similarly, we observed no meaningful difference in 6MWT between patient groups with baseline 6MWD greater than 350 meters.

Pre-specified meta-analysis. The meta-analysis combined efficacy results from the ACT DMD ITT population and Phase 2b ambulatory decline phase subgroup. The Phase 2b ambulatory decline phase group includes the patients from our randomized, double-blind, placebo-controlled, Phase 2b clinical trial in patients with nmDMD who would have met the enrollment criteria of ACT DMD.

Results from the meta-analysis showed a statistically significant 21 meter improvement in 6MWD (p = 0.015) favoring Translarna.

Additionally, the meta-analysis showed statistically significant benefit for Translarna over placebo across each timed function test including time to run/walk 10 meters (1.4 seconds; p=0.025), time to climb four stairs (1.6 seconds; p =0.018) and time to descend four stairs (2.0 seconds; p=0.004). The hazard ratio for Translarna versus placebo was 0.66 (p=0.023) for 10% 6MWD worsening. We believe that we are able to demonstrate a statistically significant outcome in the 6MWD

in the meta-analysis, despite the significant variability in baseline 6MWD among patients in both ACT DMD and the Phase 2b trial's ambulatory decline phase, due to the substantially larger patient population available in the pooled analysis.

Retrospective Analysis. We also looked back at the observed results in the meta-analysis for all patients with a baseline 300 to 400 meter 6MWD from ACT DMD and the Phase 2b trial. The meta-analysis of these data demonstrated a 45 meter benefit (nominal $p<0.001$) in the 6MWT as well as clinically meaningful benefits across each secondary endpoint timed function test, including benefit over placebo in time to run/walk 10 meters (2.2 seconds; nominal $p=0.008$), time to climb four stairs (3.4 seconds; nominal $p<0.001$) and time to descend four stairs (4.3 seconds; nominal $p<0.001$). This meta-analysis of patients with baseline 6MWD of 300 to 400 meters was not pre-specified and is defined post-hoc.

A retrospective analysis performed after unblinding trial results can result in the introduction of bias if the analysis is inappropriately tailored or influenced by knowledge of the data and actual results. In addition, nominal p-values cannot be compared to the benchmark p-value of 0.05 to determine statistical significance without being adjusted for the testing of multiple dose groups or analyses of subgroups. Because of these limitations, regulatory authorities typically give greatest weight to results from pre-specified analyses and adjusted p-values and less weight to results from post-hoc, retrospective analyses and nominal p-values.

Statistical Considerations. The pre-specified meta-analysis results, which favored Translarna in the 6MWT and each of the timed function tests, are considered statistically significant. In the pre-specified subgroups of ACT DMD patients with a baseline 6MWD less than 350 meters and 300 to 400 meters, the p-values for the 6MWT and each of the timed function tests are considered nominal. For information with respect to the use of nominal p-values and post-hoc analyses, see Item 1A. Risk Factors, "*Subgroup, retrospective, post-hoc, and certain statistical analyses may not be reliable and typically will not form the basis for regulatory approval."*

Participation Criteria and Stratification. Certain key inclusion criteria were specified in the ACT DMD trial protocol for enrollment: the patient had to be 7 through 16 years of age; at the screening visit the patient had to be able to walk no more than 80% of predicted 6MWD compared to healthy boys matched for age and height, but had to be able to walk at least 150 meters during the 6MWT; and the patient must have used systemic corticosteroids for a minimum of six months prior to start of treatment. The ACT DMD trial protocol provided for the exclusion of patients from the trial if, among other things, they recently used systemic aminoglycoside antibiotics, recently initiated or changed corticosteroid therapy or previously received Translarna treatment. Patients enrolled in ACT DMD underwent 48 weeks of blinded treatment prior to the final analysis and the randomization was stratified based on age (<9 years versus ≥9), baseline 6MWD (<350 versus ≥350 meters), and duration of prior use of corticosteroids (<12 months versus ≥12 months).

Study 045

In the fourth quarter of 2018, following the FDA's recommendation to collect dystrophin data using validated quantification methods, we initiated Study 045, a Phase 2 open label clinical study of 20 boys with nmDMD from ages two to seven, to evaluate the ability of ataluren to increase dystrophin protein levels in boys with nmDMD. Study 045 did not meet its pre-specified primary endpoint. Patients received baseline biopsies prior to the initiation of treatment and follow-up biopsies scheduled at 40 weeks following the start of treatment. However, certain patients were delayed in obtaining the final study muscle biopsies performed at our clinical trial site at the University of California, Los Angeles as a result of the COVID-19 pandemic. 8 of 20 patients were unable to undergo biopsies at week 40, and these patients had their second biopsies between 62 and 70 weeks of treatment. Full-length dystrophin levels were measured using both the Electrochemiluminescence, or ECL assay, as the primary endpoint and Immunohistochemistry, or IHC, assay as the secondary endpoint.

The ITT population included the 20 patients enrolled in the study. However, one subject was determined to be non-compliant, as he only took half of the study drug, and one subject did not have adequate biopsy samples to establish baseline levels. Therefore, 18 patients were compliant with the study drug and had evaluable biopsy samples. These 18 patients are considered the evaluable population. 10 of these 18 patients had their second biopsy at week 40 and 8 had their second biopsy between weeks 62 and 70. Patient characteristics, including age and steroid use were consistent across both cohorts.

Overall in the ITT population, there was an increase in dystrophin expression from baseline, on both ECL as the primary endpoint and IHC as the secondary endpoint, but these did not meet a p-value of <0.05. Nevertheless, when studying the 18 patients in the evaluable cohort, we identified a greater increase in dystrophin expression, and this increase did reach a nominal p-value of 0.04 in the analysis of the IHC assay. Also, over 80% of the evaluable subjects demonstrated an increase in dystrophin expression. 8 patients in the evaluable population had longer treatment exposure, ranging from 62-70 weeks, and these 8 patients had markedly greater levels of dystrophin increase with an average of approximately 24% in the ECL assay. We believe that these results suggest that longer duration of treatment resulted in greater biological effect, which is consistent with the long-term Translarna treatment benefit we have previously reported from our other clinical studies and our international drug registry study for nmDMD patients receiving Translarna.

We also measured creatine kinase, or CK, levels of patients in Study 045 as an objective measure of muscle damage. Dystrophin acts as a shock absorber during a muscle contraction and would be expected to protect against muscle damage and therefore reduce CK levels. Consistent with an increase in the level of dystrophin, we observed a marked reduction of approximately 20% in creatine kinase and that longer treatment with Translarna was associated with a greater magnitude of biological effect.

Study 041

Overview. As a specific obligation to our marketing authorization in the EEA, we were required to conduct and submit to the EMA the results of a three-year clinical trial to confirm the efficacy and safety of Translarna in the treatment of ambulatory patients with nmDMD aged five years or older. The trial was comprised of two stages: an 18-month randomized, double-blind, placebo-controlled clinical trial followed by an 18-month open label extension period. We refer to the 18-month clinical trial portion as "Stage 1" and the 18-month extension period as "Stage 2". We refer to Stage 1 and Stage 2 together as Study 041. In September 2022, as part of our specific obligation, we submitted a report on Stage 1 and data from Stage 2 in connection with a Type II variation to the EMA to support conversion of the conditional marketing authorization for Translarna to a standard marketing authorization.

For a discussion of the risks related to conducting clinical trials, in general, and Study 041, in particular, please see "Item 1A. Risk Factors-Risks Related to the Development and Commercialization of our Products and our Product Candidates" and "-Risks Related to Regulatory Approval of our Products and our Product Candidates".

Enrollment. According to the study protocol, Study 041 enrolled nmDMD patients aged five years and above who achieve a 6MWD equal to or greater than 150 meters at three pre-treatment evaluation times (screening, baseline day one and baseline day two), tested as set forth in the protocol. Qualified participants also needed to perform timed function tests of running/walking 10 meters, climbing/descending four stairs and standing from supine within 30 seconds at both screening and baseline, and meet the other criteria set forth in the protocol.

We completed enrollment of Study 041 in the fourth quarter of 2020. Of the 363 patients enrolled in Study 041, 185 patients meet the criteria for inclusion in the primary analysis population, which we refer to as the modified intention-to-treat population, or mITT. Patients included in the mITT must be at least 7, but less than 16, years old, with a 6MWD of equal to or greater than 300 meters and a stand from supine time of five seconds or more, each as tested at screening and baseline.

Objectives and endpoints. The primary objective of Study 041 was to evaluate the effect of Translarna on ambulation and endurance as assessed by the 6-minute walk test, or 6MWT. Based on the study protocol, the primary analysis of Stage 1 was to evaluate the difference in slope of change in 6MWD from baseline to week 72 between Translarna and placebo in the mITT population. Data from participants who did not qualify for inclusion in the mITT were used for summary and analysis of efficacy endpoints in the ITT (full date set) population.

A secondary objective of Study 041 was to determine the effects of Translarna on ambulation and burst activity as assessed by timed function tests (10-meter run/walk, 4-stair stair-climb, and 4-stair stair descend). Each timed function test was analyzed as a secondary endpoint for both the mITT and ITT populations at the end of Stage 1 and was also analyzed at the end of Stage 2. A separate analysis evaluates 10-meter run/walk results in participants with a baseline 6MWD below 300 meters. An additional analysis evaluates a composite endpoint of average change in times to run/walk 10 meters, climb

4 stairs, and descend 4 stairs. We also assess each of time to loss of ambulation, stair-climbing and stair-descending over 72 weeks and over 144 weeks.

Determination of the effects of Translarna on lower-limb muscle function as assessed by the NSAA test, serves as an additional secondary objective. NSAA scores were analyzed as secondary endpoints for both the mITT and ITT populations at the end of Stage 1 and were also analyzed as at the end of Stage 2. A separate analysis for Stage 2 evaluated changes in total score in participants with a baseline 6MWD of equal to or greater than 400 meters and under 7 years of age. We also assessed the risk of loss of NSAA items over 72 weeks and 144 weeks.

Slope of change in 6MWD over 144 weeks was also assessed as a secondary endpoint at the conclusion of Stage 2. Changes in 6MWD from baseline to week 72 and week 144 respectively were also addressed as secondary endpoints.

The safety profile of Translarna was evaluated throughout Stage 1 and Stage 2 as a secondary objective.

Certain exploratory endpoints were also assessed in Study 041. In patients aged 7 years and above, change from baseline in upper limb function is assessed using both functional testing and parent/caregiver-reported questionnaires. In patients under 7 years of age, muscle strength was assessed by change from baseline in myometry parameters. At pre-qualified sites only, magnetic resonance imaging was used to assess change from baseline in muscle fat fraction. The effects of Translarna on pulmonary function were assessed by change from baseline in forced vital capacity. In addition, subject- and parent/caregiver-reported questionnaires and at-home diaries were assessed to evaluate the effect of Translarna on health-related quality of life (HRQL) changes from baseline.

Stratification. In Stage 1, participants were randomized 1:1 to placebo or Translarna (10, 10, 20 mg/kg). The randomization was stratified based on type of concomitant corticosteroid used at baseline (deflazacort versus prednisone/prednisolone), maximum of the two valid 6-minute walk tests performed at baseline day 1 and day 2 (<300 meters versus ≥300 to <350 meters, versus ≥350 to <400 meters, versus ≥400 meters), and time to stand from supine at baseline (<5 seconds versus ≥5 seconds).

Results. In June 2022, we announced top-line results from Stage 1. Within Stage 1, Translarna showed a statistically significant treatment benefit across the entire ITT population as assessed by the 6MWT as assessed by the NSAA. Additionally, Translarna showed a statistically significant treatment benefit across the ITT population within the 10-meter run/walk and 4-stair stair climb, while also showing a positive trend in the 4-stair stair descend although not statistically significant. Within the mITT population, Translarna demonstrated a positive trend across all endpoints, however, statistical significance was not achieved. Translarna was also well tolerated with no new safety findings noted.

Multi-platform Discovery

We continue to invest in our pre-clinical product pipeline by committing resources to research and development programs to provide access to best-in-class treatments for patients who have an unmet medical need.

Our Approach

We use multiple drug discovery platforms to discover and develop therapies to target diseases with high-unmet need. Our platforms focus on identifying small molecules that intervene in pathways required for RNA processing and energy production. Careful control and manipulation of these processes allow us to address a wide range of deficiencies.

Splicing

Post-transcriptional control processes are the events that occur in a cell following the transcription of DNA into RNA. These processes regulate, for example, how long RNA molecules last in the cell, how exons in precursor messenger RNA, or pre-mRNA, molecules are spliced, and how efficiently mRNA molecules are translated to proteins. In the majority of human protein-encoding genes, the sequence encoding the mature mRNA transcript is not contiguous in the pre-mRNA but rather has intervening non-coding regions called introns that interrupt the coding sequences, called exons. These introns

are removed from the final mRNA product by a process called splicing that also joins the exons together such that only the exons are retained in the mature mRNA.

Approximately 94% of all human genes encode pre-mRNAs that undergo splicing, as such the majority of the human genome is targetable with splicing modulation. PTC's proprietary splicing discovery platform, PTSeek™, identifies small molecules that modulate splicing of specific exons in genes of therapeutic interest, including genes associated with SMA, HD and various forms of cancer. Using this technology, we have successfully identified orally bioavailable small molecules that correct splicing of SMN2 mRNA. An example of one of these molecules is Evrysdi, which was approved in August 2020 by the FDA for the treatment of SMA in adults and children two months and older. Based on our knowledge of the mechanism of splicing and how small molecules interact with the cellular splicing machinery, we have identified additional small molecule drug candidates that modify splicing of pre-mRNA, promote inclusion of specific exons into mRNA, including pseudoexons, or force skipping of undesired exons from the mature mRNA. We believe that this technology is potentially widely applicable to a large number of target genes across many therapeutic areas.

Inflammation and Ferroptosis

Energy production in cells is critical to their survival. On the other hand, processes that induce oxidative stress in cells can negatively impact cell survival. Energy production takes place in a part of the cell called mitochondria. The mitochondria use the transport of electrons via chemical reactions called redox reactions in their cell membranes to produce adenosine triphosphate, or ATP, which is the central energy molecule inside cells. This process of moving electrons to produce ATP is termed electron transfer or transport. The redox reactions, however, can also cause oxidative stress. We use our expertise in energy production via electron transfer chemical reactions and in oxidative stress to develop potentially first-in-class therapeutics for unmet medical needs. One area of our focus is on inherited mitochondrial diseases. Mitochondrial diseases often derive from defects in energy production and oxidative stress pathway. These diseases commonly result in severe neurological impairment and death at an early age. Through our screening processes, we have identified multiple drug targets which we are assessing in nonclinical studies with the aim of identifying additional product candidates to take into clinical development. Similar strategies potentially can be used for broader sets of diseases. We believe such approaches to these types of intractable diseases have the potential to lead to novel therapies to address areas of high unmet medical need.

Our Collaborations, License Agreements and Funding Arrangements

We currently have ongoing collaborations with Roche and the SMA Foundation for SMA, a license agreement with National Taiwan University, or NTU, for Upstaza, a collaboration and license agreement with Akcea for Tegsedi and Waylivra, a license agreement with Shiratori Pharmaceutical Co., Ltd., or Shiratori, relating to the manufacturing processes and technology for sepiapterin, and a license and collaboration agreement with Novartis for our PTC518 HD program.

Roche and the SMA Foundation

Overview. In November 2011, we entered into a License and Collaboration Agreement with Roche and the SMA Foundation, dated as of November 23, 2011, or the SMA License Agreement, to further develop and commercialize compounds identified under our SMA sponsored research program with the SMA Foundation and to research other small molecule compounds with potential for therapeutic use in patients with SMA. The research term of this agreement was terminated effective December 31, 2014. The ongoing collaboration is governed by a joint steering committee consisting of an equal number of representatives of us, the SMA Foundation and Roche. We, the SMA Foundation and Roche have agreed to endeavor to make decisions by consensus, but if the joint steering committee cannot reach agreement after following a specified decision resolution procedure, Roche's decision will control. However, Roche may not exercise its final decision-making authority with respect to certain specified matters, including any decision that would increase our or the SMA Foundation's obligations, reduce our or the SMA Foundation's rights, expand Roche's rights, or reduce Roche's obligations under the license and collaboration agreement.

Commercialization. We have granted Roche worldwide exclusive licenses, with the right to grant sublicenses, to our patent rights and know-how with respect to such compounds and products. Roche is responsible for pursuing worldwide

clinical development of compounds from the research program and has the exclusive right to develop and commercialize compounds from the collaboration.

Payments and Contingent Payments. Pursuant to the SMA License Agreement, Roche paid us an upfront non-refundable payment of $30.0 million. During the research term, which was terminated effective December 31, 2014, Roche provided us with funding, based on an agreed-upon full-time equivalent rate, for an agreed-upon number of full-time equivalent employees that we contributed to the research program. We are eligible to receive up to an aggregate of $135.0 million in payments if specified development and regulatory milestones are achieved and up to an aggregate of $325.0 million in payments if specified sales milestones are achieved. We are also entitled to tiered royalties ranging from 8% to 16% on worldwide net product sales of products developed pursuant to the collaboration. Roche's obligation to pay us royalties will expire generally on a country-by- country basis at the latest of the expiration of the last-to-expire patent covering a product in the given country, the expiration of regulatory exclusivity for that product in such country or 10 years from the first commercial sale of that product in such country. However, the royalties payable to us may be decreased in certain circumstances. For example, the royalty rate in a particular country is reduced if the product is not protected by patents in that country and no longer entitled to regulatory exclusivity in that country. We remain responsible for making any payments to the SMA Foundation that may become due under our pre-existing sponsored research agreement with the SMA Foundation.

As of December 31, 2024, we had recognized a total of $310.0 million in milestone payments and $545.6 million royalties on net sales pursuant to the SMA License Agreement. As of December 31, 2024, there are no remaining development and regulatory event milestones that we can receive. The remaining potential sales milestones as of December 31, 2024 are $150.0 million upon achievement of certain sales events.

In June 2024, we entered into an amendment with Royalty Pharma Investments 2019 ICAV, or Royalty Pharma, and Royalty Pharma plc, to the A&R Royalty Pharma Purchase Agreement, dated October 18, 2023, or the A&R Royalty Purchase Agreement, which amends and restates in its entirety the Royalty Purchase Agreement, dated as of July 17, 2020, and we exercised our first put option in exchange for $241.8 million in cash consideration. Pursuant to the A&R Royalty Purchase Agreement, we have sold to Royalty Pharma a portion of our right to receive sales-based royalty payments, or the Royalty, on worldwide net sales of Evrysdi and any other product developed pursuant to the SMA License Agreement under the SMA program. To date, Royalty Pharma has paid to us cash consideration of $1.9 billion (less Royalty payments received by us with respect to assigned Royalties, or the Assigned Royalty Rights) in exchange for 90.49% of the Royalty, which will be reduced to 83.33% after Royalty Pharma receives $1.3 billion in aggregate payments, or the Assigned Royalty Cap, from the Royalty assigned under the Original Royalty Purchase Agreement. We currently retain 9.51% of the Royalty, which increases to 16.67% after the Assigned Royalty Cap has been met. We have the option to sell our retained portions of the Royalty to Royalty Pharma in up to three tranches for the following payments: (1) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the Assigned Royalty Cap has been met, (2) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the Assigned Royalty Cap has been met, and (3) $50.0 million in exchange for 1.90% of the Royalty, which increases to 3.33% after the Assigned Royalty Cap has been met, in each case less Royalty payments received by us with respect to the Assigned Royalty Rights.

Termination. Unless terminated earlier, the SMA License Agreement will expire on the date when no royalty or other payment obligations are or will become due under the agreement. Roche's termination rights under the license and collaboration agreement include the right to terminate the agreement at any time after November 22, 2013 on a product-by-product and country-by-country basis upon three months' notice before the launch of the applicable product or upon nine months' notice thereafter; and the right to terminate the agreement in specified circumstances following a change of control of us. The license and collaboration agreement provides that we or Roche may terminate the agreement in the event of an uncured breach by the other party of a material provision of the agreement, or in the event of the other party's bankruptcy or insolvency. Upon termination of the collaboration agreement by Roche for convenience or termination by us as a result of Roche's breach, bankruptcy, change of control or patent challenge, we have the right to assume the development and commercialization of product candidates arising from the license and collaboration agreement. In that event, we may become obligated to pay royalties to Roche on sales of any such product.

SMA Foundation

Overview. In June 2006, we entered into a sponsored research agreement with the SMA Foundation under which we and the SMA Foundation have collaborated in the research and preclinical development of small molecule therapeutics for SMA. As discussed above, we are also collaborating with the SMA Foundation and Roche to further develop these compounds. Pursuant to the sponsored research agreement, as amended, the SMA Foundation provided us with $13.3 million in funding. The SMA Foundation is not obligated to provide any further funding under this agreement.

Continuing financial obligations. We may become obligated to pay the SMA Foundation single-digit royalties on worldwide net product sales of any collaboration product that we successfully develop and subsequently commercialize or, with respect to collaboration products we outlicense, including Evrysdi, a specified percentage of certain payments we receive from our licensee. As discussed above, we have outlicensed rights to Roche pursuant to a license and collaboration agreement. We are not obligated to make such payments unless and until annual sales of a collaboration product exceed a designated threshold. Since inception, the SMA Foundation has earned $52.5 million in royalty payments, fulfilling our obligation to make such payments, and all of which was paid as of December 31, 2024.

Reversion rights. In specified circumstances, including those involving our decision to discontinue development or commercialization of a collaboration product, our uncured failure to meet agreed timelines or those that might arise following our change of control, we may be obligated to grant the SMA Foundation exclusive or non-exclusive sublicensable rights under our intellectual property, in certain collaboration products, among other rights, to assume the development and commercialization of such collaboration products and to provide the SMA Foundation with other transitional assistance, which we refer to as a reversion. In some such cases, we may be entitled to receive licensing fee payments from the SMA Foundation and single-digit royalties on sales of the applicable collaboration product, which amounts we collectively refer to as reversion payments. In other cases, the SMA Foundation is not required to make any payments to us in connection with the licenses it receives from us.

Termination. Unless terminated earlier, the sponsored research agreement will continue until the earliest of the SMA Foundation's receipt of the repayment amount or, if there was a reversion, either our receipt of all reversion payments that the SMA Foundation may be obligated to make to us or, if the SMA Foundation is not obligated to make reversion payments, the expiration of the last-to-expire patent we licensed to the SMA Foundation in connection with such reversion. The sponsored research agreement provides that either party may terminate the agreement in the event of an uncured material breach by the other party or in the event of the other party's bankruptcy or insolvency.

National Taiwan University

Overview. Pursuant to the license and technology transfer agreement, originally entered into between Agilis Biotherapeutics, Inc., or Agilis, NTU and Professor Wuh-Liang (Paul) Hwu, in December 2015, or the NTU Licensing Agreement, NTU granted to us an exclusive, perpetual license, with the right to grant sublicenses through all tiers, to research and use the intellectual property, data, chemistry, manufacturing and controls, or CMC, records, documents, confidential information, materials and know-how pertaining to the Research, including Upstaza for the treatment of AADC deficiency, under the NTU Collaboration Agreement (as defined below), or the Technology, and to develop, make, manufacture, use, sell, import and market the Technology and any other products made, invented, developed or incorporated by or with the Technology, or the Licensed Products. Subject to any regulatory delays or issues, we are obligated to research, use and develop the Technology to manufacture Licensed Products by December 23, 2025. Additionally, we were obligated to obtain marketing approval of Upstaza for the treatment of AADC deficiency, either by the FDA or by the EMA, by December 31, 2024. In July 2022, the EC approved Upstaza for the treatment of AADC deficiency for patients 18 months and older within the EEA, satisfying that obligation.

Funding Obligations. NTU received a lump sum of $100,000 upon execution of the NTU Licensing Agreement, as well as $2.0 million milestones payments based on the achievement of certain clinical and regulatory milestones, including $1.2 million that became due and payable in July 2022 upon the EC's approval of Upstaza for the treatment of AADC deficiency. Additionally, NTU will be entitled to receive contingent payments from us based on (i) annual license maintenance fees, (ii) a low double-digit percentage royalty of annual net sales of Licensed Products, and (iii) a percentage

of sublicense revenue, ranging from low-twenties to mid-twenties. The annual license maintenance fees are non-refundable, but creditable against annual net sales payments.

Intellectual Property. All intellectual property relating to the manufacture, production, assembly, use or sale of Technology and any Licensed Products derived thereof are owned by NTU.

Termination. The NTU Licensing Agreement expires on December 23, 2035. Upon expiration, we will have a fully paid-up, perpetual, royalty-free exclusive license to the Technology. We may terminate the NTU Licensing Agreement upon 60 days' written notice to NTU in the event of (a) the failure of a pivotal clinical study, or serious adverse event in a clinical study, with respect to Upstaza for the treatment of AADC deficiency, that prevents continuing such clinical study under reasonable circumstances or (b) the rejection of a BLA with the FDA or an MAA with the EMA, or equivalent biologics approval application in another territory with respect to Upstaza for the treatment of AADC. In such termination event, we must pay $100,000 to NTU within 30 days of termination and NTU would retain all rights to the Technology. We may terminate the NTU Licensing Agreement for material breach by another party following a 30-day cure period. NTU may terminate the NTU Licensing Agreement for our failure to pay any undisputed license fees or net sales or sublicensing royalty fees within the applicable deadline following a 30-day cure period.

We are also a party to collaborative research agreements with NTU, or the NTU Collaboration Agreements, that govern the collaboration between us and NTU with respect to the research and clinical trials for AADC deficiency gene therapy. NTU is responsible for performing the research and clinical trials and we are responsible for providing related funding. As of December 31, 2024, an aggregate amount of $4.5 million in funding payments has been paid to NTU pursuant to the NTU Collaboration Agreements.

Tegsedi and Waylivra

Overview. PTC Therapeutics International Limited, our subsidiary, entered into a Collaboration and License Agreement, or the Tegsedi-Waylivra Agreement, dated August 1, 2018 by and between us and Akcea, for the commercialization by us of Tegsedi, Waylivra and products containing those compounds, which we refer to collectively as the Products, in countries in Latin America and the Caribbean, or the PTC Territory. We are responsible for all meetings, communications and other interactions with regulatory authorities in the PTC Territory. The activities of the parties pursuant to the Tegsedi-Waylivra Agreement is overseen by a Joint Steering Committee, composed of an equal number of representatives appointed by each of us and Akcea.

Commercialization. Under the terms of the Tegsedi-Waylivra Agreement, Akcea has granted to us an exclusive right and license, with the right to grant certain sublicenses, under Akcea's product-specific intellectual property to develop, manufacture and commercialize the Products in the PTC Territory. In addition, Akcea has granted to us a non-exclusive right and license, with the right to grant certain sublicenses, under Akcea's core intellectual property and manufacturing intellectual property to develop, manufacture and commercialize the Products in the PTC Territory and to manufacture the Products worldwide in accordance with a supply agreement with Akcea. Akcea has in-licensed certain of the Akcea intellectual property from its parent company, Ionis. Each party has agreed not to, independently or with any third party, commercialize any competing oligonucleotide product in the PTC Territory for the same gene target as inotersen.

Payments and Contingent Payments. We paid to Akcea an upfront licensing fee of $18.0 million, consisting of an initial payment of $12.0 million paid in connection with entering into the Tegsedi-Waylivra Agreement in August 2018, and a second payment of $6.0 million that was paid after Waylivra received regulatory approval from the EMA in May 2019. In addition, Akcea was eligible to receive milestone payments, on a Product-by-Product basis, of $4.0 million upon receipt of regulatory approval for a Product from ANVISA, subject to a maximum aggregate amount of $8.0 million for all such Products. We paid Akcea $4.0 million upon our receipt of marketing authorization from ANVISA in October 2019 for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hATTR amyloidosis in Brazil with Tegsedi and an additional $4.0 million upon our receipt of marketing authorization from ANVISA in August 2021 for the treatment of FCS. Akcea is also entitled to receive royalty payments in the mid-twenty percent range of net sales on a country-by-country and Product-by-Product basis, commencing on the earlier to occur of (1) 12 months after the first commercial sale of such Product in Brazil or (2) the date when we, our affiliates or sublicensees have recognized revenue of $10.0 million

or more in cumulative net sales for such Product in the PTC Territory. The royalty payments are subject to reduction in certain circumstances as set forth in the Tegsedi-Waylivra Agreement.

Termination. The Tegsedi-Waylivra Agreement will continue until the expiration of the last to expire royalty term with respect to all Products in all countries in the PTC Territory. Either party may terminate the Tegsedi-Waylivra Agreement on written notice to the other party if such other party is in material breach of its obligations thereunder and has not cured such breach within 30 days after notice in the case of a payment breach or 60 days after notice in the case of any other breach.

Shiratori

Overview. In connection with our acquisition of Censa Pharmaceuticals, Inc., or Censa, in May 2020, we became a party to a license agreement dated as of February 8, 2015, as amended, between Shiratori and Censa, or the Shiratori License Agreement. Pursuant to the Shiratori License Agreement, as amended, Shiratori granted Censa the sole and exclusive worldwide right and license, with the right to sublicense, under certain licensed know-how, or the Licensed Know-How, and licensed patents, or the Licensed Patents, relating to manufacturing processes and technology for sepiapterin, to research, have researched, develop, have developed, use, import, export, market, have marketed, offer for sale, sell and have sold, and otherwise commercialize any final pharmaceutical product in finished form containing sepiapterin as an active pharmaceutical ingredient, including sepiapterin, collectively the Sepiapterin Products, covered by the Licensed Patents or using the Licensed Know-How in all countries and territories of the world.

Payments and Contingent Payments. Under the Shiratori License Agreement, we are obligated to pay to Shiratori a low single digit percentage of annual net sales of the Sepiapterin Products in each country in the Sepiapterin Territory until the expiration of the last-to-expire Licensed Patent controlled by Shiratori covering the relevant country followed by an obligation to pay a reduced royalty rate for a specified period of time thereafter. We are also obligated to pay Shiratori certain regulatory and development milestones.

Termination. Unless earlier terminated, the Shiratori License Agreement will continue in full force and effect on a country-by-country and product-by-product basis until the obligation to pay royalties with respect to the sale of such Sepiapterin Product in such country expires. The parties may agree to mutually terminate the Shiratori License Agreement. Shiratori may elect to terminate the Shiratori License Agreement upon sixty days' prior written notice to us in the event that we fail to (i) achieve regulatory approval for a Sepiapterin Product in either the United States or EU by February 8, 2026 or (ii) commercially launch a Sepiapterin Product in the United States or EU by February 8, 2027. We may elect to terminate the Shiratori License Agreement upon sixty days' prior written notice to Shiratori.

Novartis Pharmaceuticals Corporation

Overview. On November 27, 2024 we and Novartis entered into the Novartis Agreement relating to our PTC518 HD program which includes related molecules. Pursuant to the Novartis Agreement, we will continue to conduct the ongoing Phase 2A Clinical Trial and the ongoing OLE Clinical Trial pursuant to its existing development plan, with the goal of transitioning the ongoing OLE Clinical Trial to Novartis within 12 months after the effective date. Novartis will be responsible for all other development of licensed compounds and licensed products and the manufacture and commercialization of licensed compounds and licensed products worldwide.

Payments and Contingent Payments. Under the Novartis Agreement, and upon the closing of the transaction contemplated by the Novartis Agreement in January 2025, we received an upfront payment of $1.0 billion on the effective date and can receive up to $1.9 billion in development, regulatory and sales milestones, a 40% share of U.S. profits and losses, and tiered double-digit royalties on ex-U.S. sales.

Termination. The Novartis Agreement, unless earlier terminated in accordance therewith, shall continue in force and effect until (a) with respect to the royalty territory, on a licensed product-by-licensed product and country-by-country basis, the royalty term end date for such licensed product in such country and (b) with respect to the profit-sharing territory, on a licensed product-by-licensed product basis, until the exploitation of such licensed product has completely terminated. Either party may terminate for material breach of the Novartis Agreement. Novartis may terminate for convenience or for

safety or regulatory issue. We may also terminate (a) solely with respect to such country or other jurisdiction, (b) in the case that such country or other jurisdiction is United States, Brazil, Switzerland, Russia, United Kingdom, France, Germany, Italy and Spain, each a Major Market, solely with respect to all Major Markets, or (c) in its entirety, for material breach of diligence obligations.

Our Ongoing Acquisition-Related Obligations

From time to time, we have engaged in strategic transactions to expand and diversify our product pipeline, including through the acquisition of assets or businesses. In connection with these acquisitions, we have entered into agreements through which we have ongoing obligations, including obligations to make contingent payments upon the achievement of certain development, regulatory and net sales milestones or upon a percentage of net sales of certain products.

Complete Pharma Holdings, LLC

On April 20, 2017, we completed our acquisition of all rights to Emflaza, or the Emflaza Transaction. The Emflaza Transaction was completed pursuant to an asset purchase agreement, dated March 15, 2017, as amended on April 20, 2017, or the Emflaza Asset Purchase Agreement, by and between us and Marathon Pharmaceuticals, LLC (now known as Complete Pharma Holdings, LLC), or Marathon. The assets acquired by us in the Emflaza Transaction include intellectual property rights related to Emflaza, inventories of Emflaza, and certain contractual rights related to Emflaza. We assumed certain liabilities and obligations in the Emflaza Transaction arising out of, or relating to, the assets acquired in the Emflaza Transaction.

In addition to the upfront consideration paid to Marathon upon the closing of the Emflaza transaction, Marathon is entitled to receive contingent payments from us based on annual net sales of Emflaza, up to a specified aggregate maximum amount over the expected commercial life of the asset, subject to the terms and conditions of the Emflaza Asset Purchase Agreement. This amount was achieved during the year ended December 31, 2024. Accordingly, no future payments will be due. In 2022, we paid Marathon a single $50.0 million sales-based milestone in accordance with the Emflaza Asset Purchase Agreement.

Agilis Biotherapeutics, Inc.

On August 23, 2018, we completed our acquisition of Agilis pursuant to an Agreement and Plan of Merger, dated as of July 19, 2018, or the Agilis Merger Agreement, by and among us, Agility Merger Sub, Inc., a Delaware corporation and our wholly owned, indirect subsidiary, Agilis and, solely in its capacity as the representative, agent and attorney-in-fact of the equityholders of Agilis, Shareholder Representative Services LLC, or the Merger.

In addition to the upfront consideration paid to Agilis equityholders upon the closing of the Merger, Agilis equityholders may become entitled to receive contingent payments from us based on the achievement of certain development, regulatory and net sales milestones, as well as based upon a percentage of net sales of certain products.

On April 29, 2020, we, certain of the former equity holders of Agilis, or the Participating Rightholders, and, for the limited purposes set forth in the agreement, Shareholder Representative Services LLC, entered into a Rights Exchange Agreement, or the Rights Exchange Agreement. Pursuant to the Right Exchange Agreement, we issued 2,821,176 shares of our common stock and paid $36.9 million, in the aggregate, to the Participating Rightholders in exchange for the cancellation and forfeiture by the Participating Rightholders of their rights to receive certain milestone-based contingent payments under the Agilis Merger Agreement.

As of December 31, 2024, we have paid former equity holders of Agilis a total of $72.4 million in connection with the achievement of certain milestone-based contingent payments under the Agilis Merger Agreement. In addition, $11.0 million in regulatory milestones were recorded in accounts payable and accrued expenses on the balance sheet as of December 31, 2024. In May 2023, as part of our strategic portfolio prioritization, we decided to discontinue our preclinical and early research programs for our gene therapy platform, which included programs for FA and Angelman syndrome. As a result, we do not expect the milestones under the Agilis Merger Agreement related to FA and Angelman syndrome to be achieved, and we do not expect to pay royalties on annual net sales related to FA and Angelman syndrome. Our outstanding

obligations under the Agilis Merger Agreement related to Upstaza/Kebilidi include obligations to pay up to a maximum aggregate amount of $50.0 million upon the achievement of certain net sales milestones.

BioElectron Technology Corporation

On October 25, 2019, we completed the acquisition of substantially all of the assets of BioElectron Technology Corporation, or BioElectron, pursuant to an Asset Purchase Agreement by and between us and BioElectron, dated October 1, 2019, or the BioElectron Asset Purchase Agreement.

In addition to the upfront consideration paid to BioElectron upon the closing of the asset acquisition, subject to the terms and conditions of the BioElectron Asset Purchase Agreement, BioElectron may become entitled to receive contingent milestone payments of up to $200.0 million (in cash or in shares of our common stock, as determined by us) from us based on the achievement of certain regulatory and net sales milestones. Subject to the terms and conditions of the BioElectron Asset Purchase Agreement, BioElectron may also become entitled to receive contingent payments based on a percentage of net sales of certain products. Upon the potential achievement in 2025 of certain regulatory milestones relating to vatiquinone, which milestones would be payable in 2026, we expect to make payments to BioElectron of $75.0 million in the aggregate, in cash or shares of our common stock, as determined by us.

Censa Pharmaceuticals, Inc.

On May 29, 2020, we acquired Censa pursuant to an Agreement and Plan of Merger, dated as of May 5, 2020, or the Censa Merger Agreement, by and among us, Hydro Merger Sub, Inc., our wholly owned, indirect subsidiary, and, solely in its capacity as the representative, agent and attorney-in-fact of the securityholders of Censa, Shareholder Representative Services LLC, or the Censa Merger.

In addition to the upfront consideration paid to the Censa securityholders upon the closing of the Censa Merger, pursuant to the Censa Merger Agreement, Censa securityholders will be entitled to receive contingent payments from us based on (i) the achievement of certain development and regulatory milestones up to an aggregate maximum amount of $217.5 million for sepiapterin's two most advanced programs and receipt of a priority review voucher from the FDA as set forth in the Censa Merger Agreement, (ii) $109 million in development and regulatory milestones for each additional indication of sepiapterin, (iii) the achievement of certain net sales milestones up to an aggregate maximum amount of $160.0 million, (iv) a percentage of annual net sales during specified terms, ranging from single to low double digits of the applicable net sales threshold amount, and (v) any sublicense fees paid to us in consideration of any sublicense of Censa's intellectual property to commercialize sepiapterin, on a country-by-country basis, which contingent payment will equal to a mid-double digit percentage of any such sublicense fees. In February 2023, we completed enrollment of our Phase 3 placebo-controlled clinical trial for sepiapterin for PKU. In connection with this event and pursuant to the Censa Merger Agreement, we paid a $30.0 million development milestone to the former Censa securityholders. We elected to pay this milestone in the form of shares of our common stock, less certain cash payments. Pursuant to such election, we issued 657,462 shares of our common stock and paid $0.4 million to former Censa securityholders. As of December 31, 2024, we have paid the former Censa securityholders a total of $65.0 million in connection with the achievement of certain regulatory milestone-based contingent payments under the Censa Merger Agreement. We expect to make payments to the former Censa securityholders of $57.5 million in the aggregate in cash upon the potential achievement in 2025 of regulatory milestones relating to sepiapterin pursuant to the Censa Merger Agreement.

Intellectual Property

Patents and trade secrets

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and certain ex-U.S. patent applications related to our proprietary technology, inventions and improvements that we believe are important to the development of our business, where patent protection is available. We also rely on trade

secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of January 31, 2025, our patent portfolio included a total of 106 active U.S. patents and 53 pending U.S. non-provisional patent applications, including continuations and divisional applications, that are owned, co-owned, or exclusively in-licensed. Our patent portfolio also includes numerous International and ex-U.S. patents and patent applications. The patent portfolio includes patents and patent applications with claims including composition of matter, pharmaceutical formulation and methods of use of our commercial products including ataluren, the active ingredient in the formulated product Translarna, and risdiplam, the active ingredient in the formulated product Evrysdi.

The patent rights relating to ataluren owned by us include 17 issued U.S. patents relating to composition of matter, methods of use, formulations, dosing regimens and methods of manufacture and multiple pending U.S. patent applications relating to methods of use, formulation, and dosing regimens. We do not license any material patent rights relating to ataluren to unaffiliated parties. The issued U.S. patents relating to composition of matter expired in April 2024 and all U.S. patents that issue from U.S. patent applications arising from the composition of matter also expired in April 2024. Issued U.S. patents relating to therapeutic methods of use are currently scheduled to expire in 2026 and 2027, including patent term adjustment. Our patent rights relating to ataluren include granted patents or pending counterpart patent applications in a number of other jurisdictions, including Canada, certain South American countries, Europe, certain Middle Eastern countries, certain African countries, certain Asian countries and certain Eurasian countries. We own five European patents relating to composition of matter, uses, dosing regimens and methods of manufacture of ataluren, as well as multiple pending European patent applications relating to composition of matter, uses and formulations. Granted European patents expired in April 2024 for those patents drawn to composition of matter, and will expire in 2026 and 2027 for those patents drawn to dosing regimen, and in 2027 for those patents drawn to the manufacturing process. Except as indicated above, the anticipated expiration dates referred to above are without regard to potential patent term extension, patent term adjustment or other marketing exclusivities that may be available to us.

The patent rights relating to risdiplam co-owned by us and Roche include seven issued U.S. patents relating to composition of matter, methods of use, and methods of manufacture and pending U.S. patent applications. We do not license any material patent rights relating to risdiplam to unaffiliated parties. The issued U.S. patents relating to composition of matter are currently scheduled to expire in 2033, 2035 and 2042. Our patent rights include granted patents or pending counterpart patent applications in a number of other jurisdictions, including Canada, certain South American countries, Europe, certain Middle Eastern countries, certain African countries, certain Asian countries and certain Eurasian countries. We co-own four European patents relating to composition of matter, and uses of risdiplam. The expiration dates of the granted European patents relating to composition of matter are currently scheduled to expire in 2033 and 2035. Except as indicated above, these anticipated expiration dates are without regard to potential patent term extension, patent term adjustment or other marketing exclusivities that may be available to us.

The patent rights relating to sepiapterin owned by us include five issued U.S. patents relating to composition of matter and methods of use, and one issued U.S. patent, co-owned by us and Shiratori, relating to methods of manufacture, as well as pending U.S. patent applications. We do not license any material patent rights relating to sepiapterin to unaffiliated parties. The last issued U.S. patent relating to composition of matter is currently scheduled to expire in September of 2038. Our patent rights include granted patents or pending counterpart patent applications in a number of other jurisdictions, including Canada, certain South American countries, Europe, certain Middle Eastern countries, certain African countries, certain Asian countries and certain Eurasian countries. We co-own one European patent relating to methods of manufacture of sepiapterin. The European patent relating to composition of matter is currently scheduled to expire in May of 2033. Except as indicated above, these anticipated expiration dates are without regard to potential patent term extension, patent term adjustment or other marketing exclusivities that may be available to us.

The patent rights relating to vatiquinone owned by us include seven issued U.S. patents relating to methods of use, formulations, dosing regimens and methods of manufacture and multiple pending U.S. patent applications relating to methods of use, formulation, and dosing regimens. We do not license any material patent rights relating to vatiquinone to unaffiliated parties. Issued U.S. patents relating to therapeutic methods of use are currently scheduled to expire in between October of 2029 and May of 2032. Our patent drawn to the manufacturing process in the U.S. will expire in October 2029. Our patent rights relating to vatiquinone include granted patents or pending counterpart patent applications in a number of other jurisdictions, including Canada, certain South American countries, Europe, certain Middle Eastern

countries, certain African countries, certain Asian countries and certain Eurasian countries. We own four European patents relating to composition of matter, uses, dosing regimens and methods of manufacture of vatiquinone, as well as multiple pending European patent applications relating to composition of matter, uses and formulations. Granted European patents will expire between June of 2026 and July of 2032 for those patents drawn to composition of matter, will expire between June of 2026 and May of 2032 for those patents drawn to dosing regimen, and in October of 2029 for the patent drawn to the manufacturing process. Except as indicated above, the anticipated expiration dates referred to above are without regard to potential patent term extension, patent term adjustment or other marketing exclusivities that may be available to us.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a U.S. patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval, or PMA, may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met.

Analogous patent term extension provisions are available in Europe and certain other ex-U.S. jurisdictions to extend the term of a patent that covers an approved drug. One means of patent term extension in Europe after EMA approval is based on obtaining a Supplementary Protection Certificate, or SPC. We have applied for SPCs for ataluren in all applicable European countries in which we have a European patent and have obtained SPCs or expect to obtain SPCs in all applicable European countries. The maximum patent term extension provided by an SPC is a total of 5 years from the date of patent term expiration. For example, in jurisdictions where an SPC with maximum patent term extension has been granted, the ataluren composition of matter patent would be scheduled to expire in 2029. To the extent a marketing authorization in any particular jurisdiction is not or cannot be maintained, the granted patent may remain in force in that jurisdiction until its natural expiration date, although a granted SPC in that jurisdiction may be withdrawn. To the extent an underlying granted patent may be invalidated in that jurisdiction prior to its natural expiration date, the associated SPC will be invalidated as well. In the future, if and when our product candidates receive approval by the FDA or other non-European ex-U.S. regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors.

We have no patents covering Emflaza or the approved use of Emflaza. See "Item 1. Business-Government Regulation" for further information regarding the exclusivity periods we expect to rely on for patients aged 2-5.

We rely on orphan drug exclusivity in the EEA for Upstaza for the treatment of AADC deficiency. We rely on the non-patent market exclusivity periods under the Orphan Drug Act and the BPCIA to commercialize Kebilidi in the United States. If approved elsewhere, we expect to rely on orphan drug exclusivity in other countries or regions where such exclusivity is available. See "Item 1. Business-Government Regulation" for further information regarding the exclusivity periods that we expect to rely on.

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, using confidentiality agreements with our employees, consultants, scientific advisors, contractors and collaborators. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, such agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees, former employees, consultants, scientific advisors, contractors or collaborators use intellectual property owned by us or licensed to us by others in their work for us, trade secret disputes may arise. If such disputes arise in the U.S., we may protect our trade secrets and pursue remedies available under federal statute using either the Economic Espionage Act of 1996 and/or the Defend Trade Secrets Act of 2016 and, if necessary, under state law using either the Uniform Trade Secrets Act or other State law available in the applicable venue. If such disputes arise ex-US, we may protect our trade secrets and pursue remedies available under local or international law.

License agreements

We are a party to a number of license agreements under which we license patents, patent applications and other intellectual property from third parties. We enter into these agreements to augment our proprietary intellectual property portfolio. The licensed intellectual property covers some of the compounds that we are researching and developing, some post-transcriptional control targets and some of the scientific processes that we use. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future.

We exclusively in-licensed know-how and materials related to the production and use of Upstaza/Kebilidi. For a further discussion of the material agreements relating to our in-licensing of Upstaza/Kebilidi for the treatment of AADC deficiency, see "Item 1. Business-Our Collaborations, License Agreements and Funding Arrangements-National Taiwan University." Additionally, we exclusively in-license or jointly own patent applications with claims directed to composition of matter, formulation and methods of use of other gene therapy products candidates currently in development.

Manufacturing

We do not currently own or operate functional manufacturing or distribution facilities for the production of clinical or commercial quantities of our products or product candidates or compounds that we are testing in our preclinical programs. We currently rely, and expect to continue to rely, on third parties for the manufacture, packaging, labeling and distribution of clinical and commercial supplies of our products or product candidates that we may develop, other than small amounts of compounds that we may synthesize ourselves for preclinical testing. We have personnel with manufacturing and quality experience to oversee our contract manufacturers.

The active pharmaceutical ingredients in our products and product candidates are provided by third-parties. We currently rely on a single source for the production of some of our raw materials and we obtain our supply of the drug substance for Translarna from two third-party manufacturers. For sepiapterin we rely on two sources for the production of our raw materials and we obtain our supply of the drug substance from two third-party manufacturers. For vatiquinone we rely on one source for the production of our raw materials, and we obtain our supply of the drug substance for vatiquinone from one third-party manufacturer.

We engage two separate manufacturers to provide bulk drug product for Translarna. We have a relationship with three manufacturers that are capable of providing primary and secondary packaging services for our finished commercial and clinical Translarna product. We currently engage one manufacturer each to provide bulk drug product for sepiapterin and vatiquinone.

We currently obtain our supplies of Translarna, sepiapterin and most of our other products and product candidates from our third-party manufacturers pursuant to agreements that include specific supply timelines and volume expectations. If a manufacturer should become unavailable to us for any reason, we would seek to obtain supply from another manufacturer engaged by us for the applicable product or service. In the event that we were unable to procure the applicable supply from a validated manufacturer, we believe that there are a number of potential replacements for each of our outsourced services, however we likely would experience delays in our ability to supply Translarna, sepiapterin or vatiquinone to patients or in advancing our clinical trials while we identify and qualify replacement suppliers.

We obtain our supply of the drug substance for Emflaza through a third-party manufacturer that is currently the only third-party manufacturer qualified to provide Emflaza drug substance for use in the United States. All of our drug product manufacturing, processing and packaging needs for Emflaza tablet and suspension product are fulfilled pursuant to two different exclusive supply agreements assumed by us in connection with our acquisition of Emflaza. We expect to fulfill all of our requirements for Emflaza tablets as well as secondary packaging of Emflaza oral suspension bottles pursuant to one of these agreements, which has an automatic renewal provision subject to the termination rights of each party. We expect to fulfill all of our requirements for Emflaza suspension product pursuant to the other agreement. We are obligated to pay to the manufacturer of the Emflaza suspension product royalty payments, on a quarterly basis, based on a percentage (ranging from low to middle-low double digits) of, or a fixed payment with respect to, our annual net sales of suspension product in the United States, subject to reduction in accordance with the terms of the agreement.

If our drug substance provider or either of our drug product manufacturers was to be unable to provide drug substance or manufacture Emflaza product in sufficient quantities to meet projected demand, future sales could be adversely affected, which in turn could have a detrimental impact on our ability to maintain our marketing authorization in the United States and on our ability to commercialize Emflaza, which in turn would have a material adverse effect on our business, financial results and results of operations. Further, Emflaza received a seven-year exclusive marketing period in the United States for its approved indications, commencing on the date of FDA approval, under the provisions of the Orphan Drug Act. Emflaza's seven-year period of orphan drug exclusivity related to the treatment of DMD in patients five years and older expired in February 2024. Emflaza's orphan drug exclusivity related to the treatment of DMD in patients two years of age to less than five expires in June 2026. As the holder of orphan exclusivity, we are required to assure the availability of sufficient quantities of Emflaza to meet the needs of patients. Failure to do so could result in loss of the drug's remaining orphan exclusivity in the United States.

Translarna, Emflaza and sepiapterin are manufactured in reliable and reproducible synthetic processes. Our raw materials are not scarce and are readily available subject to supply chain disruptions. We currently rely on a single source for the production of some raw materials for Translarna and Emflaza, and switching to an alternative source could, in some instances, take time and could lead to delays in manufacturing. We currently rely on multiple sources for the production of raw materials for seipaipterin. We maintain inventories for such materials such that any delays with raw materials will not affect or delay our manufacturing. No material shortages or delays of raw materials were encountered in 2024 and no manufacturing delays are currently expected in 2025. The chemistry is amenable to scale up and does not require unusual equipment in the manufacturing process. We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities or internally, in the case of our gene therapy platform.

We have agreements with third-party manufacturers for the long-term commercial supply of Translarna, sepiapterin and vatiquinone. In the event that we are unable to procure supply from a validated manufacturer, we would seek to identify and qualify replacement suppliers, however this process would likely delay our ability to supply these products to patients or advance our clinical trials. We may be unable to conclude agreements for commercial or clinical supply of these products with third-party manufacturers, or we may be unable to do so on acceptable terms.

We currently have contracts with multiple pharmacy and hospital distributors in the EU that distribute Translarna for limited commercial and EAP programs. We have engaged with third-party logistic providers, or 3PLs, which distribute Translarna for the majority of our commercial and EAP programs on our behalf.

We utilize third parties for the commercial distribution of Emflaza, including a 3PL to warehouse Emflaza as well as specialty pharmacies to sell and distribute Emflaza to patients. The specialty pharmacies provide us with third-party call center services to provide patient support and financial services, prescription intake and distribution, reimbursement adjudication, and ongoing compliance support.

Pursuant to the Tegsedi-Waylivra Agreement, we have entered into a master supply agreement with Akcea whereby Akcea or its affiliates will manufacture and supply, or cause to be manufactured and supplied, Tegsedi and Waylivra in quantities sufficient to support the commercialization of Tegsedi and Waylivra in the PTC Territory. This is currently the only manufacturing and supply agreement that we have entered into for the drug substance of Tegsedi and Waylivra. If the master supply agreement is terminated and we are unable to find an alternative third-party contractor, we may encounter delays in manufacturing Tegsedi and Waylivra.

We have a commercial manufacturing services agreement with MassBiologics of the University of Massachusetts Medical School, or MassBio, to provide sufficient quantities of our Upstaza/Kebilidi materials to meet commercial scale demands. If MassBio is unable to perform its obligations under the commercial manufacturing services agreement, identifying a replacement gene therapy manufacturer would likely be challenging and time-consuming. However, we believe that we have sufficient supply of Upstaza/Kebilidi to meet our near-term commercial needs in such an event.

In June 2024, we sold our gene therapy manufacturing business in Hopewell Township, New Jersey. Accordingly, we do not expect to have manufacturing revenue going forward. For the years ended December 31, 2024 and 2023, we recognized $1.7 million and $7.7 million of manufacturing revenue, respectively, related to plasmid DNA and AAV vector production for external customers. No manufacturing revenue was recognized for the year ended December 31, 2022.

Manufacturers and suppliers of product candidates are subject to the FDA's current Good Manufacturing Practices, or cGMP, requirements, and other rules and regulations prescribed by ex-U.S. regulatory authorities. We depend on our third-party suppliers and manufacturers for continued compliance with cGMP requirements and applicable ex-U.S. standards.

Commercial Matters

Sales and marketing team

Our product revenue has primarily been attributable to sales of Translarna for the treatment of nmDMD in territories outside of the United States and to sales of Emflaza for treatment of DMD in the United States. We have employees across the globe, with the largest concentrations being in the United States, Latin America and Europe.

In addition, in select territories, we have engaged full-time consultants, marketing partners and distribution partners to assist us with our international commercialization efforts for our products. We continue to evaluate new territories to determine in which geographies we might, if approved, choose to commercialize our products ourselves and in which geographies we might choose to collaborate with third parties. We expect that our internal team and partnership network will continue to grow, as needed, to maximize access to patients.

Customers

During 2024, our product revenue was primarily attributable to Translarna for the treatment of nmDMD and to Emflaza for treatment of DMD. Translarna for the treatment of nmDMD was available on a commercial basis or via reimbursed EAP programs or similar styled programs in multiple territories outside of the United States. In some territories, orders for Translarna are placed directly with us and in other territories we have engaged with third-party distributors. As a result, orders for Translarna are generally received from hospital and retail pharmacies and, in some cases, one of our third-party partner distributors. Our third-party distributors act as intermediaries between us and end-users and do not typically stock significant quantities of Translarna. The ultimate payor for Translarna is typically a government authority or institution or a third-party health insurer. The payment terms are generally 30 to 90 days after receipt of products.

Emflaza for treatment of DMD is available on a commercial basis throughout the United States. We utilize five specialty pharmacies to sell and distribute Emflaza to patients. The specialty pharmacies receive prescription orders for Emflaza directly from physicians and ship Emflaza directly to the end-user upon fulfillment of the order. As such, there is very little inventory of Emflaza stocked. The ultimate payor for Emflaza is typically a state health insurance program or a third-party health insurer. The payment terms are generally 30 to 90 days after receipt of products.

During 2024, two of our distributors each accounted for over 10% of our net product sales. Financial information about our net product revenues and other revenues generated in the principal geographic regions in which we operate and our long-lived assets is set forth in our financial statements and in Note 15, "Segment and geographic information" to our consolidated financial statements included in this Annual Report on Form 10-K.

Translarna and Emflaza can generally only be returned if agreed upon in writing by us and the product is not opened nor in receipt by the final user, except in the case of quality issues associated with the product. Product is generally shipped when a specific patient is approved by the applicable government or insurer and an individual prescription has been written. The right of return is eliminated as a matter of course when the product is dispensed to patients. Other than in connection with our transition to a new third-party distributor, we have never had a request for a return of a material amount of product for either Translarna or Emflaza.

In some countries, orders for named patient sales may be for multiple months of therapy, which can lead to an unevenness in orders which could result in significant fluctuations in quarterly net product sales. For example, almost all of our Brazilian product revenue for Translarna is attributable to centralized group purchase orders through the Brazilian Ministry of Health that are intended to cover multiple months of therapy. Similarly, Translarna orders placed through a distributor for the Ministry of Health of the Russian Federation are also intended to cover multiple months of therapy. Any fluctuations in quarterly net product sales in Brazil and Russia resulting from these centralized group purchase orders may also be exacerbated by any delays.

Translarna for the treatment of nmDMD is currently available on a commercial basis in multiple countries outside of the United States. We consider our products to be commercially available when we are permitted to market treatment to patients.

Translarna for the treatment of nmDMD is also currently available through EAP or similar styled programs in select countries where funded named patient or cohort programs exist, both within the EEA and in other territories. These programs generally reference the EMA's determinations with respect to our marketing authorization in the EEA. As of today, Translarna is available under EAP or similar styled programs in various countries outside of the United States. Generally, EAP programs allow for access to Translarna pursuant to a named patient program, under which a physician requests access to Translarna on behalf of the specific, or "named" patient or pursuant to a cohort program, which allows for a broader temporary authorization for use for nmDMD meeting the inclusion criteria. Our EAP programs are named patient or similar styled programs in all territories other than France, which is a cohort program.

Our ability to make Translarna available via commercial or EAP programs or through similar styled programs is largely dependent upon our ability to maintain our marketing authorization in the EEA for Translarna for the treatment of nmDMD in ambulatory patients aged two years and older. The marketing authorization is subject to annual review and renewal by the EC following reassessment by the EMA. In September 2022, we submitted a Type II variation to the EMA to support conversion of the conditional marketing authorization for Translarna to a standard marketing authorization, which included a report on the placebo-controlled trial of Study 041 and data from the open-label extension as further described below. In February 2023, we also submitted an annual marketing authorization renewal request to the EMA. In September 2023, the CHMP gave a negative opinion on the conversion of the conditional marketing authorization to full marketing authorization of Translarna for the treatment of nmDMD and a negative opinion on the renewal of the existing conditional marketing authorization of Translarna for the treatment of nmDMD. In January 2024, the CHMP issued a negative opinion for the renewal of the conditional marketing authorization following a re-examination procedure. In May 2024, the EC decided not to adopt the CHMP's negative opinion for the renewal of the conditional marketing authorization of Translarna and returned such opinion to the CHMP for re-evaluation. In June 2024, following the EC's request for re-review, the CHMP issued a negative opinion on the renewal of the conditional marketing authorization of Translarna for the treatment of nmDMD. On October 18, 2024, the CHMP maintained its negative opinion for the renewal of the conditional marketing authorization following the requested reexamination procedure. In accordance with EMA regulations, the EC has 67 days from the date of issuance to adopt the opinion. At this time, the EC has not yet adopted the negative opinion. If the EC adopts the negative opinion, Translarna would no longer have marketing authorization in the member states of the EEA. The marketing authorization for Translarna remains in effect, pending the EC's potential adoption of the negative opinion. See "Item 1. Business-Global commercial footprint-Global DMD franchise" and "Risk Factors-Risks Related to Regulatory Approval of our Products and our Product Candidates" for further information regarding the marketing authorization in the EEA and related risks.

Market Access Considerations

Our future revenues from our products and any other product candidates we may develop depends largely on our ability to obtain and maintain reimbursement from governments and third-party insurers. Each country in the EEA has its own pricing and reimbursement regulations and many countries in the EEA have other regulations related to the marketing and sale of pharmaceutical products in the applicable country. The pricing and reimbursement process varies from country to country and can take a substantial amount of time from initiation to completion. As a result, our commercial launches of products in the EEA has been and is expected to continue to be on a country-by-country basis and we generally will not be able to commence commercial sales of our products pursuant to our marketing authorizations in the EEA in any particular member state of the EEA until we conclude the applicable pricing and reimbursement negotiations and comply with any licensing, employment or related regulatory requirements in that country. The price that is approved by local governmental authorities pursuant to commercial pricing and reimbursement processes may be lower than the price for purchases of product in that country pursuant to a reimbursed early access program.

In some instances, reimbursement may be subject to challenge, reduction or denial by the government and other payers. For example, in France, EAP programs and commercial sales of a product can begin while pricing and reimbursement rates are under discussion with the applicable government health programs. In the event that the negotiated price of the product is lower than the amount reimbursed for sales made prior to the conclusion of price negotiations, we may become

obligated to repay such excess amount to the applicable government health program. Such retroactive reimbursement would be made following the conclusion of price negotiations with the applicable government health authority.

For Emflaza, which is approved in the United States, we are engaged in pricing, coverage and reimbursement discussions with third-party payors, such as state and federal governments, including Medicare and Medicaid, managed care providers, private commercial insurance plans and pharmacy benefit management plans. Decisions regarding the extent of coverage and the amount of reimbursement to be provided for Emflaza are made on a plan-by-plan, and in some cases, on a patient-by-patient basis. Coverage and reimbursement decisions by third-party payors, including the processing and adjudication of prescriptions, may vary from weeks to several months. Certain third-party payors routinely impose additional requirements before approving reimbursement of a prescription, including prior authorization and the requirement to try another therapy first. The specialty pharmacies we utilize provide patient services programs to support product access and, when eligible, out-of-pocket assistance.

We have generated revenue from net sales of Upstaza for the treatment of AADC deficiency in the EEA since May 2022. Upstaza is approved for the treatment of AADC deficiency for patients 18 months and older within the EEA and the United Kingdom. In November 2024, the FDA granted accelerated approval for this gene therapy for the treatment of AADC deficiency in the United States. This gene therapy is marketed with the brand name Kebilidi in the United States. We expect to generate revenue from net sales of Kebilidi for the treatment of AADC deficiency in the United States during the year ending December 31, 2025. Our future revenues from Upstaza/Kebilidi depend largely on our ability to obtain and maintain reimbursement from governments and third-party insurers as described above.

Tegsedi for the treatment of hATTR amyloidosis and Waylivra for the treatment of FCS are currently available on a commercial basis in multiple countries outside of the United States and we have the right to commercialize these products in the PTC Territory. We have received marketing authorization from ANVISA for Tegsedi for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hATTR amyloidosis in Brazil and Waylivra for the treatment of FCS and FPL in Brazil. We make commercial sales of Tegsedi for the treatment of hATTR amyloidosis in Brazil and Waylivra for the treatment of FCS and FPL in Brazil. The marketing authorizations of Tegsedi and Waylivra in Brazil are subject to renewal every five years. We have also made both Tegsedi and Waylivra available in certain countries within the PTC Territory through EAP Programs. Our ability to make Tegsedi and Waylivra available within the PTC Territory is largely dependent upon the maintenance of the marketing authorizations in the EU and the United States by the licensor.

We record revenue net of estimated third-party discounts and rebates. Allowances are recorded as a reduction of revenue at the time revenues from product sales are recognized. These allowances are adjusted to reflect known changes in factors and may impact such allowances in the quarter those changes are known.

For important information regarding market access and pricing and reimbursement considerations see “Item 1. Business-Government Regulation-Pharmaceutical Pricing and Reimbursement” and “Item 1A. Risk Factors-Risks Related to the Development and Commercialization of our Products and our Product Candidates” and “-Risks Related to Regulatory Approval of our Products and our Product Candidates”.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies and private and public research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller

or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop. In addition, our ability to compete may be affected because in some cases insurers or other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers.

The key competitive factors affecting the success of our products and product candidates are likely to be its efficacy, safety, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

The competition for our products and product candidates includes the following:

- ***Translarna for nmDMD.*** There is currently no marketed therapy specifically for nmDMD, other than Translarna in the EEA. Santhera Pharmaceuticals has received approval of Agramee (vamorolone) in the United States for DMD patients ages 2 and up and in the EU and United Kingdom for patients ages 4 years and older. Sarepta Therapeutics has received approval of Elevidys for DMD patients 4 to 5 years of age with a confirmed mutation in the "DMD gene" in the United States and United Arab Emirates and Qatar. Sarepta Therapeutics has also received approval in the United States for two treatments (Exondys 51 (eteplirsen) and Vyondys 53 (golodirsen)) addressing the underlying cause of disease for different mutations in the DMD gene. Additionally, the FDA granted accelerated approval to Viltepso (viltolarsen) from NS Pharma for the treatment of DMD in patients with exon 53 skipping and Sarepta (Casimersen (SRP 4045) for the treatment of DMD in patients with exon 45 skipping. Viltepso (viltolarsen) from NS Pharma is also approved in Japan. Other biopharmaceutical companies are developing treatments addressing the underlying cause of disease for different mutations in the DMD gene, including Dyne Therapeutics (DYNE-251), Wave Life Sciences (WVE-N53), Daiichi Sankyo (DS-5141)), Nippon Shinyaku (Viltolarsen (NS-065/NCNP-01) and NS-089/NCNP-02)), and Astellas (AT-702). Additionally, other pharmaceutical companies are developing micro dystrophin gene therapies for patients with DMD regardless of genotype, including Pfizer (PF-06939926) and Solid Biosciences (SGT-001).
- ***Emflaza for DMD.*** With the expiration of Emflaza's orphan exclusivity for treatment of DMD in patients five years and older in February 2024, we face competition from generic versions of Emflaza for this indication. The FDA has not approved a corticosteroid specifically for DMD in the United States other than Emflaza. However, prednisone/prednisolone, which is not approved for DMD in the United States, is generically available and has been prescribed off label for DMD patients. Santhera has received approval of Agramee (vamorolone), in the United States for DMD patients ages 2 and up and in the EU and United Kingdom for patients ages 4 years and older.
- ***Upstaza/Kebilidi.*** Currently, no other treatment options are available for the underlying cause of AADC deficiency. Additionally, we are not aware of any late-stage development product candidates for AADC deficiency.
- ***Waylivra for FCS.*** Ionis is developing Olezarsen for the treatment of FCS.
- ***Waylivra for FPL.*** Waylivra faces competition from Myalept (metreleptin) produced by Cheisi Farmaceutica, Inc., which is currently approved in Brazil for use in generalized lipodystrophy patients. We are not aware of any late-stage development product candidates for FPL.
- ***Tegsedi.*** Tegsedi faces competition from drugs like Onpattro (patisiran) which was launched by Alnylam Pharmaceuticals in the United States in 2018 and received approval in Brazil for the treatment of hATTR amyloidosis in 2020 as well as AMVUTTRA (vutrisiran) which Alnylam Pharmaceuticals received approval for in the United States and Brazil in 2022 for the treatment of the polyneuropathy of hATTR amyloidosis in adults. Vyndaqel (tafamids meglumine) and Vyndamax (tafamidis) are commercialized in the United States, EU and some countries in Latin America by Pfizer. Other companies are also pursuing product candidates for the treatment of ATTR Amyloidosis with polyneuropathy including BridgeBio Pharma (AG 10), Intellia Therapeutics (NTLA2001), Proclara Biosciences (NPT 189) and SOM Biotech (tolcapone).
- ***Evrysdi.*** Evrysdi, an orally bioavailable treatment, faces competition from treatments that are not orally bioavailable, including Spinraza (nusinersen), a drug developed by Ionis and marketed by Biogen, which is

approved to treat SMA and Zolgensma (onasemnogene abeparvovec), a gene therapy drug developed by AveXis, Inc., (acquired by Novartis in 2018), which is approved in the United States and Japan for the treatment of SMA in patients under 2 years of age and in Europe for babies and young children who weigh up to 21 kilograms. Novartis is also developing OAV-101, an intrathecal administration of Zolgensma, for SMA patients ages ≥ 2 to < 18 years of age. Biogen is developing a higher dose regimen of nusinersen with potential for improved efficacy and evaluating an implantable medical device to enable subcutaneous delivery of nusinersen. Other companies are also pursuing product candidates for the treatment of SMA, including Scholar Rock (apitegromab, SRK-015), Biohaven (Taldefgrobep alfa), Roche Pharmaceuticals (RO-7204239/GYM-329), Biogen / Ionis (BIIB-115/ION-306) and NMD Pharma (NMD-670).

- ***Sepiapterin for PKU.*** If approved, sepiapterin could face competition from Kuvan (sapropterin dihydrochloride), including generic versions, and Palynziq (pegvaliase-pqpz), each of which is approved for the treatment of PKU. Other companies are also pursuing product candidates for the treatment of PKU, including Otsuka Pharmaceutical (JNT-517), SOM Biotech (SOM-1311), Maze Therapeutics (MZE-782) and Agios (AG-181).
- ***PTC518 for HD.*** There are currently no disease-modifying therapies approved to delay the onset or slow the progression of HD. However, uniQure (AMT-130), Roche and Ionis (tominersen), Skyhawk Therapeutics (SKY 0515), Vico Therapeutics (VO659) and Wave Life Sciences (WVE-003) are all developing product candidates for treatment of Huntington disease.
- ***Vatiquinone for FA.*** If approved, vatiquinone could face competition from Skyclarys (omaveloxolone) from Biogen, which is approved in the United States and the EU. There are also two assets in early development: LX-2006 (Lexeo/Frataxin AAVrh10) and CTI-1601 (Larimar Therapeutics).

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, quality control, approval, manufacturing, labeling, post-approval monitoring and reporting, recordkeeping, packaging, promotion, storage, advertising, distribution, marketing and sales and export and import of biopharmaceutical products such as those we are developing and marketing. In addition, sponsors of biopharmaceutical products and drug products participating in Medicaid and Medicare are required to comply with mandatory price reporting, discount, and rebate requirements. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and ex-U.S. statutes and regulations require the expenditure of substantial time and financial resources. If we do not comply with applicable requirements, we may be subject to civil penalties, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, fined, the government may refuse to approve our marketing applications, supplemental applications, or allow us to manufacture or market our products, we may be criminally prosecuted and we may be debarred or excluded from participation in government healthcare programs. These requirements are continually evolving. See "Item 1A. Risk Factors-Risks Related to Regulatory Approval of our Product and our Product Candidates" for important information regarding some of the risks to our business arising as a result of government regulation.

U.S. government regulation

In the United States, the FDA regulates drugs and biologic products, including gene therapy products, under the Federal Food, Drug, and Cosmetic Act, or the FDCA, the Public Health Service Act, or the PHSA, and regulations and guidance implementing these laws. The FDCA, PHSA and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving drugs and biologic products. Failure to comply with the applicable FDA requirements at any time pre- or post-approval may result in a delay of approval or administrative or judicial sanctions.

Regulatory requirements governing our business are also evolving. For example, the FDA has issued a growing body of guidance documents on CMC, clinical investigations and other areas of gene therapy development, all of which are intended to facilitate the industry's development of gene therapy products. Moreover, the FDA also continually issues guidance documents that provide the FDA's interpretation of its laws and regulations, as well as the FDA's approach to scientific issues and questions. While the FDA's guidance is not binding, it does provide the FDA's current interpretation and approach.

The new drug and biologic approval process

In the United States, an NDA is the vehicle through which the FDA approves a new pharmaceutical drug product for sale and marketing in the United States. A BLA is the vehicle through which the FDA approves a new biologic product for sale and marketing in the United States.

To market a new drug or biologic product in the United States, a sponsor generally must undertake the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies under the FDA's Good Laboratory Practice, or GLP, regulations and other applicable laws or regulations;
- submission to the FDA of an investigational new drug application, or IND, for clinical testing, which must become effective before clinical trials may begin at United States clinical trial sites;
- approval by an independent Institutional Review Board, or IRB, and in the case of certain gene therapy studies, an Institutional Biosafety Committee, or IBC, prior to initiation and subject to continuing review;
- completion of adequate and well-controlled clinical trials to establish safety and efficacy, in the case of a drug product candidate, or safety purity, and potency, in the case of a biologic product candidate for its intended use, performed in accordance with Good Clinical Practices, or GCP, and the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, or ICH, E6 GCP guidelines. Certain gene therapy research must also be conducted in accordance with the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines;
- development of manufacturing processes to ensure the product candidate's identity, strength, quality, purity, and potency;
- submission and FDA acceptance of an NDA or BLA, and satisfactory completion of an FDA Advisory Committee meeting, if applicable;
- satisfactory completion of an FDA inspection or remote regulatory assessment of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMPs, which require that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity, as well as satisfactory completion of an FDA inspection or remote regulatory assessment of selected clinical sites and selected clinical investigators to determine GCP compliance;
- FDA review and approval of the NDA or BLA to permit commercial marketing for particular indications for use; and
- compliance with any post approval requirements and commitments, including Risk Evaluation and Mitigation Strategies, or REMS, and post approval studies required by the FDA.

Nonclinical Studies and IND Submission

Nonclinical tests include laboratory evaluations of product chemistry, pharmacology, stability, toxicity and product formulation, as well as animal or other nonclinical studies to assess potential safety and efficacy. In order to begin clinical testing, a sponsor must submit an IND to the FDA, which includes, among other things, the results of the nonclinical tests, manufacturing information, analytical data, proposed clinical protocols, and any available clinical data or literature on the product candidate. Some nonclinical testing may continue after the IND is submitted. The IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. Clinical holds also may be imposed by the FDA at any time before or during trials due to safety concerns or non-compliance.

Clinical Trials

Clinical trials involve the administration of an investigational product to human subjects under the supervision of qualified investigators. Clinical trials are conducted in accordance with protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, the effectiveness criteria to be evaluated, and a statistical analysis plan. A protocol for each clinical trial and subsequent protocol amendments must be filed with the FDA as part of the IND.

Sponsors will also be required to provide FDA with diversity action plans. In accordance with GCP requirements, all research subjects or their legally authorized representatives must provide their informed consent in writing prior to their participation in a clinical trial. Each clinical trial must be reviewed and approved by an IRB and is subject to ongoing IRB monitoring. The IRB must approve the protocol, protocol amendments, the informed consent form, and communications to study subjects before a study commences at the site. An IRB considers among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to anticipated benefits, and whether the planned human subject protections are adequate. The IRB must continue to oversee the clinical trial while it is being conducted. Special clinical trial ethical considerations also must be taken into account if a study involves children. In the case of certain gene therapy studies, an IBC at the local level may also review and maintain oversight over the particular study, in addition to the IRB. If the product candidate is being investigated for multiple intended indications, separate INDs may also be required. Progress reports detailing the results of the clinical trials must be submitted at least annually to FDA and the IRB and more frequently if serious adverse events or other significant safety information is found. Certain reports may also be required to be submitted to the IBC.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group regularly reviews accumulated data and advises the study sponsor regarding the continuing safety of the trial. This group may also review interim data to assess the continuing validity and scientific merit of the clinical trial. The data safety monitoring board receives special access to unblinded data during the clinical trial and may advise the sponsor to halt the clinical trial if it determined there is an unacceptable safety risk for subjects or on other grounds, such as no demonstration of efficacy.

Information about certain clinical trials must be submitted within specific timeframes to the NIH to be publicly posted on the Clinicaltrials.gov website. Sponsors or distributors of investigational products for the diagnosis, monitoring, or treatment of one or more serious disease or conditions must also have a publicly available policy on evaluating and responding to requests for expanded access. Investigators must also provide certain information to clinical trial sponsors to allow the sponsors to make certain financial disclosures to the FDA.

The manufacture of investigational drugs and biologics for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and biologics and active ingredients and therapeutic substances imported into the United States are also subject to regulation by the FDA. Further, the export of investigational products outside the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FDCA.

In general, for the purposes of NDA and BLA approval, human clinical trials typically are conducted in three sequential phases, but the phases may overlap, be divided, or be combined. Phase 1 clinical trials may be conducted in patients or healthy volunteers to evaluate the product's safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism distribution, excretion, and pharmacokinetics and, if possible, seek to gain an early indication of its effectiveness. Phase 2 clinical trials usually involve controlled trials in a larger but still relatively small number of subjects from the relevant patient population to evaluate dosage tolerance and appropriate dosage; identify possible short-term adverse effects and safety risks; and provide a preliminary evaluation of the efficacy of the drug or biologic product for specific indications. Phase 3 clinical trials usually further evaluate clinical efficacy and test further for safety in an expanded patient population at geographically dispersed clinical trial sites, to generate enough data to provide statistically significant evidence of clinical efficacy and safety of the product candidate for approval. These trials are well-controlled and are intended to establish the overall risk- benefit profile of the product or product candidate and provide an adequate basis for physician labeling. Phase 3 clinical trials are usually larger, more time consuming, more complex and more costly than Phase 1 and Phase 2 clinical trials. The FDA typically requires that an NDA or BLA include data from two adequate and well-controlled clinical trials, but, in certain circumstances, approval may be based upon a single adequate and well-controlled clinical trial plus confirmatory evidence or a single large multicenter trial without confirmatory evidence. In some cases, the FDA may condition approval of an NDA or BLA on the applicant's agreement to conduct additional clinical trials to further assess the product's safety and effectiveness after NDA or BLA approval. Such post-approval trials are typically referred to as Phase 4 studies. The results of Phase 4 studies can confirm or refute the effectiveness of a product candidate, and can provide important safety information.

Additional kinds of data may also help support a BLA or NDA, such as patient experience data and real world evidence. Real world evidence may also be used to assist in clinical trial design or support an NDA for already approved products.

For genetically targeted populations and variant protein targeted products intended to address an unmet medical need in one or more patient subgroups with a serious or life-threatening rare disease or condition, the FDA may allow a sponsor to rely upon data and information previously developed by the sponsor or for which the sponsor has a right of reference, that was submitted previously to support an approved application for a product that incorporates or utilizes the same or similar genetically targeted technology or a product that is the same or utilizes the same variant protein targeted drug as the product that is the subject of the application. A program has also been established whereby a platform technology that is incorporated within or utilized by an approved drug or biologic product may be designated as a platform technology, provided that certain conditions are met, which are outlined in an FDA guidance, in which case development and approval of subsequent products using such technology may be expedited.

Concurrent with clinical trials, companies usually complete additional nonclinical studies and must also develop additional information about the physical characteristics of the drug or biologic product candidate as well as finalize a process for manufacturing the product candidate 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 requirements, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biologic product. Additionally, appropriate packaging must be selected and tested and adequate stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Additional FDA Expedited Review and Approval Programs

The FDA has various programs that are intended to expedite or simplify the process for the development and FDA review of certain products that are intended for the treatment of serious or life-threatening diseases or conditions, and demonstrate the potential to address unmet medical needs or present a significant improvement over existing therapy. The purpose of these programs is to provide important new therapeutics to patients earlier than under standard FDA review procedures.

To be eligible for a Fast Track designation, the FDA must determine, based on the request of a sponsor, that a product candidate is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. If Fast Track designation is obtained, sponsors may be eligible for more frequent development meetings and correspondence with the FDA. In addition, the FDA may potentially initiate a rolling review of sections of an application before the application is complete. This ‘‘rolling review’’ is available if the applicant provides and the FDA approves a schedule for the remaining information. Applicable user fees must also be paid before the FDA will commence its review. In some cases, a Fast Track product may be eligible for accelerated approval or priority review.

The FDA may give a priority review designation to product candidates that are intended to treat serious conditions and, if approved, would provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of the serious condition. A priority review means that the goal for the FDA is to review an application within six months, rather than the standard review of ten months under current PDUFA guidelines.

The FDA’s accelerated approval process allows for potentially faster development and approval of certain drugs or biologic products intended to treat serious or life-threatening illnesses that provide meaningful therapeutic benefit to patients over existing treatments. Under the accelerated approval process, the adequate and well-controlled clinical trials conducted with the drug or biologic product establish that the drug or biologic product has an effect on a “surrogate” endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity, that is reasonably likely to predict an effect on irreversible morbidity or mortality, taking into account the severity, rarity, or prevalence of the condition and availability or lack of alternative treatments. Drugs or biologic products approved through the accelerated approval process are subject to certain post-approval requirements, including completion of Phase 4 clinical trials to demonstrate clinical benefit. By the date of approval of an accelerated approval product, FDA must specify the conditions for the required post approval studies, including enrollment targets, the study protocol, milestones, and target completion dates. The FDA may also, and frequently does, require that the confirmatory Phase 4 studies be commenced prior to the FDA granting a product accelerated approval. Reports on the progress of the required Phase 4 confirmatory studies must be submitted to the FDA every 180 days after approval. If the trials fail to verify the clinical benefit of the drug or biologics product, the FDA may withdraw approval of the application through a statutorily defined streamlined process. Failure to conduct the required Phase 4 confirmatory studies or to conduct such studies with due diligence, as well as failure to submit the required update reports can subject a sponsor to

penalties. Promotional materials for a drug or biologic approved under the accelerated approval pathway are subject to the FDA prior review.

Sponsors can also request designation of a product candidate as a ‘‘breakthrough therapy.’’ A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Products designated as breakthrough therapies are eligible for intensive guidance on an efficient development program beginning as early as Phase 1 trials, a commitment from the FDA to involve senior managers and experienced review staff in a proactive collaborative and cross-disciplinary review, rolling review, and the facilitation of cross-disciplinary review.

Another expedited pathway is the Regenerative Medicine Advanced Therapy, or RMAT, designation. Qualifying products must be a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or a combination of such products, and not a product solely regulated as a human cell and tissue product. The product must be intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and preliminary clinical evidence must indicate that the product has the potential to address an unmet need for such disease or condition. Advantages of the RMAT designation include all the benefits of the Fast Track and breakthrough therapy designation programs, including early interactions with the FDA. These early interactions may be used to discuss potential surrogate or intermediate endpoints to support accelerated approval.

Companion Diagnostics and Other Combination Products

A drug or biologic product may be regulated as combination product if it is intended for use in conjunction with a medical device, such as a drug delivery device or in vitro diagnostic device, as further discussed below. In such cases, the use of the two products together (i.e., the drug/biological product and the device) must be shown to be safe and effective for the proposed intended use and the labeling of the two products must reflect their combined use. In some cases, the device component may require a separate premarket submission; for example, when the device component is intended for use with multiple drug products. Sponsors of clinical studies using investigational devices are required to comply with FDA’s investigational device exemption regulations. Once approved or cleared, the sponsor of the device component submission (or the combination product submission, if both components are covered by one premarket submission) would need to comply with FDA’s post-market device requirements, including establishment registration, device listing, device labeling, unique device identifier, quality system regulation, medical device reporting, and reporting of corrections and removals requirements.

If the safety or effectiveness of a drug or biologic product candidate for its proposed indication is dependent on the measurement or detection of specified biomarkers, the FDA may require the contemporaneous approval or clearance of an in vitro companion diagnostic device that measures such biomarkers, and require the labeling of both the drug/biological product and the companion diagnostic to including instructions for use of the two products together. The FDA has explained in guidance that in vitro companion diagnostic devices may be used for a number of purposes, including identifying appropriate subpopulations for treatment. The type of premarket submission required for a companion diagnostic device will depend on the FDA classification of the device. A premarket approval, or PMA, application is required for high risk devices classified as Class III; a 510(k) premarket notification is required for moderate risk devices classified as Class II; and a de novo request may be used for novel devices not previously classified by FDA that are low or moderate risk. It is also possible that an in vitro companion diagnostic device could be subject to the FDA enforcement discretion from compliance with the FDCA if it meets the definition of a Laboratory Developed Test, or LDT. However, the FDA issued a final rule in April 2024 to end enforcement discretion for LDTs and actively regulate such products as medical devices. Under this final rule, LDTs are required to come into compliance with the FDA’s medical device regulatory requirements in a staged approach over the course of four years. The implementation of this LDT final rule could potentially be affected by the Executive Order, *Regulatory Freeze Pending Review*, issued on January 20, 2025 and/or the anticipated change in leadership at the FDA under the new administration.

The FDA’s guidance states that the FDA generally will not approve a drug or biologic that is dependent upon the use of a companion diagnostic device if no such device is contemporaneously FDA-approved or -cleared for the relevant indication.

According to the guidance, however, the FDA may approve such a drug/biologic product without an approved/cleared companion diagnostic when the drug/ biologic "is intended to treat a serious or life-threatening condition for which no satisfactory alternative treatment exists" and the FDA determines that the benefits from the use of the drug/biologic "are so pronounced as to outweigh the risks from the lack of an" approved/cleared companion diagnostic. Under these circumstances, the FDA expects that a companion diagnostic would be subsequently approved/cleared, and that the drug/biologic labeling would be revised "to stipulate the use of the" companion diagnostic device. The FDA would also consider whether additional protections, such as risk evaluation and mitigation strategies, or REMS, or post-approval requirements, are necessary.

In a separate guidance, specific to DMD and related dystrophinopathies, the FDA has stated that a sponsor should contemporaneously develop a companion diagnostic device in situations where (1) the safety or efficacy of the drug or biologic product "may be related to the patient's specific dystrophin mutation or to another type of finding related to a biomarker," and (2) a suitable companion diagnostic device is not currently available. However, given "the serious and life-threatening nature of dystrophinopathies and the lack of satisfactory alternative treatments that currently exist," the guidance further states that the FDA may approve a drug/biologic "even if a companion diagnostic device is not yet approved or cleared, if the benefits are so pronounced as to outweigh the risks from the lack of an approved or cleared in vitro companion diagnostic device." During the review, the "FDA will determine the need for clearance or approval of the device." The FDA guidance documents represent the FDA's current thinking on a topic but do not establish legally enforceable responsibilities.

FDA Approval Process

Assuming successful completion of the required clinical testing, the results of the preclinical studies and of the clinical trials, together with other detailed information, including proposed labeling and information on the chemistry, manufacture and composition of the product, are submitted to the FDA in the form of an NDA or BLA requesting approval to market the product for one or more indications. In most cases, the NDA or BLA must be accompanied by a substantial user fee, though a waiver of such fees may be obtained under certain limited circumstances. Product candidates that are designated as orphan products are not subject to application user fees unless the application includes an indication other than the orphan indication. The user fees must be paid at the time of the first submission of the application, even if the application is being submitted on a rolling basis. The FDA has 60 days from its receipt of an NDA or BLA to determine whether the application will be accepted for filing based on the FDA's threshold determination that it is sufficiently complete to permit a substantive review.

If the FDA determines that the NDA or BLA is incomplete, the FDA may refuse to file the application. If the FDA refuses to file an NDA or BLA, the applicant may refile the application with information addressing the FDA identified deficiencies, which refiling would be subject to FDA review before it is accepted for filing. After the NDA or BLA submission is accepted for filing, the FDA reviews the NDA or BLA to determine, among other things, whether a product meets FDA's approval standard and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. Under the goals and policies agreed to by the FDA under the PDUFA, the FDA has set the review goal of completing its review of 90% of all standard applications for new molecular entities and original BLAs within ten months of the 60 day filing date. Under the FDA's priority review program, however, the FDA set a review goal of completing its review of 90% of all applications within 6 months of the 60 day filing date. The FDA does not always meet its PDUFA goal dates. The review process and the PDUFA goal date may be extended by additional three-month review periods whenever the FDA requests or the NDA or BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission at any time during the review cycle.

NDAs or BLAs or supplements to NDAs or BLAs for a new active ingredient, dosage form, dosage regimen, or route of administration, unless subject to the below requirement for molecularly targeted cancer products, must contain data to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of data or full or partial waivers. This requirement does not generally apply to products for an indication for which orphan designation has been granted.

However, compliance may be required if approval is sought for other indications for which the product has not received orphan designation.

Product candidates intended for the treatment of adult cancer which are directed at molecular targets that the FDA determines to be substantially relevant to the growth or progression of pediatric cancer, must submit, with the marketing application, reports from molecularly targeted pediatric cancer investigations designed to yield clinically meaningful pediatric study data, gathered using appropriate formulations for each applicable age group, to inform potential pediatric labeling. The FDA may, on its own initiative or at the request of the applicant, grant deferrals or waivers of some or all of this data, as above. Orphan products are not exempt from this requirement.

The FDA will typically inspect or conduct an inspection or remote regulatory assessment of one or more clinical sites to assure compliance with GCP before approving an NDA or BLA. The FDA also will inspect or conduct a remote regulatory assessment of the facility or the facilities at which the product is manufactured before the NDA or BLA is approved. The FDA will not approve the product unless cGMP compliance is satisfactory.

The FDA may refer applications for novel drug products or biologic products to an advisory committee for recommendation as to whether the application should be approved and under what conditions. Specifically, for a product candidate for which no active ingredient (including any ester or salt of active ingredients) has previously been approved by the FDA, the FDA must either refer that product candidate to an advisory committee or provide in an action letter, a summary of the reasons why the FDA did not refer the product candidate to an advisory committee. The FDA may also refer other product candidates to an advisory committee if FDA believes that the advisory committee's expertise would be beneficial. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully, particularly any negative recommendations or limitations, when making drug or biologic product approval decisions.

After evaluating the marketing application and all related information, including the advisory committee recommendation, if any, and inspection or remote regulatory assessment reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a CRL. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL indicates that the review cycle of the application is complete and the application is not ready for approval and describes all of the specific deficiencies that the FDA identified. A CRL generally contains a statement of specific conditions that must be met in order to secure final approval of the marketing application, and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. The deficiencies identified may be minor, for example, requiring labeling changes; or major, for example, requiring additional clinical trials. If a CRL is issued, the applicant may either: resubmit the marketing application, addressing all of the deficiencies identified in the letter; withdraw the application; or request an opportunity for a hearing. The FDA has the goal of reviewing 90% of application resubmissions in either two or six months of the resubmission date, depending on the kind of resubmission. Even with submission of additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

Additional regulation for gene therapy clinical trials

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving the use of gene therapy. The FDA has issued, and continues to issue, various guidance documents regarding the development and commercialization of gene therapies, which outline additional factors that the FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical and nonclinical assessment of gene therapies; the design and conduct of clinical trials, the CMC information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and long term patient and clinical study subject follow up and regulatory reporting. The FDA also issued guidance documents that address guidance specific to the development of gene therapy products for neurodegenerative diseases and with respect to the use of human and animal derived materials.

Post-approval requirements

After FDA approval of a product is obtained, we are required to comply with a number of post-approval requirements, including, among other things, establishment registration and product listing, record-keeping requirements, reporting certain adverse reactions and production problems to the FDA, providing updated safety and efficacy information, and complying with requirements concerning advertising and promotional labeling. As a condition of approval of an NDA or BLA, the FDA may require the applicant to conduct additional clinical trials or other post market testing and surveillance to further monitor and assess the product's safety and efficacy. There also are continuing annual program user fee requirements for approved products, though orphan products may receive exemptions if certain criteria are met.

The FDA also has the authority to require a specific REMS to ensure that a product's benefits outweigh its risks. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate healthcare providers of the product's risks, limitations on who may prescribe or dispense the product, or other measures that the FDA deems necessary to assure the safe use of the drug. The FDA may also impose a REMS requirement on an approved product if the FDA determines, based on new safety information, that a REMS is necessary to ensure that the product's benefits outweigh its risks.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Although physicians may prescribe a drug or biologic for off-label uses, manufacturers may only promote the product for the approved indications and in accordance with the approved labeling. All statements regarding products must be consistent with the FDA approved label, must be truthful and non-misleading, and must be adequately substantiated with a fair balance between product benefit claims and risks, among other requirements. This means, for example, that a manufacturer cannot make claims about the use of its marketed products or their relative benefits compared to other treatments outside of their FDA approved indications and label and without adequate comparative studies, and it would not be able to discuss or provide information on off-label uses or off-label safety benefits of such products in a promotional context. Over the last few years, the FDA has taken a number of actions in the advertising and promotional spaces, including issuing a final rule and a guidance on risk and efficacy disclosures in direct to consumer advertising, and a guidance on communication of off-label scientific information about approved products. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with the laws and regulations governing advertising and promotion can have negative consequences, including FDA and other governmental authority enforcement actions.

In addition, the distribution of prescription pharmaceutical product samples is subject to the Prescription Drug Marketing Act, or PDMA, in addition to state requirements. Reports must also be submitted to the FDA on sample distribution. The Drug Supply Chain Security Act, or DSCSA, added sections in the FDCA that require manufacturers, repackagers, wholesale distributors, dispensers, and third-party logistics providers to take steps to identify and trace certain prescription drugs and biologics to protect against the threats of counterfeit, diverted, stolen, contaminated, or otherwise harmful products in the supply chain. The DSCSA regulates the distribution of prescription pharmaceutical drugs and biologics, requiring passage of documentation to track and trace each prescription product at the saleable unit level through the distribution system. This documentation must be transferred electronically. The FDA is also phasing in requirements with respect to the interoperable exchange of electronic product tracing at the package level. Products subject to the DSCSA must only be transferred to appropriately licensed purchasers. The DSCSA also requires manufacturers and repackagers to affix or imprint a unique product identifier on product packages in both a human-readable and on a machine-readable data carrier. The DSCSA also establishes several requirements relating to the verification of product identifiers. Further, under this legislation, sponsors have product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products that would result in serious adverse health consequences or death to humans, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Also, quality control and manufacturing procedures must continue to conform to cGMPs after approval, including quality control and quality assurance and maintenance of records and documentation. Changes to the manufacturing process are strictly regulated and often require prior FDA approval or notification before being implemented. The FDA has issued a guidance specifically on demonstrating product comparability, and the management and reporting of manufacturing changes for investigational and licensed cellular and gene therapy products. FDA regulations also require investigation

and correction of any deviations from cGMP and specifications, and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use.

Manufacturers and others involved in the manufacture and distribution of such products also must register their establishments with the FDA and certain state agencies, and provide information regarding the products that they manufacture. The information that must be submitted to the FDA regarding manufactured products was expanded through the Coronavirus Aid, Relief, and Economic Security, or CARES, Act to include the volume of drugs produced during the prior year.

Establishments may be subject to periodic, unannounced inspections or remote regulatory assessments by government authorities to ensure compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. The FDA may take into account results of inspections performed by certain counterpart ex-U.S. regulatory agencies in assessing compliance cGMPs. The FDA has entered into international agreements with ex-U.S. agencies, including in the EU, in order to facilitate this type of information sharing.

Sponsors are further subject to various requirements related to FDA drug shortage and manufacturing volume reporting, supply chain security, such as risk management plan requirements, and the promotion of supply chain redundancy. Legislation and executive actions have also been issued to encourage domestic manufacturing.

Additional controls for biologics

To help reduce the risk of the introduction of adventitious agents or of causing other adverse events with the use of biologic products, the PHSA emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the United States and between states.

After a BLA is approved, the product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

Other regulatory agencies may also regulate our use of biological materials, which may necessitate that we, our manufacturers, or other third parties with whom we work obtain permits and otherwise comply with regulatory requirements.

Orphan drug designation.

We have received orphan drug designation from the FDA for Translarna for the treatment of nmDMD, Emflaza for the treatment of DMD, Kebilidi for the treatment of AADC deficiency, Evrysdi for the treatment of SMA, vatiquinone for the treatment of FA, sepiapterin for the treatment of hyperphenylalaninemia, including hyperphenylalaninemia caused by PKU, and PTC518 for the treatment of HD. The FDA may grant orphan drug designation to drugs and biologics intended to treat a "rare disease or condition," which is defined as a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a product for this type of disease or condition will be recovered from sales in the United States for that product. Additionally, sponsors must present a plausible hypothesis for clinical superiority to obtain orphan designation if there is a product already approved by the FDA that that is considered by the FDA to be the same as the already approved product and is intended for the same indication. This hypothesis must be demonstrated to obtain orphan exclusivity. Orphan drug designation must be requested before submitting an application

for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Orphan drug designation can provide opportunities for grant funding towards clinical trial costs, tax advantages and FDA user-fee benefits.

The FDA's regulations provide flexibility in meeting approval standards for new therapies intended to treat persons with life-threatening and severely-debilitating illnesses, especially where no satisfactory alternative therapy exists, such that the FDA may exercise scientific judgment in determining the kind and quantity of data required for approval and during development programs. Per guidance issued by the FDA with respect to rare diseases, "[t]his flexibility extends from the early stages of development to the design of adequate and well-controlled clinical investigations required to demonstrate effectiveness to support marketing approval and to establish safety data needed for the intended use." The FDA states that it "is committed to helping sponsors create successful drug development programs that address the particular challenges posed by each disease…."

If a product which has an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug or biologic for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or the same drug or biologic for different indications. However, competitors may receive approval of different drugs or biologics for the indications for which the orphan product has exclusivity.

Notably, the exact scope of orphan drug exclusivity may be an evolving space. A 2021 judicial decision, Catalyst Pharms., Inc. v. Becerra, challenged and reversed an FDA decision on the scope of orphan product exclusivity for the drug, Firdapse. Under this decision, orphan drug exclusivity for Firdapse blocked approval of another company's application for the same drug for the entire disease or condition for which orphan drug designation was granted, not just the disease or condition for which approval was received. In a January 2023 Federal Register notice, however, the FDA stated that it intends to continue to apply its regulations tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved. The exact scope of orphan drug exclusivity will likely be an evolving area.

Orphan product sameness decisions are also an evolving space. The FDA issued a final guidance document on how the agency will determine the "sameness" of gene therapy products. Pursuant to the guidance, "sameness" will depend on the products' transgene expression, viral vectors groups and variants, and other product features that may have a therapeutic effect. Generally, minor differences between gene therapy products will not result in a finding that two products are different. Any FDA sameness determinations could impact our ability to receive approval for our product candidates and to obtain or retain orphan drug exclusivity.

Rare Pediatric Disease Voucher Program

Under the FDCA, the FDA awards priority review vouchers to sponsors of rare pediatric disease products that meet certain criteria. To qualify, the rare disease must be serious or life-threatening in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years. Also, the product must contain no active ingredient (including any ester or salt of the active ingredient) that has been previously approved in any other application and the application must meet certain additional qualifying criteria, including eligibility for FDA priority review. If FDA determines that a product is for a rare pediatric disease and the qualifying application criteria are met, upon a sponsor's request, the FDA may award the sponsor a priority review voucher. This voucher may be redeemed to receive priority review (i.e., a review time of 6 months as compared to 10 months for standard review) of a subsequent marketing application for a different product. Use of a priority review voucher is subject to an FDA user fee. These vouchers are transferable. Accordingly, sponsors may sell these vouchers for substantial sums of money. Vouchers may also be revoked by the FDA under certain circumstances and sponsors of approved rare pediatric disease products must submit certain reports to the FDA.

The FDA's ability to issue pediatric priority review vouchers may, however, be limited, as the program lapsed in December 2024 and has not yet been reauthorized by Congress. Under the law's sunset provision, the drug or biologic was required to be designated by the FDA for a rare pediatric disease no later than December 20, 2024, and approved no later than September 30, 2026. While, as of December 2024, the FDA continued to grant rare pediatric disease designations, unless

there is further Congressional action, the FDA will not be able to award priority review vouchers to products that received a designation after December 20, 2024. We may not be able to obtain rare pediatric disease designation for products in the future and may also not be able to qualify for priority review vouchers.

Hatch-Waxman Act for Drugs.

Section 505 of the FDCA describes three types of drug marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained the right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application, or ANDA. An ANDA provides for marketing of a generic drug product that generally has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product, called the reference listed drug. Certain differences, however, between the reference listed drug and ANDA product may be permitted pursuant to a suitability petition. Certain labeling differences may also be permitted if information in the reference listed drug's label is protected by patent or exclusivities. ANDAs are termed "abbreviated" because they are generally not required to include nonclinical and clinical data to establish safety and efficacy. Instead, generic applications must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo, or other testing. The generic version must deliver the same amount of active ingredients to the site of action in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug. In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's drug or a method of using the drug. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's list of Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an ANDA or 505(b)(2) NDA. In an effort to clarify which patents must be listed in the Orange Book, in January 2021, Congress passed the Orange Book Transparency Act of 2020, which largely codifies FDA's existing practices into the FDCA. Listing patents in the Orange Book that do not qualify for listing can be considered to be anticompetitive conduct and, in 2023, the Federal Trade Commission sent letters to a number of companies with respect to certain patents that the agency asserted were improperly listed or inaccurate and improper listings have been the subject of recent court cases.

Upon submission of an ANDA or 505(b)(2) NDA, an applicant must certify to the FDA that (1) no patent information has been submitted to the FDA; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed upon by the manufacturer, use or sale of the drug product for which the application is submitted. The applicant may also elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. Generally, the ANDA or 505(b)(2) NDA approval cannot be made effective until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification, also known as a paragraph IV certification.

If the ANDA or 505(b)(2) NDA applicant has provided a paragraph IV certification to the FDA, the applicant must send notice of the certification to the NDA and patent holders. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification, in which case the FDA may not make an approval effective until the earlier of 30 months from the patent or application owner's receipt of the notice of the paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent is favorably decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30 month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owner(s) regularly take action to trigger the 30 month stay. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation.

Exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the therapeutic activity of the drug substance. During the exclusivity period, the FDA generally may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company that contains the new chemical entity. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

The FDCA also provides a shorter three-year period of exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. Three-year exclusivity may be granted for example, for new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

BPCIA Exclusivity

The 2010 Patient Protection and Affordable Care Act included the BPCIA as a subtitle. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. The FDA has issued a number of guidance documents outlining an approach to review and approval of biosimilars, including guidance documents on the demonstration of interchangeability and the licensure of biosimilar and interchangeable products for fewer than all of the reference product's licensed conditions of use.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there is a high degree of similarity to the reference product, notwithstanding minor differences in clinically inactive components, and that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity and potency. Biosimilarity must be shown through analytical studies, animal studies, and at least one clinical trial, absent a waiver by the FDA. There must be no difference between the reference product and a biosimilar in mechanism of action, conditions of use, route of administration, dosage form, and strength. For the FDA to approve a biosimilar product as interchangeable with a reference product, the FDA must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. However, certain changes and supplements to an approved BLA, and subsequent applications filed by the same sponsor, manufacturer, licensor, predecessor in interest, or other related entity do not qualify for the 12 year exclusivity period. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own nonclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products.

The BPCIA also includes provisions to protect reference products that have patent protection. The biosimilar product sponsor and reference product sponsor may exchange certain patent and product information for the purpose of determining whether there should be a legal patent challenge. Based on the outcome of negotiations surrounding the exchanged information, the reference product sponsor may bring a patent infringement suit and injunction proceedings

against the biosimilar product sponsor. The biosimilar applicant may also be able to bring an action for declaratory judgment concerning the patent.

The FDA maintains a publicly available online database of licensed biological products, which is commonly referred to as the "Purple Book." The Purple Book lists product names, dates of licensure, and applicable periods of exclusivity. Further, the reference product sponsor must provide patent information and patent expiry dates to the FDA following the exchange of patent information between biosimilar and reference product sponsors. This information is then published in the Purple Book.

In an effort to increase competition in the drug and biologic product marketplace, Congress, the executive branch, and the FDA have taken certain legislative and regulatory steps. For example, measures have been proposed and implemented to facilitate product importation. Moreover, the 2020 Further Consolidated Appropriations Act included provisions requiring that sponsors of approved drug and biologic products, including those subject to REMS, provide samples of the approved products to persons developing 505(b)(2) NDA or ANDA drug products, or biosimilar products within specified timeframes, in sufficient quantities, and on commercially reasonable market-based terms. Failure to do so can subject the approved product sponsor to civil actions, penalties, and responsibility for attorney's fees and costs of the civil action. This same bill also includes provisions with respect to shared and separate REMS programs for reference and generic drug products.

Patent Term Restoration

If approved, drug and biologic products may also be eligible for periods of U.S. patent term restoration if an application is timely filed with the Patent and Trademark Office. If granted, patent term restoration extends the patent life of a single unexpired patent, that has not previously been extended, for a maximum of five years, and only those claims reading on the approved drug may be extended. The total patent life of the product with the extension also cannot exceed fourteen years from the product's approval date. Subject to the prior limitations, the period of the extension is calculated by adding half of the time from the effective date of an IND to the initial submission of a complete marketing application, and all the time between the submission of the marketing application and its approval. This period may also be reduced by any time that the applicant did not act with due diligence.

Pediatric exclusivity

Pediatric exclusivity is another type of non-patent market exclusivity in the United States and, if granted, provides for the attachment of an additional six months of market protection to the term of any existing Orange Book- listed patents or regulatory exclusivity, including the non-patent exclusivity periods described above. This six-month exclusivity may be granted based on the voluntary completion of a pediatric study or studies in accordance with an FDA-issued "Written Request" for such a study or studies within a specified timeframe prior to the expiration of the underlying patent or market exclusivity period to be extended.

Regulation outside the United States

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of ex-U.S. countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. And, even if regulatory approval is granted, it may be withdrawn or limited under certain circumstances or post-approval requirements may be imposed by the applicable regulatory authority. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Regulation in the European Union

We have obtained an orphan medicinal product designation from the EC, following an evaluation by the EMA's Committee for Orphan Medicinal Products, for Translarna for the treatment of nmDMD, Upstaza for the treatment of AADC deficiency, Evrysdi for the treatment of SMA, vatiquinone for the treatment of FA, sepiapterin for the treatment of patients with hyperphenylalaninemia, including hyperphenylalaninemia caused by PKU and PTC518 for the treatment of HD. The EC can grant orphan medicinal product designation to products for which the sponsor can establish that it is intended for the diagnosis, prevention, or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the EU, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that sales of the drug in the EU would generate a sufficient return to justify the necessary investment. In addition, the sponsor must establish that there is no other satisfactory method approved in the EU of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation is not a marketing authorization. It is a designation that provides a number of benefits, including fee reductions, regulatory assistance, and, in the event of a successful application for a centralized EU marketing authorization, 10 years of EU market exclusivity. During this market exclusivity period, neither the EMA, nor the EC nor any EU member states can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, a competing similar medicinal product may in limited circumstances be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to our product. Our product candidates can lose orphan designation, and the related benefits, prior to us obtaining a marketing authorization if it is demonstrated that the orphan designation criteria are no longer met.

The EC has conducted a review of the Orphan Drug Regulation together with the Paediatric Regulation. The outcome of this review is intended to guide future legislative changes and shape the EU's pharmaceutical strategy.

Clinical Trial Developments. The structure and general regulation of clinical trials for both small molecule and biological medicines in the EU is similar to that in the United States. Separately, a new regulation, (EU) No.536/2014, regarding clinical trials of medicinal products for humans is included in the European regulatory framework and fills a series of regulatory gaps in the clinical trials regime through the creation of a uniform framework for the authorization of clinical trials by all interested EU member states with a single assessment of the results. The regulation (which came into effect on January 31, 2022) is thus intended to facilitate cross-border cooperation through streamlining of the rules on clinical trials across the EU, including by requiring the submission of clinical trial authorization applications via a new electronic EU portal.

Alongside the portal, a database has been created containing information on clinical trial data. The information on the database is publicly accessible unless the trial data's confidentiality can be justified on the basis of protection of commercially confidential information, protection of personal data, protection of confidential communication between EU countries, or ensuring effective supervision of the conduct of clinical trials by EU countries. A sponsor of a trial conducted in the EU under the new regulation is required to submit a summary of the clinical trial results to the EU database within a year of the end of the trial. In addition, where the trial was intended to be used for obtaining a marketing authorization (whether through the centralized procedure or via the national authorities), the applicant must submit the clinical study report within 30 days after the marketing authorization has been granted (or refused or withdrawn).

Overview of application process. To obtain regulatory approval of a drug under the EU's regulatory systems and authorization procedures, an applicant may submit marketing authorization applications under a centralized, decentralized, or national procedure. The centralized procedure is compulsory for certain medicinal products, including orphan medicinal products, like Translarna for the treatment of nmDMD, and medicinal products produced by certain biotechnological processes, and optional for certain other innovative products. The centralized procedure enables applicants to obtain a marketing authorization that is valid in all EU member states based on a single application. Under the centralized procedure, the EMA's Committee for Human Medicinal Products, or CHMP, is required to adopt an opinion on a valid

application within 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions.

More specifically, on day 120 of the procedure, once the CHMP has received the preliminary assessment reports and opinions from the rapporteur and co-rapporteur, it prepares a list of potential outstanding issues, referred to as "other concerns" or "major objections". These are sent to the applicant together with CHMP's recommendation. In addition, in relation to advanced therapy medicinal products, or ATMPs, which are medicines based on genes, cells or tissues, the Committee for Advanced Therapies, or CAT, EMA's committee responsible for assessing the quality, safety and efficacy of ATMPs, prepares a draft opinion on the ATMP application that is submitted to EMA before the CHMP adopts a final opinion on the marketing authorization of the applicable medicine. The CHMP can make one of two recommendations: (1) the marketing authorization could be granted provided that satisfactory answers are given to the "other concerns" and/or "major objections" identified and that all conditions outlined in the list of outstanding issues are implemented and complied with; or (2) the product is not approvable since there are "major objections".

Applicants have three months from the date of receiving the potential outstanding issues to respond to the CHMP, and can request a three-month extension if necessary. The granting of a marketing authorization will depend on the recommendations and potential major objections identified by the CHMP as well as the ability of the applicant to adequately respond to these findings. An accelerated assessment can be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days. After the adoption of the CHMP opinion, a decision on the marketing authorization application must be adopted by the EC, after consulting the EU member states, which in total can take more than 60 days.

An applicant for a marketing authorization application may request a re-examination in the event of a negative opinion, in connection with which CHMP appoints new rapporteurs. Within 60 days of receipt of the negative opinion, the applicant must submit a document explaining the basis for its request for re-examination. The CHMP has 60 days to consider the applicant's request for re-examination. The applicant may request an oral explanation before the CHMP, which is routinely granted, following which CHMP will adopt a final opinion. The final opinion, whether positive or negative, is published by the CHMP shortly following the CHMP meeting at which the oral explanation takes place. The EMA publishes a European Public Assessment Report, or EPAR, for every medicine granted a central marketing authorization by the EC following an assessment by the CHMP. EPARs are full scientific assessment reports of medicines authorized by the EMA.

Conditional marketing authorizations. In specific circumstances, as with Translarna for the treatment of nmDMD, EU legislation enables applicants to obtain a marketing authorization on a conditional basis prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for products designated as orphan medicinal products, if (1) the benefit-risk balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs, and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the benefit-risk balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization. The granting of a conditional marketing authorization will depend on the applicant's ability to fulfill the conditions imposed within the agreed upon deadline.

For important information about matters that may adversely affect our ability to renew our conditional marketing authorization for Translarna, see "Item 1A. Risk Factors-Risks Related to the Development and Commercialization of our Products and our Product Candidates."

Variations to conditional marketing authorizations. After the granting of a conditional marketing authorization, the marketing authorization holder may submit an application to vary the conditional marketing authorization under a variation

procedure. In the case of the introduction of an additional therapeutic indication, the timeframe for the variation procedure for the initial assessment of the dossier is generally 90 days (plus up to 20 days for validation).

However, in the framework of a variation application assessment procedure, the EMA may send one or more requests for supplementary information to the marketing authorization holder, requiring that additional information be provided by the marketing authorization holder to support its variation application. Such supplementary requests will be sent together with a timetable stating the date by when the marketing authorization holder must submit the requested data and, where appropriate, the extended evaluation period to be applied to such variation procedure. The 90-day variation procedure may be suspended for up to three months for the marketing authorization holder to submit its responses to such supplementary requests. The marketing authorization holder will be notified of the outcome of the CHMP's assessment of the variation procedure within 15 days from the adoption of the CHMP opinion. If unfavorable, the CHMP opinion may be subject to a re-examination procedure upon the marketing authorization holder's request. This may imply an additional minimum two-month procedure. If the CHMP opinion is favorable, the EC will usually vary the marketing authorization to introduce the additional therapeutic indication within approximately two months from the receipt of the final CHMP opinion.

Exceptional Circumstances. Similarly, certain of our product candidates may be eligible for a marketing authorization under exceptional circumstances. Such an authorization may be granted where the applicant can demonstrate in its application that it is unable to provide comprehensive data on efficacy and safety under normal conditions of use, because: 1) the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence; 2) in the present state of scientific knowledge, comprehensive information cannot be provided; or 3) it would be contrary to generally accepted principles of medical ethics to collect such information. Authorizations under exceptional circumstances are annually reassessed and granted subject to a requirement for the applicant to implement certain procedures, in particular, competent authority notification in the event of any safety issue. After 5 years, the authorization is renewed under exceptional circumstances for an unlimited period, unless the EMA decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. A marketing authorization under exceptional circumstances will not be granted when a conditional marketing authorization is more appropriate. Orphan products are further eligible for approval under exceptional circumstances only if the criteria considered for the approval under exceptional circumstances are fulfilled.

Additional requirements and considerations. Prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver, or (3) a deferral for one or more of the measures included in the PIP. In the case of orphan medicinal products, completion of an approved PIP can result in an extension of the aforementioned market exclusivity period from ten to twelve years.

In the EU there is also a procedure which allows member states to authorize the distribution of an unauthorized medicinal product in response to the spread of pathogens. The UK (but no EU countries) used this procedure with two COVID-19 vaccines during December 2020. Notwithstanding the UK's subsequent full departure from the EU, the EU provision is mirrored in UK medicines legislation.

In the EU, for a period of eight years from the grant of a marketing authorization of an innovative product (the "reference medicinal product"), competent authorities may not accept marketing authorization applications from applicants seeking to market "generic medicinal products" where such applications rely on the data in the marketing authorization dossier of the reference product. Moreover, generic medicinal products that rely on the independently generated data of the reference product may not be placed on the market for 10 years from the granting of the initial marketing authorization for that reference medicinal product. This is extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications considered to offer a significant clinical benefit in comparison with existing therapies. These periods of data exclusivity do not prevent other companies from obtaining a marketing authorization based on their own independently generated data. The data exclusivity regime is currently under review. The EC intends to strike a balance between providing incentives for innovation and supporting timely patient access to medicinal products across the EU. To do so, the EC has published a proposal for a revised Directive on the Union Code Relating to Medicinal Products for Human Use, which proposes replacing the regulatory data protection system with a new regime that will offer innovators variable durations of data exclusivity. Under the new rules, if implemented, new medicinal products will have a minimum period of regulatory protection of eight years,

which includes six years of regulatory data protection and two years of market protection. Such products may benefit from additional periods of regulatory data protection if they satisfy certain criteria, which may increase the total period of regulatory protection up to a maximum of 12 years (as compared to the current maximum of 11 years).

If a marketing authorization is granted in the EEA for a medicinal product, such as the marketing authorization granted for Translarna for the treatment of nmDMD by the EC, the marketing authorization holder is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal products that are in addition to the other conditions of the marketing authorization described above. The marketing authorization holder must, for example, comply with the EU's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. Other requirements relate to, for example, the manufacturing of products and active pharmaceutical ingredients in accordance with good manufacturing practice standards. Competent authorities of EU member states may conduct inspections to verify compliance with applicable requirements, and the marketing authorization holder will have to continue to expend time, money and effort to remain compliant. Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties in the EU Similarly, failure to comply with the EU's requirements regarding the protection of individual personal data can also lead to significant penalties and sanctions. Individual EU member states may also impose various sanctions and penalties in case we do not comply with locally applicable requirements. The CAT is involved in any procedure regarding the provision of advice on the conduct of efficacy follow-up, pharmacovigilance and risk management systems of ATMPs as provided for in ATMP legislation.

Off-label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU member states also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict our promotional activities with healthcare professionals. In addition, legislation adopted at the EU level and by individual EU member states require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. Promotion of indications not covered by the SmPC is specifically prohibited. ATMP legislation lays down certain minor extra labelling requirements for ATMPs.

The EMA is responsible for coordinating inspections to verify compliance with the principles of GCP, good manufacturing practice, or GMP, GLP, and good pharmacovigilance practice. These inspections are also intended to verify compliance with other aspects of the supervision of authorized medicinal products in use in the EU. The EMA coordinates any inspection by the relevant member state regulatory authority as requested by the CHMP in connection with the assessment of marketing authorization applications or matters referred to these committees. Inspections may be routine or triggered by issues arising during the assessment of the dossier or by other information, such as previous inspection experience. Inspections usually are requested during the initial review of a marketing authorization application, but could arise post-authorization.

Inspectors are drawn from the regulatory authorities of member states of the EU and the EEA. Following an inspection, the inspectors provide a written inspection report to the inspected site or applicant and provide an opportunity for response. Some inspection reports require follow-up and may result in additional adverse consequences due to critical or major findings. The inspectors and the CHMP will comment on any response from an inspected site or applicant and may monitor future compliance with any proposed corrective action plan.

In the GCP area, inspectors grade their findings according to the following scale:

- Critical: Conditions, practices or processes that adversely affect the rights, safety or well-being of the subjects or the quality and integrity of data. Observations classified as critical may include a pattern of deviations classified as major.
- Major: Conditions, practices or processes that might adversely affect the rights, safety or well-being of the subjects and/or the quality and integrity of data. Observations classified as major may include a pattern of deviations or numerous minor observations.

- Minor: Conditions, practices or processes that would not be expected to adversely affect the rights, safety or wellbeing of the subjects or the quality and integrity of data. Minor observations indicate the need for improvement of conditions, practices and processes.
- Comments: Suggestions on how to improve quality or reduce the potential for a deviation to occur in the future.

Possible consequences of critical and major findings include rejection of clinical trial data, causing significant delays in obtaining final marketing authorization, or other direct action by national regulatory authorities.

Falsified Medicines Directive – As of February 2019, new legislation required manufacturers of marketed prescription medicines to place safety features on all medicines and contribute financially to the establishment of a verification system allowing the authenticity of a medicine to be assessed at the time of supply to the patient. Under the legislation, all packages of prescription medicines placed on the market in Europe have to bear two safety features: a unique identifier in the form of a two-dimensional data matrix (barcode) and an anti-tamper device. In addition, ATMP legislation requires a procedure for tracing the product and its starting and raw materials from its source to the site where the product is used.

Early access programs

Many jurisdictions allow the supply of unauthorized medicinal products in the context of strictly regulated and exceptional EAP programs, and some countries may provide reimbursement for drugs provided in the context of such programs. In the EU, the legal basis for EAP programs, also referred to as named-patient and compassionate use programs, is set out in the EU legislation regulating the authorization, manufacture, distribution and marketing of medicinal products. Detailed regulatory requirements applicable to EAP programs have been adopted and implemented by EU member states in their national laws. The promotion, advertising and marketing of unauthorized medicinal products is generally prohibited, and authorization for EAP programs must generally be obtained from national competent authorities, which might not grant such authorization. Obtaining authorization for an EAP program in one country does not ensure that authorization will be obtained in another country.

U.S. law permits "expanded access" (also known as compassionate use and treatment use) for certain patients with serious diseases who have no comparable alternative treatment options. The potential patient benefit must justify the potential risks of the treatment use and those potential risks must not be unreasonable in the context of the disease or condition to be treated. Moreover, providing the investigational drug or biologic for the requested use must not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use. Additional requirements apply depending on the size of the expanded access population. To provide expanded access, sponsors, including individual physicians, must submit detailed regulatory information to the FDA and receive the agency's approval for the use. However, if there is an emergency that requires that a patient be treated before a written submission can be made, the FDA may authorize the expanded access use by telephone. In such a case, a written expanded access submission must be submitted to the FDA within fifteen working days of the FDA's authorization. Following approval for expanded access use, both the sponsor of the use and the investigator (i.e., physician) must comply with certain FDA requirements. Sponsors may not promote products as safe or effective for expanded-access uses.

Pharmaceutical Pricing and Reimbursement

The containment of healthcare costs has become a priority of federal, state and ex-U.S. governments, and the prices of pharmaceuticals have been a focus of this effort. Ex-U.S. governments, the U.S. government, and state legislatures have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls (e.g., inflation penalties and price caps), increases in rebates paid, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs.

In some countries, particularly the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing and reimbursement negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product and there is only limited EU-level control over the decision-making autonomy of the government authorities including in relation to timing, justification and the ability to challenge such decisions. In addition, there can be considerable pressure by governments and other stakeholders on prices

and reimbursement levels, including as part of cost containment measures. In some countries, governments can set conditions that must be satisfied for prices to be set at a certain value. Political, economic and regulatory developments may further complicate pricing and reimbursement negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel distribution (arbitrage between low-priced and high- priced member states), can further reduce prices. In some countries we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product or product candidate to other available therapies in order to obtain reimbursement or pricing approval.

In the United States, federal price reporting laws require manufacturers to calculate and report complex pricing metrics (e.g., average manufacturer price, Best Price, and average sales price) used to determine prescription rebates paid under the Medicaid Drug Rebate Program and amounts reimbursed pharmacies and other providers by the Medicaid and Medicare programs. Various state healthcare programs similarly obligate us to report drug pricing information that is used as the basis for their reimbursement of pharmacies and other healthcare providers and the negotiation of supplemental rebates. Payment for a manufacturer's drugs by these programs is conditioned on submission of this pricing information. Some government healthcare programs impose penalties if drug price increases exceed specified percentages or inflation rates, and these penalties can result in mandatory penny prices for certain federal and 340B program customers. States, such as California, have also enacted transparency laws that require manufacturers to report price increases and related information, and may cap price increases, or require negotiation of supplemental rebates for new drugs entering the market at price points determined to be high. Refusal to negotiate supplemental rebates can negatively affect market access and provider reimbursement. States, such as Maryland, have also established Drug Affordability Review Boards for the purpose of establishing upper payment limits for certain high-cost drugs which, if implemented, could result in reduced reimbursement for those products. Failure to comply with the rules for calculating and submitting pricing information or otherwise overcharging the government or its beneficiaries may result in criminal, civil, or administrative sanctions or enforcement actions, and expose us to federal civil False Claims Act, or the False Claims Act, liability.

The Veterans Health Care Act of 1992 requires, as a condition of payment by certain federal agencies and the Medicaid program, that manufacturers of "covered drugs" (including all drugs approved under an NDA) enter into a Master Agreement and Federal Supply Schedule (FSS) contract with the Department of Veterans Affairs through which their covered drugs must be offered for sale at a mandatory calculated ceiling price to certain federal agencies, including the VA and Department of Defense. FSS contracts require compliance with applicable federal procurement laws and regulations, including disclosure of commercial prices during contract negotiations and maintenance of price relationships during the term of the contract, and subject manufacturers to contractual remedies as well as administrative, civil, and criminal sanctions. The Veterans Health Care Act also requires manufacturers to enter into pricing agreements with the Department of Health and Human Services to charge no more than a different ceiling price (derived from the Medicaid rebate percentage) to covered entities participating in the 340B drug discount program. Failure to accurately report drug pricing or to provide the mandatory discount may subject the manufacturer to specific civil monetary penalties. Termination of either of these agreements also jeopardizes payment by Medicaid and Medicare for the manufacturer's drugs in an outpatient setting. Certain states have also enacted drug price transparency laws that require reporting of pricing information, including certain increases in a drug's wholesale acquisition cost and the reasons causing the price increase.

Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. For example, in the United States, healthcare reform measures under the Affordable Care Act, contain provisions that may affect the profitability of drug products. However, since its passage, Congress has repealed and amended certain provisions of the Affordable Care Act, repeal efforts may occur again, and legal challenges to the Affordable Care Act may contribute to the uncertainty of the ongoing implementation and impact of the Affordable Care Act and underscore the potential for additional reform going forward. Certain provisions of enacted or proposed legislative changes may negatively impact coverage and reimbursement of, or rebates paid by manufacturers for, healthcare items and services. We cannot assure that the Affordable Care Act, as currently enacted or as amended in the future, will not adversely affect our business and financial results and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

Legislators and regulators at both the federal and state level are increasingly focused on containing the cost of drugs, and there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been recent U.S. Congressional inquiries and proposed bills designed to, among other

things, bring more transparency to drug pricing, penalize companies that do not agree to cap prices paid for certain drugs, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, in 2016, the Centers for Medicare and Medicaid Services, or CMS, issued a final rule regarding the Medicaid Drug Rebate Program (MDRP), which among other things, revises the manner in which the "average manufacturer price" or AMP is to be calculated by manufacturers participating in the program and implements certain amendments to the Medicaid rebate statute created under the Affordable Care Act, or ACA. More recently, Congress amended the Medicaid statute, effective October 1, 2019, to exclude prices paid by secondary manufacturers for an authorized generic drug (but not a product approved under the BLA process) from the NDA holder's AMP for the brand, thereby increasing the rebate amount and the 340B price for the brand. This was implemented by CMS in a final rule issued December 31, 2020. The rule also expanded the definition of products identified as "line extensions" and, in certain circumstances, required inclusion of patient copay assistance in Medicaid best price (effective January 1, 2023), thereby potentially increasing Medicaid rebates paid by manufacturers for such drugs. 340B program guidance regulations on civil monetary penalties for statutory violations, which had been finalized in early 2017 but deferred, also recently went into effect.

On November 27, 2020, CMS issued an interim final rule implementing a Most Favored Nation payment model under which reimbursement for certain Medicare Part B drugs and biologicals will be based on a price that reflects the lowest per capita Gross Domestic Product-adjusted (GDP-adjusted) price of any non-U.S. member country of the Organization for Economic Co-operation and Development (OECD) with a GDP per capita that is at least sixty percent of the U.S. GDP per capita. This rule now has been rescinded, but other efforts to address the costs of pharmaceuticals have been adopted, including the Inflation Reduction Act of 2022, or the IRA. The Inflation Reduction Act of 2022 requires manufacturers of selected drugs to negotiate discounted prices with the Secretary of the Department of Health and Human Services. Failure to reach an agreement can subject manufacturers to an excise tax or withdraw of all drug products from coverage under Medicare and Medicaid. Drug price negotiations and other program implementation measures could potentially be affected by the Executive Order, *Initial Rescissions of Harmful Executive Orders and Actions,* issued on January 20, 2025 and/or the anticipated change in leadership at Health and Human Services (HHS) and the Centers for Medicare and Medicaid Services (CMS) under the new administration. These and any additional healthcare reform measures could further constrain our business or limit the amounts that federal and state governments will pay for healthcare products and services, which could result in additional pricing pressures.

Any regulatory approval of a product is limited to specific diseases and indications for which such product has been deemed safe and effective by the FDA. Coverage by federal healthcare programs, however, may be more limited than the indications for which a drug is approved by the FDA or comparable ex-U.S. regulatory authorities' coverage of the same products. Sales of any products for which we may receive regulatory approval for commercial sale will depend in part on the extent to which the costs of the products will be covered and reimbursed by third-party payors, including government healthcare programs (such as, in the United States, Medicare and Medicaid), private health insurers and other organizations. Obtaining reimbursement for orphan drugs may be particularly difficult because of the significant research and development challenges and costs and resulting pricing considerations typically associated with drugs developed to treat conditions that affect a small population of patients. Certain drugs with an orphan designation may also become subject to price negotiations under the IRA. In addition, third-party payors are likely to impose strict requirements for reimbursement in connection with drugs that are perceived as having high costs. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors.

The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third- party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. Third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our product or product candidates or conduct direct head-to-head studies to demonstrate clinical superiority and cost-effectiveness. Our products and product candidates may not be considered clinically superior and cost-effective to competitor products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and other third-party payors fail to provide adequate coverage and reimbursement.

Freedom of Information Requests and Affirmative Disclosures

We are also subject, in the U.S. and many other countries, to various regulatory schemes that require disclosure of clinical trial data or allow access to our data via freedom of information requests. We have been and may, from time to time, be notified by regulators, such as the EMA or the competent authorities of EU member states that they have received a freedom of information request for documents that they hold relating to our company, including information related to our product or our product candidates. For example, in 2015, we were notified by the EMA that it had received from another pharmaceutical company a request under Regulation (EC) No 1049/2001 seeking access to aspects of our marketing authorization application for Translarna for the treatment of nmDMD. Following the decision of the EMA to release such documentation with only minimal redactions we initiated litigation before the General Court of the EU to prevent disclosure of this information. In the first quarter of 2018, the Court ruled in favor of the EMA, allowing the EMA to release the documentation. We appealed the General Court's decision to the Court of Justice of the EU, or CJEU, but the CJEU dismissed our appeal in January 2020 and released the information to the requester. In addition, under policies recently adopted in the EU, clinical trial data submitted to the EMA in MAAs that were traditionally regarded as confidential commercial information is now subject to automatic public disclosure. Further, under the Clinical Trials Regulation 536/2014, the sponsor of an EU trial must submit a summary of the results to an EU database within a year of the end of the trial. In addition, where the trial was intended to be used for obtaining a marketing authorization the applicant must submit the clinical study report 30 days after MA has been granted, refused or withdrawn. Subject to our limited ability to review and redact a narrow sub-set of confidential commercial information, these new EU policies will result in the EMA's public disclosure of certain of our clinical study reports, clinical trial data summaries and clinical overviews for recently completed and future MAA submissions. The move toward public disclosure of development data could adversely affect our business in many ways, including, for example, resulting in the disclosure of our confidential methodologies for development of our products, preventing us from obtaining intellectual property right protection for innovations, requiring us to allocate significant resources to prevent other companies from violating our intellectual property rights, adding even more complexity to processing health data from clinical trials consistent with applicable privacy and data protection regulations, and enabling competitors to use our data to gain approvals for their own products.

Fraud and Abuse Laws

Any present or future arrangements or interactions with third-party payors, healthcare professionals, healthcare organizations, patients and other customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may restrict certain marketing and contracting practices. These laws include, and are not limited to, anti-kickback and false claims statutes and civil monetary penalties.

Both the federal Foreign Corrupt Practices Act, or FCPA, and the UK Bribery Act of 2010, or Bribery Act are broad in scope and will require companies to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls. The FCPA prohibits the offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official, political party or candidate for public office in order to improperly influence any act or decision, secure any other improper advantage, or obtain or retain business. The FCPA also prohibits any U.S. person from corruptly acting outside the U.S. in furtherance of such offer, promise or payment. Under the UK Bribery Act, companies which carry on a business or part of a business in the United Kingdom may be held liable for bribes given, offered or promised to any person, including non-UK government officials and private persons, by employees and persons associated with the company in order to obtain or retain business or a business advantage for the company. Similar statutes have been adopted, or may be adopted in the future, by other countries in which we operate and with which we are or may be required to comply.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, in cash or kind, to induce or reward either the referral of an individual for, or the purchase, or order or recommendation of, any good or service, for which payment may be made in whole or in part under federal and state healthcare programs such as Medicare and Medicaid. This statute imposes criminal penalties and has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others. Although a number of statutory exemptions and regulatory safe harbors exist to protect certain common activities from prosecution, the exemptions and safe harbors for this statute are narrow, and practices that involve

compensation intended to induce prescriptions, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. HHS recently promulgated a regulation that is effective in two phases. First, the regulation excludes from the definition of "remuneration" limited categories of (a) PBM rebates or other reductions in price to a plan sponsor under Medicare Part D or a Medicaid Managed Care Organization plan reflected in point-of sale reductions in price and (b) PBM service fees. Second, the regulation expressly provides that rebates to plan sponsors under Medicare Part D either directly to the plan sponsor under Medicare Part D, or indirectly through a pharmacy benefit manager will not be protected under the anti-kickback statute discount safe harbor. The effective date of the two new safe harbors and the revision to the discount safe harbor was delayed by court order until January 1, 2023. Recent legislation further delayed implementation of the new safe harbors and the revision to the discount safe harbor until January 1, 2032. Our practices may not always meet all of the criteria for safe harbor protection. A person or entity need not have knowledge of the statutes or the specific intent to violate it in order to have committed a violation. In addition, the government may assert as a matter of law 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 federal civil False Claims Act. Federal enforcement agencies have shown increased interest under the federal Anti-Kickback Stature and the federal civil False Claims Act in pharmaceutical companies' product and patient assistance programs, including reimbursement and co-pay support services and donations to independent charitable patient assistance programs. A number of investigations into these programs have resulted in significant civil and criminal settlements. Most states have adopted laws similar to the federal Anti-Kickback Statute, which apply to items and services reimbursed under Medicaid and other state programs; furthermore, in several states, these statutes and regulations apply regardless of the payor, including to commercial plans. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer and its products from participation in federal healthcare programs, debarment from federal government procurement and non-procurement programs, criminal fines, and imprisonment. Several other countries, including the United Kingdom, have enacted similar anti-kickback, fraud and abuse laws and regulations.

The federal civil False Claims Act imposes civil liability and penalties on individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim, or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Claims under the federal civil False Claims Act may be initiated by whistleblowers, who receive substantial financial incentives to come forward, through "qui tam" actions that can be pursued by the whistleblower even if the government declines to prosecute the case. Intent to deceive or actual knowledge of falsity is not necessary to establish civil liability, which may be predicated on deliberate indifference or reckless disregard for the truth. The federal government continues to use the False Claims Act, and the accompanying threat of significant liability, in investigations against pharmaceutical and healthcare companies. These investigations have involved, for example, allegations of improper financial relationships with referral sources, providing free product to customers with the expectation that the customers would bill federal programs for the free product, as well as the promotion of products for unapproved uses and reporting false pricing information. A violation of the federal Anti-Kickback Statute is a per se violation of civil False Claims Act. Potential liability under the federal civil False Claims Act includes treble damages and significant per claim penalties. The criminal federal False Claims Act imposes criminal fines or imprisonment against individuals or entities who make or present a claim to the government knowing such claim to be false, fictitious or fraudulent. Conviction or civil judgment for violation of the False Claims Act can also result in debarment from federal government procurement and non-procurement programs and exclusion from participation in federal healthcare programs. The majority of states also have statutes or regulations similar to the federal False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs.

The Affordable Care Act included a provision requiring certain providers and suppliers of items and services to federal healthcare programs to report and return overpayments within sixty days after they are "identified" (the "Overpayment Statute"), after which the recipient of the overpayment incurs federal civil False Claims Act liability. The law prohibits a recipient of a payment from the government from keeping an overpayment when the government mistakenly pays more than the amount to which the recipient is entitled even if the overpayment is not caused by any conduct of the recipient. In 2014 and 2016, the CMS released regulatory guidance (in the form of final rules) to Medicare providers, suppliers and managed care and prescription drug plans regarding how to comply with the Overpayment Statute. Although these Medicare providers, suppliers and plans have faced federal False Claims Act liability since 2010 for failures to comply with the Overpayment Statute, these final rules interpreting the Overpayment Statute provide guidance regarding how to comply with applicable obligations, and guidance to government regulators and enforcement authorities regarding

monitoring and prosecuting suspected violations. These final rules are not directly applicable to manufacturers, unless a manufacturer is a direct recipient of payment by an agency such as a research grant, but may impact a manufacturer's customers and potential customers who are Medicare providers, suppliers, and plans. In a final rule issued on December 9, 2024, CMS set revised standards for identifying and returning overpayments to Medicare, clarifying the sixty-day overpayment refund obligation. Among other changes, the rule clarifies and modifies when an overpayment is identified and when the 60-day timeclock for reporting the overpayment begins, adopting the False Claims Act liability standard that does not consider the time needed to quantify the potential overpayment, thereby increasing the risk of incurring federal civil False Claims Act liability. The final rule does, however, allow for suspension of the sixty-day clock for 180 days for the purpose of conducting a timely, good faith investigation to determine the existence of related overpayments that may arise from the same or similar cause or reason as the initially identified overpayment.

The federal Physician Payments Sunshine Act, enacted as part of the Affordable Care Act, and its implementing regulations, require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to certain payments and other transfers of value made to or at the request of covered recipients, such as, but not limited to, physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and certified nurse midwives licensed in the United States and to US teaching hospitals, as well as ownership and investment interests held by physicians and members of their immediate family. Payments made to physicians, other principal investigators and certain research institutions for research, including clinical trials, are included within the ambit of this law. Such information is made publicly available by CMS in a searchable format, with data collected in each calendar year published the following June. Failure to submit required information may result in civil monetary penalties, with increased penalties for "knowing failures," for each payment, transfer of value or ownership or investment interest not timely and accurately reported in an annual submission. If not preempted by this federal law, several states currently require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to healthcare professionals in those states. Depending on the state, legislation may prohibit various marketing-related activities, such as gift bans, or require the posting of information relating to clinical studies and their outcomes. In addition, certain states, such as California, Nevada, Connecticut and Massachusetts, require pharmaceutical companies to implement compliance programs or marketing codes of conduct and several other states are considering similar proposals. Manufacturers that fail to comply with these state laws can face civil penalties.

Statutory requirements to disclose publicly payments made to healthcare professionals and healthcare organizations have also been enacted in certain European Union member states. In addition, self-regulatory bodies of the pharmaceuticals industry, such as the European Federation of Pharmaceutical Industries and Associations, or EFPIA, have published codes of conduct to which its members have agreed to abide, that require the public disclosure of payments made to healthcare professionals and healthcare organizations. In some countries (including France, Denmark and Portugal) such requirements are enforceable by law.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, a healthcare benefit program, regardless of whether the payor is public or private, in connection with the delivery of, or payment for, healthcare benefits, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items, or services relating to healthcare matters. Additionally, the Affordable Care Act amended the intent requirement of certain of these criminal statutes under HIPAA so that a person or entity no longer needs to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH Act, also imposes obligations on certain entities with respect to safeguarding the privacy and security of certain individually identifiable health information, known as protected health information. Among other things, the HITECH Act and its implementing regulations make HIPAA's security and certain privacy standards directly applicable to "business

associates", defined as persons or organizations who, on behalf of covered entities create, receive, maintain or transmit protected health information for a function or activity regulated by HIPAA. The HITECH Act also strengthened the civil and criminal penalties that may be imposed against covered entities, business associates and individuals, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, other federal and state laws, such as the California Consumer Privacy Act, or CCPA, may regulate the privacy and security of personal information that we maintain, many of which may differ from each other in significant ways. Since the CCPA was signed into law in 2018, numerous other states, including Virginia, Colorado, Utah and Connecticut, have enacted similar privacy laws that may apply to personal information that we collect or maintain. As well, beginning in 2023, several states have enacted privacy laws specific to consumer health data, which may also apply to personal information that we collect or maintain.

Outside of the U.S., additional privacy and data protection laws may apply to our operations. For example, the EU General Data Protection Regulation, the UK General Data Protection Regulation and related data protection, cybersecurity and e-privacy laws in the EU/EEA and the UK, collectively, the GDPR, and equivalent Swiss laws may apply to some or all of the clinical or other personal data obtained, transmitted, or stored from those jurisdictions. These laws require in many circumstances specific, freely given and fully informed consent to be obtained from patients or clinical study participants or other lawful bases for processing. There are also other requirements for lawful processing, including transparency obligations, data minimization requirements, data transfer restrictions and compliance obligations with individuals' stringent rights to access their personal data and to otherwise control the processing of their personal data. There are data breach notification obligations, to supervisory authorities and to individuals, where certain risk thresholds to them have occurred. The GDPR and Swiss laws only permit transfer of personal data to countries where there is adequate protection as determined by the relevant EU/UK/Swiss governmental authorities or where other mechanisms are in place such as Standard Contractual Clauses or the EU/UK/Swiss-US Data Privacy Framework.

The GDPR and Swiss law, among others, allow supervisory authorities to potentially impose high regulatory fines in the event of violations, for example, under the GDPR up to 4% of global annual group turnover or EUR 20 million (whichever is the higher amount). Supervisory authorities in the EU/EEA, Switzerland and UK may potentially levy such fines directly upon on the non-compliant entity and/or on the parent company of the non-compliant entity. Supervisory authorities also possess other wide-ranging powers, including conducting unannounced inspections of our facilities and system (so-called "dawn raids"), and issuing "stop processing" orders to us. Separate from regulatory enforcement actions, individuals may bring private actions (including potentially group or representative actions) against us. There is no statutory cap in the GDPR on the amount of compensation or the damages which individuals may recover. Overall, the significant costs of GDPR and Swiss law compliance, risk of regulatory enforcement actions and private litigation under, and other burdens imposed by these laws as well as under other regulatory schemes throughout the world related to privacy and security of health information and other personal and private data could have an adverse impact on our business, reputation, financial condition, and results of operations. We may also be subject to additional industry-specific privacy, cybersecurity, data protection, operational and information systems resilience, and artificial intelligence-related laws in the EU/EEA, Switzerland and the UK which may subject us to additional similar risks and impacts.

In addition, interactions between pharmaceutical companies and physicians are also governed by industry self-regulation codes of conduct and physicians' codes of professional conduct. In the United States, some state laws require pharmaceutical companies to comply with these industry and physician codes and the relevant compliance guidance for pharmaceutical manufacturers promulgated by the federal government. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU. The provision of benefits or advantages to physicians is also governed by the national laws of the EU member states, as well as codes of conduct issued by self-regulatory industry bodies. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, their competent professional organization, and the competent authorities of the individual EU member states. These requirements are provided in the national laws, industry codes, or professional codes of conduct, applicable in the EU member states.

Any continuing efforts to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act, could have an impact on fraud and abuse provisions and other requirements, including the Physician Payments Sunshine Act, that were authorized and enacted under the Affordable Care Act.

Human Capital Resources

As of December 31, 2024, we had 939 employees and 66 consultants and contractors. None of our U.S. based employees are represented by labor unions or covered by collective bargaining agreements, although certain international employees are covered by collective labor agreements established under local law. We consider our relationship with our employees to be good.

We believe that our growth and success is dependent on the contributions of our employees, as led by our executive officers. We focus significant attention on attracting, retaining, engaging, and further developing talented and experienced individuals to manage and support our operations. In particular, recruiting and retaining qualified scientific, clinical, manufacturing, commercial, marketing and support personnel is critical to our success. Competition for these skilled personnel is high. We believe that our strong culture of teamwork and desire to be ever better help us attract and retain employees. Our employees complete Gallup, Inc.'s Clifton Strengths talent assessment and attend related training sessions. These tools have been implemented to help our employees identify their core strengths and learn how to use these strengths to become more engaged and productive at work as well as to lead an overall more satisfying and healthier lifestyle. Our Brazilian office was recognized as a "great place to work" by the Great Place to Work Institute in 2022, 2023 and 2024.

Based on external benchmarks, we offer employees a number of additional resources and tools to help in their personal and professional development, including career coaching, targeted leadership development for identified current and emerging leaders, internal and external development programs, professional assessment tools, a paid subscription to a digital on-demand career and management learning solutions platform and a wellness website through which employees may access information regarding scheduled healthy lifestyle activities, articles and other beneficial resources. To help newly hired employees, our global onboarding team conducts monthly surveys and focus groups and each newly hired employee is paired with a "buddy" to assist in their transition. Also, we require specialized leadership training for all employees responsible for managing others within our organization. In 2023, we established a center of excellence for coaching and mentoring, with 60 mentorships in place as of December 31, 2024. In 2024, we delivered more than 4,000 training hours (excluding compliance and role-specific training), offered 28 learning sessions to all employees, and 30 customized training sessions to teams. We have also delivered more than 130 coaching hours with internal coaches. Our executive team routinely reviews employee turnover throughout the organization to monitor employee satisfaction. Over the last four years, our voluntary turnover rate has been below 10%.

We believe that we provide a competitive total reward offering to our employees, with market competitive cash compensation, equity, and industry competitive company-paid benefits, including subsidized medical, and dental insurance and retirement plans, as well as group vision insurance, tuition reimbursement, and benefits and policies to support parental leave, mental health and wellness, family planning and child bonding. In 2023, we implemented a program that offers financial support and access to high quality fertility care and family forming benefits to our employees. Total rewards offerings are established by employee positions, skill levels, experience, knowledge, and geographic location. We also provide flexible work arrangements for our employees, including remote work options when practicable. In addition, to assist our employees during times of personal disasters that impact them and their families, we have established an employee relief program that is funded by our employees with corporate matches.

We are committed to hiring, developing, and supporting a diverse and inclusive workplace, and continue to focus on extending our equality, diversity, and inclusion initiatives across our workforce. All of our employees are required to adhere to our Code of Business Conduct and Ethics, and all relevant country regulations which sets forth the high level of integrity, legal compliance and patient-centric focus expected of all our employees. We have a team of professionals that oversees our culture and community program. The mission of our culture and community team is to collaborate with cross functional partners and create intentional efforts to connect and engage with employees who want to find community and apply their passion to make a difference. A core element of this mission is our equality, diversity and inclusion, or ED&I, program which is managed by an ED&I professional, who routinely meets with our executive committee. Our ED&I program seeks to enable all employees to feel a sense of purpose and belonging through their connections with our internal

communities. This program is guided by a steering committee comprised of senior leaders, volunteer ED&I ambassadors and representatives from our seven Employee Resource Groups, or ERGs, each of which associates with a different underrepresented community. Our ERGs meet monthly and serve to offer a safe place for our employees to have conversations about social issues, celebrate cultural observances and to grow as individuals. We believe that our ERGs and our ED&I program help our employees to better understand and celebrate each other, resulting in a more cohesive work environment.

We continue to provide opportunities for talented individuals through our global Talent Pipeline Program, or the TPP. The TPP is a global fellowship program aimed at providing recent diverse graduates real-world experience in the biopharmaceutical industry and related professions, including research, clinical, finance, commercial, marketing, compliance, quality, legal, information technology, human resources, government affairs, and communications. Participants are recruited from a diverse global group of institutions and networks and are provided mentorship, job coaching, career counseling, and leadership training for one year. Participants from the TPP are often offered full-time positions based upon our workforce needs. The TPP was originally established in 2020 to benefit students that graduated during the COVID-19 pandemic.

Our Corporate Information

Our principal executive offices are located at 500 Warren Corp Center Drive, Warren, New Jersey 07059. Our telephone number is (908) 222-7000. We maintain a website at www.ptcbio.com.

Additional Information

We make available, free of charge on our website, www.ptcbio.com, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file those reports with, or furnish them to, the Securities and Exchange Commission, or SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. Such reports, proxy statements and other information may be obtained through the SEC's website (www.sec.gov). The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K.

Item 1A. Risk Factors

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to the Development and Commercialization of our Products and our Product Candidates

If we are unable to continue to execute our commercial strategy for our products, fail to obtain renewal of, or satisfy the conditions of our marketing authorization for our products, or if we experience significant delays in accomplishing such goals, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources to bring our products to market through research and development, collaborations and acquisitions. Our ability to continue to generate product revenues will depend heavily on the successful commercialization of our products.

If we do not successfully maintain our marketing authorizations for our products and obtain new marketing authorizations for our product candidates and new uses of our approved products, our ability to generate additional revenue will be

jeopardized and, consequently, our business will be materially harmed. Additionally, our ability to make our licensed products available within the relevant territories is largely dependent upon the maintenance of the marketing authorizations by the licensor. The success of our products will depend on a number of additional factors, including the following:

- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms on a timely basis, or at all;
- the timing, scope and outcome of commercial launches;
- the maintenance and expansion of a commercial infrastructure capable of supporting product sales, marketing and distribution;
- the implementation and maintenance of marketing and distribution relationships with third parties in territories where we do not pursue direct commercialization;
- our ability to establish and maintain commercial manufacturing arrangements with third-party manufacturers;
- our ability or the ability of our third-party manufacturers to successfully produce commercial and clinical supply of drug on a timely basis sufficient to meet the needs of our commercial and clinical activities;
- successful identification of eligible patients;
- acceptance of the drug as a treatment for the approved indication by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- global trade policies;
- a continued acceptable safety profile of the drug;
- the costs, timing and outcome of post-marketing studies and trials required for our products;
- protecting our rights in our intellectual property portfolio, obtaining and maintaining regulatory exclusivity and whether we are able to maintain market exclusivity periods under the Orphan Drug Act or equivalent protections in other jurisdictions;
- whether negative results from our clinical or pre-clinical trials of a product for one indication affect the perception of such product in another indication, including with respect to determinations by regulators, including the FDA and EMA, with respect to our ongoing or future regulatory submissions for marketing authorization of our products for any indication;
- whether, with respect to Translarna, we are able to continue to satisfy our obligations under, and maintain, the marketing authorization in the EEA for Translarna for the treatment of nmDMD, including whether the EMA determines on an annual basis that the benefit-risk balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label;
- whether, and within what timeframe, we are able to advance Translarna for the treatment of nmDMD in the United States;
- our ability to complete certain FDA post-marketing requirements in connection with our marketing authorization of Kebilidi;
- our ability to obtain additional and maintain existing reimbursed named patient and cohort EAP programs for our products on adequate terms;
- our ability to successfully prepare and advance regulatory submissions for marketing authorizations for our products in additional territories and for additional or expanded indications and whether and in what timeframe we may obtain such authorizations; and
- the ability and willingness of patients and healthcare professionals to access our products through alternative means if pricing and reimbursement negotiations in the applicable territory do not have a positive outcome.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to continue to commercialize our products, either of which would have a material adverse effect on our business, results of operations and financial condition.

Delays or failures in obtaining regulatory approval would prevent us from commercializing our product candidates in the applicable territory and our ability to generate revenue will be materially impaired. Moreover, should we need to conduct additional development work, other than those we have planned, we expect to incur significant costs, which may have a material adverse effect on our business and results of operations.

There is significant risk that we will be unable to obtain approval for our product candidates on a timely basis or at all, and we may be required to perform additional clinical trials, non-clinical studies or CMC assessments, work, or analyses at significant cost. Product development is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. This is especially true for rare and/or complicated diseases and new or novel products. A failure of one or more clinical or preclinical trials, or manufacturing development can occur at any stage. Preclinical and clinical studies may also reveal unfavorable product candidate characteristics, including safety concerns, or may not demonstrate product candidate efficacy. There can be significant variability in results between different clinical trials of the same product candidate due to numerous factors. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing authorization of their products.

The approval process is also subject to the substantial discretion of regulatory authorities and the approval procedures vary among countries, can involve additional testing, and the time for approval may materially differ and be subject to administrative delays that we cannot control. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, the failure to obtain approval in one jurisdiction may compromise our ability to obtain approval elsewhere.

In response to changes in the regulatory environment or requests from regulators, we may elect, or be obliged, to postpone a regulatory submission to include additional analyses, which could cause delays in getting our products to market and substantially increase our costs. Securing marketing authorization also requires the submission of information about the product manufacturing process to, and inspection or conduct of remote regulatory assessments of manufacturing facilities by, the regulatory authorities. Changes to manufacturers, product candidate formulation, manufacturing processes and other product candidate attributes, such as the method of delivery, during product candidate development may also require additional studies to demonstrate the comparability of the product candidate using prior processes, formulation, or manufacturers, or with the prior attributes, to the product candidate using new the processes, formulation, or manufacturers, or with the new attributes.

For example, we have been seeking FDA approval for Translarna for nmDMD with the FDA since 2010 and the FDA has repeatedly disagreed with our interpretation of our results. In October 2017, the Office of Drug Evaluation I of the FDA issued a CRL for the NDA, stating that it was unable to approve the application in its current form. In response, we filed a formal dispute resolution request with the Office of New Drugs of the FDA. In February 2018, the Office of New Drugs of the FDA denied our appeal of the CRL. In its response, the Office of New Drugs recommended a possible path forward for the ataluren NDA submission based on the accelerated approval pathway. This would involve a re-submission of an NDA containing the current data on effectiveness of ataluren with new data to be generated on dystrophin production in nmDMD patients' muscles. We followed the FDA's recommendation and collected, using newer technologies via procedures and methods that we designed, such dystrophin data in a new study, Study 045, and announced the results of Study 045 in February 2021. Study 045 did not meet its pre-specified primary endpoint. In June 2022, we announced top-line results from the placebo-controlled trial of Study 041. Following this announcement, we submitted a meeting request to the FDA to gain clarity on the regulatory pathway for a potential re-submission of an NDA for Translarna. The FDA provided initial written feedback that Study 041 does not provide substantial evidence of effectiveness to support NDA re-submission. We held a Type C meeting with the FDA in the fourth quarter of 2023 to discuss the totality of Translarna data. Based on feedback from the FDA, we re-submitted the NDA in July 2024, based on the results from Study 041 and from our international drug registry study for nmDMD patients receiving Translarna. In October 2024, the FDA accepted for review the resubmission of the NDA for Translarna for the treatment of nmDMD. As this was an NDA resubmission following a CRL to the NDA which was filed over protest in 2016, the FDA is not obligated to follow the review timelines under PDUFA guidelines and an action date has not been provided.

There is no guarantee that we will be able to achieve our milestones at all or within our anticipated timeframes, or that regulators may have additional questions to which we will need to respond. There is also substantial risk that the results of our future or current studies will not ultimately support the approval of a product candidate. Regulators may also request additional studies, data and information, that we may need to develop and which were not originally planned for. Any delays in obtaining regulatory approval, or if we never obtain regulatory approval, could have a material adverse effect on our business, financial condition and results of operations.

We may be unable to continue to commercialize Translarna for nmDMD in the EEA if the EC adopts the negative opinion issued by the CHMP for the renewal of the existing conditional authorization for Translarna.

Our marketing authorization for Translarna for the treatment of nmDMD in ambulatory patients aged two years and older in the EEA is subject to annual review and renewal by the EC following reassessment by the EMA of the benefit-risk balance of the authorization. In September 2022, we submitted a Type II variation to the EMA to support conversion of the conditional marketing authorization for Translarna to a standard marketing authorization, which included a report on the placebo-controlled trial of Study 041 and data from the open-label extension. In February 2023, we also submitted an annual marketing authorization renewal request to the EMA. In September 2023, the CHMP gave a negative opinion on the conversion of the conditional marketing authorization to full marketing authorization of Translarna for the treatment of nmDMD and a negative opinion on the renewal of the existing conditional marketing authorization of Translarna for the treatment of nmDMD. In January 2024, the CHMP issued a negative opinion for the renewal of the conditional marketing authorization following a re-examination procedure. In May 2024, the EC decided not to adopt the CHMP's negative opinion for the renewal of the conditional marketing authorization of Translarna and returned such opinion to the CHMP for re-evaluation. In June 2024, following the EC's request for re-review, the CHMP issued a negative opinion on the renewal of the conditional marketing authorization of Translarna for the treatment of nmDMD. On October 18, 2024, the CHMP maintained its negative opinion for the renewal of the conditional marketing authorization following the requested reexamination procedure. In accordance with EMA regulations, the EC has 67 days from the date of issuance to adopt the opinion. At this time, the EC has not yet adopted the negative opinion. If the EC adopts the negative opinion, Translarna would no longer have marketing authorization in the member states of the EEA.

Given the negative opinion from the CHMP, we believe that it is likely that the EC will refuse to renew the marketing authorization for Translarna. While we are exploring other potential mechanisms in which we may provide Translarna to nmDMD patients in the EEA, we may be unable to identify processes that are both possible within the regulatory frameworks of individual EEA countries and commercially viable. As such, there is substantial risk to our ability to maintain our conditional marketing authorization in the EEA and our ability to commercialize Translarna for the treatment of nmDMD in the EEA. If we are unable to renew our conditional marketing authorization in the EEA or we are unable to identify other potential mechanisms in which we may provide Translarna to nmDMD patients in the EEA, we would lose all, or a significant portion of, our ability to generate revenue from sales of Translarna in the EEA, which would have a material adverse effect on our business, results of operations and financial condition.

Additionally, the CHMP's negative opinion for Translarna and potential loss of the Translarna marketing authorization in the EEA may influence regulatory entities in other jurisdictions in which Translarna has been approved to reassess such approvals. For example, certain countries reference or depend on the determination by the EMA when considering the grant of a marketing authorization. There is substantial risk that we would be unable to maintain our marketing authorizations in these countries in the event the EC decides not to renew or otherwise varies, suspends or withdraws our marketing authorization in the EEA. Even in countries where our marketing authorization is maintained, there may be an impact on pricing and reimbursement of Translarna within those countries. Any potential reassessments or scheduled renewals of our marketing authorizations or impacts to pricing and reimbursement may lead to additional regulatory costs, requirements to complete additional clinical trials, restrictions on or removal of our marketing authorizations or loss of a significant portion of our revenue for Translarna in other jurisdictions, which could have a material adverse effect on our business, results of operations and financial condition.

We may use certain specialized pathways to develop our product candidates or to seek approval. We may not qualify for these pathways or such pathways may not ultimately speed the time to approval or result in product candidate approval.

In the United States, we may pursue the accelerated approval pathway for certain of our product candidates. However, the FDA may find that our product candidates do not qualify for accelerated approval. Moreover, even if we do ultimately receive accelerated approval, we would need to meet certain post approval requirements, such as completing a post-approval study confirming our product candidates' clinical benefit that may require substantial time, effort, and funds. The FDA must specify the conditions for the required post approval studies, including enrollment targets, the study protocol, milestones, and target completion dates, by the time of approval and the FDA may require that the post-approval studies be commenced before the date of approval. If this study does not confirm the product's clinical benefit or if the study is not conducted in accordance with the FDA's requirements, it would be subject to the risk of expedited FDA withdrawal. Additional regulatory requirements also include the pre-submission of promotional materials to the FDA and potential restrictions, such as distribution restrictions, to assure the product's safe use. In recent years, the accelerated approval pathway has come under significant governmental and public scrutiny. Accordingly, depending on the results of our studies, the FDA may be more conservative in granting accelerated approval or, if granted, may be more apt to withdrawal approval if clinical benefit is not confirmed. Due to these and other uncertainties, we are unable to estimate the timing or potential for product candidates for which we may use the accelerated approval pathway or the cost or effort required to receive FDA approval. Further, even if we receive accelerated approval, there is no guarantee that we would be able to maintain such approval. For instance, our confirmatory studies may not confirm a product's clinical benefit, in which case, the FDA could withdraw the product from the market, we may choose to voluntarily withdraw the product from the market, or we may need to conduct further studies to determine whether the product has a clinical benefit.

Moreover, we may pursue other product designations or programs that are designed to facilitate drug development. There is no guarantee that we will be able to obtain any such designations or, if obtained, that we will be able to maintain them. For instance, the FDA may find that, following designation, our product candidates no longer qualify for the designation due to changed circumstances or study results. This may result in the FDA rescinding a designation that we previously received. Any such designation also may not expedite or otherwise facilitate product development.

If we or our collaborators experience any of a number of possible unforeseen events in connection with clinical trials related to our products or our product candidates, maintenance of our existing marketing authorization for our products and any additional potential marketing authorization or commercialization of our products or our product candidates could be delayed or prevented.

We or our collaborators may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing authorization or commercialize our products or our product candidates, including:

- clinical trials may produce negative or inconclusive results, regulators may disagree with our interpretation of results, our studies may fail to reach the necessary level of statistical significance, or we may not be able to demonstrate that our product candidates are safe, effective, or provide an advantage over current standard of care or other therapies;
- our clinical trials may not meet their primary endpoints. For example, for Translarna, the primary efficacy endpoint in the intent to treat, or ITT, population did not achieve statistical significance in the Phase 2b trial (completed in 2009), Phase 3 trial in ACT DMD (completed in 2015), or Study 045 (completed in 2021);
- there may be flaws in our clinical trials' design that may not become apparent until the clinical trials are well advanced or regulators may not agree with the design of our studies or our analysis of the resulting data;
- clinical trial sites or enrolled patients, as well as the resulting data, may be negatively affected by outbreaks of contagious disease, resulting in delays and disruptions in completing clinical trials, such as the delays we experienced in 2021 and 2022 in enrolling a Phase 2/3 placebo-controlled trial of vatiquinone in children with mitochondrial disease associated seizures trial as some patients were unable or hesitant to travel to clinical trial sites due to the COVID-19 pandemic. The exact impact of any contagious disease outbreak may not be fully known until the applicable trials are complete or are submitted to the applicable regulatory authorities;

- we may be unable to enroll a sufficient number of patients in our clinical trials, the number of patients required for clinical trials may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials, not comply with trial procedures, misrepresent their eligibility, or be lost to follow-up at a higher rate than we anticipate;
- we may enroll patients in foreign countries in which clinical sites may have less experience with studies or the disease at issue, or may use a different standard of care;
- regulatory authorities may not accept the data generated at foreign sites or may find that such data is not sufficiently representative of the population of the approving country;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or we may be required to engage in additional clinical trial site monitoring;
- regulators, institutional review boards, institutional biosafety committees, or independent ethics committees may not authorize us or our investigators to commence or continue a clinical trial, may require additional data or studies, or may require changes to our studies, including applications and protocols;
- we may be unable to engage trial sites and contract research organizations or they may withdraw from our studies;
- we, regulators, institutional review boards, institutional biosafety committees, or independent ethics committees may require the suspension or termination of studies for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our products or our product candidates may be greater than we anticipate or we may have insufficient funds for a clinical trial or to pay the substantial user fees required by the FDA upon the filing of a marketing application;
- the supply or quality of our products or our product candidates or other materials necessary to conduct clinical trials of our products or our product candidates may be insufficient or inadequate;
- regulators may require us to perform additional or unanticipated studies, develop additional manufacturing information, or make changes to our manufacturing process to obtain approval;
- there may be changes in the applicable regulatory authorities' approval requirements, which may render our data insufficient to obtain marketing approval;
- the FDA or comparable regulatory authorities may disagree with our intended indications;
- regulators may fail to approve or subsequently find fault with the manufacturing processes or facilities for clinical and future commercial supplies;
- the FDA or comparable regulatory authorities may take longer than we anticipate to make a decision on our product candidates; or
- we may decide to abandon the development of a product candidate or development program.

These risks may be increased for product candidates intended for the treatment of diseases for which there is little clinical experience, where we are using new endpoints or methodologies, or where the product candidates are new or novel. For example, there are no marketed therapies approved to treat the underlying cause of nmDMD and there is limited clinical trial experience with respect to drugs to treat nmDMD and other diseases that we are studying or have studied. As a result, the design and conduct of clinical trials for these diseases, particularly for drugs to address the underlying nonsense mutations causing these diseases in some subsets of patients, is subject to increased risk. Furthermore, because gene therapy products are a relatively new development, less is known about such products and product candidates and, accordingly there is an increased risk that such products may not perform as expected. Regulatory review agencies and the requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional or larger studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval studies, limitations or restrictions.

We may also experience increased risks to the extent that products or product candidates require a specialized delivery device or method. For example, Upstaza/Kebilidi is administered directly to the putamen in the brain using stereotactic surgery, a brain surgery requiring significant skill and training. There is little experience with such surgeries being used to deliver drugs and for such surgeries being performed on children. We may need to train sufficient brain surgeons to perform the procedure properly, which may expose us to additional regulatory risks as our interactions with such healthcare providers must comply with all applicable laws and regulations. As a result, we will need to invest significant resources to ensure all personnel and contractors are adequately trained on these requirements and to monitor their conduct. Delivery of Upstaza/Kebilidi to the putamen also requires certain medical devices, which can increase our regulatory compliance obligations.

Our product development costs will increase if we experience delays in testing or marketing authorizations, and we may not have sufficient funding to complete the testing and approval process for any of our product candidates. We may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our products and product candidates. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our products or our product candidates and allow our competitors to bring products to market before we do or impair our ability to successfully commercialize our products or our product candidates, and so may harm our business, results of operations and financial condition.

Subgroup, retrospective, post-hoc, and certain statistical analyses may not be reliable and typically will not form the basis for regulatory approval.

In the event that a study's primary endpoint is not met, companies may undertake certain analyses to further understand the data and potential reasons for the study results, including retrospective, post-hoc, and subgroup analyses. Because these analyses are not pre-planned and studies may not be adequately designed for these analyses, they may not be reliable and typically will not form the basis for regulatory approval. For example, after determining that we did not achieve the primary efficacy endpoint with the pre-specified level of statistical significance in our completed ACT DMD and Phase 2b clinical trials of Translarna for the treatment of nmDMD, we performed subgroup, retrospective, and meta-analyses. We submitted these analyses to the FDA as part of our NDA, taking the position that the totality of clinical data from these trials support the clinical benefit of Translarna for the treatment of nmDMD. The FDA, however, did not agree that these analyses supported approval.

Some of our favorable statistical data from these trials also are based on nominal p-values. Nominal p-values are subject to certain limitations, and which, because of these limitations, regulatory authorities typically give less weight to nominal p-values, compared to regular p-values. For example, the p-values in ACT DMD for change from baseline at week 48 in the 6-minute walk test, or 6MWT (which we also refer to as 6-minute walk distance, or 6MWD) and each secondary end point timed function test were nominal p-values. The FDA found that certain post-hoc adjustments, our retrospective analyses and our reliance on nominal p-values for some of our statistical data did not support approval.

An unfavorable view of our data and analyses by regulatory authorities has and could continue to negatively impact our ability to obtain or maintain marketing authorizations, which would have a material adverse effect on our revenue and would materially harm our business, financial results and results of operations.

If we experience delays or difficulties in the enrollment of patients in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates, including clinical trials due to the inability to enroll a sufficient number of patients. Patient enrollment is affected a number of factors including:

- the size of the patient population (many of our studies concern rare conditions with small patient populations);
- the availability of approved treatments;
- severity of the disease under investigation;
- eligibility criteria for the study in question;
- perceived benefits and risks of the product candidate under study;

- disruptions caused by and the willingness of patients to enroll in a clinical trial during outbreaks of contagious disease;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- competition from other clinical trials;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

For example, we previously experienced delays in 2021 and 2022 enrolling a Phase 2/3 trial of vatiquinone in children with mitochondrial disease associated seizures as some patients were unable or hesitant to travel to clinical trial sites due to the COVID-19 pandemic.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates. Our inability to enroll, timely or at all, a sufficient number of patients in our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

If serious adverse side effects are identified during the development of any product candidate or for any product for which we have or may obtain marketing approval, we may need to abandon or limit our development and/or marketing of that product or product candidate.

If our products or our product candidates are associated with undesirable side effects or have characteristics that are unexpected, regulatory authorities, institutional review boards, institutional biosafety committees, or independent ethics committees may place our studies on clinical hold, withdraw or suspend study approvals, or require that we modify our protocols. We may also need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a benefit-risk perspective. Adverse events or side effects may also result in study recruitment challenges, marketing authorization denial, limitations on the indicated use of a product, the inclusion of warnings, contraindications, or precautions on the label of any approved products, or significant conditions imposed on any approval, including the requirement of a risk evaluation and mitigation strategies, or REMS, costly post-marketing studies or clinical trials and surveillance to monitor the safety of the product. Adverse effects may also prevent the adoption of a product, if it is approved. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects that prevented further development of the compound. Furthermore, we may be sued and held liable for harm caused by our products to patients as a result of the identification of undesirable side effects, which may cause reputational harm.

For example, although we did not observe a pattern of liver enzyme elevations in our Phase 2 or Phase 3 clinical trials of Translarna, we did observe modest elevations of liver enzymes in some subjects in one of our Phase 1 clinical trials. These elevated enzyme levels did not require cessation of Translarna administration, and enzyme levels typically normalized after completion of the treatment phase. We did not observe any increases in bilirubin, which can be associated with serious harm to the liver, in the Phase 1 clinical trial.

In addition, in Study 009, our first Phase 3 clinical trial of Translarna for the treatment of nmCF, five adverse events in the Translarna arm of the trial that involved the renal system led to discontinuation. As compared to the placebo group, the Translarna treatment arm also had a higher incidence of adverse events of creatinine elevations, which can be an indication of impaired kidney function. In the Translarna treatment arm, more severe clinically meaningful creatinine elevations were reported in conjunction with cystic fibrosis pulmonary exacerbations. These creatinine elevations were associated with concomitant treatment with antibiotics associated with impaired kidney functions, such as aminoglycosides or vancomycin. This led to the subsequent prohibition of concomitant use of Translarna and these antibiotics, which was successful in addressing this issue in the clinical trial.

The risk of finding adverse side effects may be particularly heightened in the case of gene therapies. For instance, new gene copies may produce too much or too little of the desired protein or RNA, or the production of the desired protein or RNA may change over time. Because the treatment is irreversible, there may be challenges in managing side effects. Adverse effects would not be able to be reversed or relieved by stopping dosing and might require us to develop additional clinical safety procedures. Furthermore, new gene copies may disrupt other normal biological molecules and processes.

Adverse side effects may also be experienced by patients as a result of the process for administering the therapy or related procedures.

There have been several significant adverse side effects in gene therapy treatments in the past, including reported cases of leukemia, immune- and complement-mediated responses, and death seen in other trials using other vectors. While new recombinant vectors have been developed to potentially reduce these side effects, gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. For instance, possible adverse side effects that could occur include an immunologic or complement-mediated reactions early after administration which, could substantially limit the effectiveness of the treatment. Depending on the vector, additional manufacturing, clinical, and preclinical testing may be required, as well as additional analyses, assessments, and potential long-term patient and clinical study subject monitoring and sample testing and associated regulatory reporting. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could further adversely impact our product candidates in the form of increased government regulation, unfavorable public perception, potential regulatory delays, stricter labeling requirements, and a decrease in demand.

If, following approval, we or others identify previously unknown side effects, if such side-effects are severe, or if known side effects are more frequent or severe than in the past then our marketing authorizations may be restricted or withdrawn, changes may be required to the product's label, sales may be adversely impacted, we may be required to undertake additional studies or trials, and government investigations or litigation, including product liability claims, may be brought against us. Additionally, if the safety warnings in our product labels are not followed, adverse medical situations in patients may arise, resulting in negative publicity and potential lawsuits. Any of these occurrences would limit or prevent us from commercializing our products, which would have a material adverse effect on our business, financial results and operations.

Certain of our products and product candidates may be difficult to produce, presenting manufacturing challenges that may delay product development and regulatory approval.

Manufacturers of pharmaceutical products must comply with strictly enforced manufacturing and quality requirements, including cGMP requirements, state and federal regulations, as well as ex-U.S. requirements when applicable. These may be particularly difficult to meet for complex products such as biologic and gene therapy products. Any failure to meet the applicable manufacturing and quality requirements could lead to a delay or interruption in development programs, delays in receiving regulatory approval, and consequences should we receive marketing approval.

The manufacture of drugs, and especially biologic and gene therapy products is technically complex, requires extreme precision to meet specification requirements and necessitates substantial expertise and capital investment. Production difficulties caused by unforeseen events, even if seemingly minimal, may delay the availability of material for clinical studies and commercial product. For example, given the nature of biologics manufacturing, there is a risk of contamination. Any contamination could materially adversely affect our ability to produce our gene therapy product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage.

In addition, gene therapy products have only in limited cases been manufactured at scales sufficient for pivotal trials and commercialization. Few pharmaceutical contract manufacturers specialize in gene therapy products and those that do are still developing appropriate processes, controls and facilities for large-scale production. While we believe that there are alternative sources of supply that can satisfy our commercial requirements for Upstaza/Kebilidi, we cannot be certain that we will be able to identify and establish relationships with such sources, if necessary, in a timely manner or at all, and what the terms and costs of such new arrangements would be, or that such alternative suppliers would be able to supply our potential commercial needs. Any switch from our current manufacturer would result in a significant delay, would require regulatory authority approval, and cause material additional costs.

Furthermore, some of the raw materials and other components required in our manufacturing process are derived from diverse biologic sources that may be difficult to procure and may be subject to contamination or recall. Any material shortage, supply chain disruption, contamination recall or restriction on the use of biologically derived substances in the

manufacture of our product candidates could adversely impact or disrupt the production and commercialization of products.

Finally, we and our third-party manufacturers may experience any number of unforeseen issues, unforeseen delays, including equipment failure, labor shortages, natural disasters, power failures, transportation difficulties, quality control or other issues, including those resulting from compliance with regulatory requirements, as further described in these risks, that could prevent us from realizing the intended benefits of our manufacturing strategy.

Any of our products or any other product candidate that receives marketing authorization may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Even if we are successful in obtaining and maintaining marketing authorizations, our products may not gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Third-party payors may require prior authorizations or failure on another type of treatment before covering a particular drug, particularly with respect to higher-priced drugs. Decreases in third-party reimbursement for a product or a decision by a third-party payor to not cover a product could reduce physician usage of the product. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations.

The degree of market acceptance of our products or product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages, as well as cost effectiveness compared to alternative treatments;
- the prevalence and severity of any side effects, as well as perceived safety;
- limitations or warnings contained in, as well as permitted claims based on the product's FDA-approved labeling;
- whether patients may be ineligible to receive a particular product or whether a particular product, especially in the case of gene therapies, may preclude future treatments;
- distribution and use restrictions imposed by the FDA or which we voluntarily implement;
- the ability to offer our products or product candidates for sale at competitive prices;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies. For example, gene therapy remains a novel technology and Upstaza/Kebilidi must be administered directly to the brain via a surgery and public perception may be influenced by claims that gene therapy is unsafe, which may cause gene therapy to not gain acceptance by the public or the medical community;
- the convenience and ease of administration compared to alternative treatments;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement and, where applicable, our ability to obtain pricing approvals which is separate from the marketing authorization process;
- adverse publicity about our and our competitors' products or product candidates or favorable publicity about competitive products or product candidates. For example, earlier gene therapy trials conducted by other organizations have led to several well-publicized adverse events, including cases of leukemia, immune- and complement-mediated adverse events, and death seen in other such organizations' trials using vectors;
- the results of studies of the product in other indications or similar products; and
- any restrictions on concomitant use of other medications.

Obtaining coverage and reimbursement for a product from third-party payers is a time-consuming and costly process. Failure to obtain adequate reimbursement may significantly impact the adoption and sale of products. Market acceptance and obtaining reimbursement coverage may be particularly challenging in the case of gene therapies, where the cost of a single administration may be substantial and adequate coverage and reimbursement will be essential for patients to afford the treatment. Payors may require us to provide supporting scientific, clinical and cost-effectiveness data, which we may not be able to provide. Moreover, ethical, social and legal concerns about certain treatments, such as gene therapy, could result in additional regulations restricting or prohibiting sale of our products.

In the United States, third-party payers, including government payers such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. Expensive specialty drugs in particular are often subject to restriction. The Medicare and Medicaid programs increasingly are used as models for how private payers and government payers develop their coverage and reimbursement policies. We cannot be assured that Medicare or Medicaid will cover our product candidates that may be approved or provide reimbursement without restriction and at adequate levels to realize a sufficient return on our investment. Our rebate payments may increase or our prices be adjusted under value-based purchasing arrangements based on evidence-based measures or outcomes-based measures for a patient or beneficiary based on use of our drug. Moreover, reimbursement agencies in the EU may be more conservative than CMS. It is difficult to predict what third-party payers will decide with respect to the coverage and reimbursement for our products for which we obtain marketing approval. Additionally, within Europe, each country has its own reimbursement regime employing various health technology assessment approaches to assess the cost-effectiveness of the product (for example, in the United Kingdom a HTA assessment is conducted by NICE) which may significantly affect the effective access to the market.

Our ability to negotiate, secure and maintain third-party coverage and reimbursement may also be affected by political, economic and regulatory developments. Governments continue to impose cost containment measures, and third-party payors are increasingly challenging prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. These and other similar developments could significantly limit the degree of market acceptance of our products or any of our other product candidates that receive marketing authorization.

If we are unable to establish or maintain sales, marketing and distribution capabilities or enter into agreements with third parties to market, sell and distribute our products or product candidates, we may not be successful in our continuing efforts to commercialize our products or any other product candidate if and when they are approved.

Our ongoing commercial strategy for our products and any other product candidate that may receive marketing authorization involves the development of a commercial infrastructure that spans multiple jurisdictions and is heavily dependent upon our ability to continue to build an infrastructure that is capable of implementing our global commercial strategy. The establishment and development of our commercial infrastructure will continue to be expensive and time consuming, and we may not be able to develop our commercial organizations in all intended territories, including in the United States, in a timely manner or at all. Doing so will require a high degree of coordination and compliance with laws and regulations in numerous territories, including restrictions on advertising practices, enforcement of intellectual property rights, restrictions on pricing or discounts, transparency laws and regulations, and unexpected changes in regulatory requirements and tariffs. If we are unable to effectively coordinate such activities or comply with such laws and regulations, our ability to commercialize our products or any other product candidates that may receive marketing authorization will be adversely affected. If we are unable to establish and maintain adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue consistent with our expectations and may not become profitable.

There are risks involved with establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training an internal commercial team is expensive and time consuming and could delay commercialization efforts. If a commercial launch for any product or product candidate for which we recruit a commercial team and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition such personnel.

The arrangements that we have entered into, or may enter into, with third parties to perform sales and marketing services will generate lower product revenues or profitability of product revenues to us than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our products or product candidates. Factors that may materially affect our efforts to commercialize our products include:

- our ability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- our ability to monitor the legal and regulatory compliance of sales and marketing personnel;
- an inability to secure adequate coverage and reimbursement by government and private health plans;
- reduced realization on government sales from mandatory discounts, rebates and fees, and from price concessions to private health plans and pharmacy benefit managers necessitated by competition for access to managed formularies;
- the clinical indications for which the products are approved and the claims that we may make for the products;
- limitations or warnings, including distribution or use restrictions, contained in the products' approved labeling;
- any distribution and use restrictions imposed by the FDA or to which we agree as part of a mandatory REMS or voluntary risk management plan;
- liability for sales or marketing personnel who fail to comply with the applicable legal and regulatory requirements;
- our ability to implement third-party marketing and distribution relationships on favorable terms, or at all, in territories where we do not pursue direct commercialization;
- the ability of our commercial team to obtain access to or persuade adequate numbers of physicians to prescribe our current or any future products;
- the lack of complementary products to be offered by our commercial team, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercial organization.

Any of these factors, individually or as a group, if not resolved in a favorable manner may have a material adverse effect on our business and results of operations. Similar risks apply in those territories where any of our products are available on a reimbursed basis under an EAP program.

A substantial portion of our commercial sales currently occurs in territories outside of the United States which subjects us to additional business risks that could adversely affect our revenue and results of operations.

We commercialize Translarna, Upstaza, Tegsedi and Waylivra outside of the United States. We have operations in multiple European countries, Latin America and other territories. We expect that we will continue to expand our international operations in the future, including in emerging growth markets, pending successful completion of the applicable regulatory processes. International operations inherently subject us to a number of risks and uncertainties, including:

- political, regulatory, compliance and economic developments that could restrict our ability to manufacture, market and sell our products, including the Russia-Ukraine conflict and related sanctions that have been imposed by various countries in response thereto;
- financial risks such as longer payment cycles, difficulty collecting accounts receivable, potentially high inflation rates, sustained high interest rates and exposure to fluctuations in foreign currency exchange rates;
- difficulty in staffing and managing international operations;
- potentially negative consequences from changes in or interpretations of tax laws;
- changes in international medical reimbursement policies and programs;
- unexpected changes in healthcare policies of ex-U.S. jurisdictions;
- trade protection measures, including import or export licensing requirements and tariffs;
- our ability to develop relationships with qualified local distributors and trading companies;
- political and economic instability in particular ex-U.S. economies and markets, in particular in emerging markets, for example in Brazil;
- diminished protection of intellectual property in some countries outside of the United States;
- differing labor regulations and business practices;

- regulatory and compliance risks that relate to maintaining accurate information and control over sales and distributors' and service providers' activities that may fall within the purview of the Foreign Corrupt Practices Act, UK Bribery Act or similar local regulation; and
- various effects and responsive measures relating to outbreaks of contagious disease.

For example, the Brazilian Ministry of Health has previously experienced significant administrative delays processing centralized group purchase orders. Almost all of our product revenue for Translarna in Brazil is attributable to such purchase orders. These centralized group purchase order delays have caused, and may continue to cause, fluctuations in our ability to generate revenue in Brazil.

In addition, some countries in which a product candidate is not approved allow patients access to the product candidate through other legal mechanisms, including court intervention or EAP programs, if the product is approved in another jurisdiction. The price that is ultimately approved by governmental authorities in any country pursuant to commercial pricing and reimbursement processes may be significantly lower than the price we are able to charge for sales under such legal mechanisms and we may become obligated to repay such excess amount.

Some of the countries in which our products are available for sale are in emerging markets. Some countries within emerging markets, including those in Latin America, may be especially vulnerable to periods of global or regional financial instability or may have very limited resources to spend on. We also may be required to increase our reliance on third-party agents within less developed markets. In addition, many emerging market countries have currencies that fluctuate substantially and if such currencies devalue and we cannot offset the devaluations, our financial performance within such countries could be adversely affected.

Furthermore, in some countries, including Brazil and Russia, orders for named patient sales may be for multiple months of therapy, which can lead to an unevenness in orders which could result in significant fluctuations in quarterly net product sales. Other factors may also contribute to fluctuations in quarterly net product sales including a product's availability in any particular territory, government actions, economic pressures, political unrest and other factors. Net product sales are impacted by factors such as the timing of decisions by regulatory authorities and our ability to successfully negotiate favorable pricing and reimbursement processes on a timely basis in the countries in which we have or may obtain regulatory approval, including the United States, EEA and other territories.

Any of these factors may, individually or as a group, have a material adverse effect on our business and results of operations. As we continue to expand our existing international operations, we may encounter new risks.

Laws and regulations governing export restrictions and economic sanctions may preclude us from developing and selling certain products, generating revenue from such products, and manufacturing certain materials outside of the United States.

Many countries, including the United States, restrict the export or import of products to or from certain countries through, for example, bans, sanction programs, and boycotts. Such restrictions may preclude us from supplying products or generating revenue in certain countries or may require an export license prior to the export of the controlled item. Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Furthermore, if we, or third parties acting on our behalf, do not comply with these restrictions, we may be subject to substantial civil and criminal penalties and suspension or debarment from government contracting.

Our activities outside of the United States, require that we dedicate resources to comply with these laws. Many of our customers and suppliers are ex-U.S. entities or have significant ex-U.S. operations. Although these restrictions have not affected our operations in the past, there is a risk that they could do so in the future as additional geographic regions and entities may become subject to such restrictions. The imposition of new or additional economic and trade sanctions against our major customers or suppliers or financial counterparties or intermediaries could result in our inability to sell to, and generate revenue from such customers or purchase materials from such suppliers. For example, we make sales of Translarna through a distributor to the Ministry of Health of the Russian Federation to access Russian nmDMD patients.

Our ability to generate and realize revenue in Russia may be materially and adversely impacted as many countries, including the United States, have imposed and may continue to consider imposing additional enhanced export controls on certain products and sanctions on certain industry sectors and parties in Russia in connection with the Russia-Ukraine conflict. We also contract with government-owned hospitals and third-party manufacturers located in China, which has recently been involved in political conflict with the United States. This conflict has increased the likelihood of restrictions that could materially and adversely affect our clinical trial sites located in China, our ability to obtain certain supplies, our ability to manufacture certain product candidates and our ability to potentially commercialize products in China. If our activities are affected because of these or other such restrictions, sanctions, or controls, our business, financial condition and results of operations could be materially and adversely affected. As a result of restrictive export laws, our customers may also seek to obtain a greater supply of similar or substitute products from our competitors that are not subject to these restrictions, which could materially and adversely affect our business, financial condition and results of operations.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current products and product candidates and any products we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Other gene therapy companies may in the future decide to utilize existing technologies to address unmet needs that could potentially compete with our product candidates.

There is currently no marketed therapy specifically for nmDMD, other than Translarna in the EEA. Santhera Pharmaceuticals has received approval of Agramee (vamorolone) in the United States for DMD patients ages 2 and up and in the EU and United Kingdom for patients ages 4 years and older. Sarepta Therapeutics has received approval of Elevidys for DMD patients 4 to 5 years of age with a confirmed mutation in the "DMD gene" in the United States and United Arab Emirates and Qatar. Sarepta Therapeutics has also received approval in the United States for two treatments (Exondys 51 (eteplirsen) and Vyondys 53 (golodirsen)) addressing the underlying cause of disease for different mutations in the DMD gene. Additionally, the FDA granted accelerated approval to Viltepso (viltolarsen) from NS Pharma for the treatment of DMD in patients with exon 53 skipping and Sarepta (Casimersen (SRP 4045) for the treatment of DMD in patients with exon 45 skipping. Viltepso (viltolarsen) from NS Pharma is also approved in Japan. Other biopharmaceutical companies are developing treatments addressing the underlying cause of disease for different mutations in the DMD gene, including, Dyne Therapeutics (DYNE-251), Wave Life Sciences (WVE-N53), Daiichi Sankyo (DS 5141)), Nippon Shinyaku (Viltolarsen (NS 065/NCNP 01) and NS 089/NCNP 02)), and Astellas (AT 702). Additionally, other pharmaceutical companies are developing micro dystrophin gene therapies for patients with DMD regardless of genotype, including Pfizer (PF 06939926) and Solid Biosciences (SGT 001).

With the expiration of Emflaza's orphan exclusivity for treatment of DMD in patients five years and older in February 2024, we face competition from generic versions of Emflaza for this indication. Although the FDA has not approved a corticosteroid specifically for DMD in the United States other than Emflaza, we face competition in the United States in the DMD market from prednisone/prednisolone, which, while not approved for DMD in the United States, is generically available and has been prescribed off label for DMD patients. Santhera has received approval of Agramee (vamorolone), in the United States for DMD patients ages 2 and up and in the European Union and United Kingdom for patients ages 4 years and older.

Currently, no other treatment options are available for the underlying cause of AADC deficiency. Additionally, we are not aware of any late-stage development product candidates for AADC deficiency.

There are several pharmaceutical and biotechnology companies engaged in the development or commercialization of products against targets that are also targets of Tegsedi and Waylivra. For example, Ionis is developing Olezarsen for the treatment of FCS. Additionally, Waylivra faces competition from Myalept (metreleptin) produced by Chesi Farmaceutica, Inc., which is currently approved in Brazil for use in generalized lipodystrophy patients. Tegsedi faces competition from drugs like Onpattro (patisiran) which was launched by Alnylam Pharmaceuticals in the United States in 2018 and received approval in Brazil for the treatment of hATTR amyloidosis in 2020 as was well as AMVUTTRA (vutrisiran) which Alnylam Pharmaceuticals received approval for in the United States and Brazil in 2022 for the treatment of the

polyneuropathy of hATTR amyloidosis in adults. Vyndaqel (tafamids meglumine) and Vyndamax (tafamidis) are commercialized in the United States, EU and some countries in Latin America by Pfizer. Other companies are also pursuing product candidates for the treatment of ATTR Amyloidosis with polyneuropathy including BridgeBio Pharma (AG 10), Intellia Therapeutics (NTLA2001), Proclara Biosciences (NPT 189) and SOM Biotech (tolcapone). For Waylivra, Ionis is developing Olezarsen for the treatment of FCS. Waylivra also faces competition from Myalept, (metreleptin) produced by Cheisi Farmaceutica, Inc., currently approved in Brazil for use in generalized lipodystrophy patients.

Evrysdi, an orally bioavailable treatment, faces competition from treatments that are not orally bioavailable, including Spinraza (nusinersen), a drug developed by Ionis and marketed by Biogen, which is approved to treat SMA and Zolgensma (onasemnogene abeparvovec), a gene therapy drug developed by AveXis, Inc., (acquired by Novartis in 2018), which is approved in the United States and Japan for the treatment of SMA in patients under 2 years of age and in Europe for babies and young children who weigh up to 21 kilograms. Novartis is also developing OAV-101, an intrathecal administration of Zolgensma, for SMA patients ages ≥ 2 to < 18 years of age. Biogen is developing a higher dose regimen of nusinersen with potential for improved efficacy and evaluating an implantable medical device to enable subcutaneous delivery of nusinersen. Other companies are also pursuing product candidates for the treatment of SMA, including Scholar Rock (apitegromab, SRK-015), Biohaven (Taldefgrobep alfa), Roche Pharmaceuticals (RO-7204239/GYM-329), Biogen / Ionis (BIIB-115/ION-306) and NMD Pharma (NMD-670).

If approved, sepiapterin could face competition from Kuvan (sapropterin dihydrochloride), including generic versions, and Palynziq (pegvaliase-pqpz), each of which is approved for the treatment of PKU. Other companies are also pursuing product candidates for the treatment of PKU, including Otsuka Pharmaceutical (JNT-517), SOM Biotech (SOM-1311), Maze Therapeutics (MZE-782) and Agios (AG-181).

If approved, vatiquinone could face competition from Skyclarys (omaveloxolone) from Biogen, which is approved in the United States and the EU. There are also two assets in early development: LX-2006 (Lexeo/Frataxin AAVrh10) and CTI-1601 (Larimar Therapeutics).

For additional discussion regarding the competition we face with respect to our current product candidates, see “Item 1. Business-Competition.”

Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are marketing or developing or that would render our products or product candidates obsolete or non-competitive. Our competitors may also obtain marketing authorization for their products more rapidly than we may obtain approval for our products and product candidates, which could result in our competitors establishing a strong market position before we are able to enter the market.

We believe that many competitors are attempting to develop therapeutics for the target indications of our products and product candidates, including academic institutions, government agencies, public and private research organizations, large pharmaceutical companies and smaller more focused companies.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to or necessary for our programs.

Our products or product candidates may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

We may not obtain adequate coverage or reimbursement for our products, or we may be required to sell our products at an unsatisfactory price. In addition, obtaining pricing, coverage and reimbursement approvals can be a time consuming and

expensive process. Our business would be materially adversely affected if we do not receive these approvals on a timely basis.

The regulations and practices that govern marketing authorizations, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries, including almost all of the member states of the EEA, require approval of the sale (list) price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some ex-U.S. markets, including the European market, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing authorization for a product in a particular country, but then be subject to price regulations, in some countries at national as well as regional levels, that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more products or other product candidates, even following marketing authorization.

Our ability to successfully commercialize our products or product candidates that may receive marketing authorization will depend in large part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, managed healthcare organizations and other third-party payors and organizations. Government authorities and other third-party payors, such as private health insurers and managed healthcare organizations, decide which medications they will pay for and establish reimbursement conditions and rates. A primary trend in the EU and U.S. healthcare industries and elsewhere is cost containment. Government authorities, including the United States government and state legislatures, and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Prices at which our products are reimbursed can be subject to challenge, reduction or denial by the government and other payers. Increasingly, third-party payors are requiring that drug companies provide them with discounts off the products' sale (list) prices and are challenging the prices manufacturers charge for medical products. We cannot be sure that coverage will be available for any product or product candidate that we may commercialize and, if coverage is available, the level of reimbursement is also uncertain.

Reimbursement levels may impact the demand for, or the price of, any product or product candidate for which we obtain marketing authorization. Obtaining reimbursement for our products has been and is expected to continue to be, particularly difficult due to price considerations typically associated with drugs that are developed to treat conditions that affect a small population of patients. In addition, third-party payors are likely to impose strict requirements for reimbursement of a higher priced drug, such as prior authorization and the requirement to try other therapies first (i.e., step edits), or high co-payments which can result in patient rejection. Decreases in third-party reimbursement for a product or a decision by a third-party payor to not cover a product could reduce physician usage of the product. If reimbursement is not available or is available only on a limited basis, we may not be able to successfully commercialize any product or product candidate for which we have obtained or may obtain marketing authorization.

There may be significant delays in obtaining coverage for newly approved drugs, and coverage may be more limited than the drug's approved indications as determined by the applicable regulatory authority. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent, and programs intended to provide patient assistance until coverage is established can be very costly and limited in duration by law. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Further, coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws, enforcement policies or administrative determinations with respect to the importation of drugs into the United States from other countries where they may be sold at lower prices.

In the United States, third-party payors include federal healthcare programs, such as Medicare, Medicaid, TRICARE, and Veterans Health Administration programs; managed care providers, private health insurers and other organizations. Several of the U.S. federal healthcare programs establish ceiling prices or require that drug manufacturers extend discounts or pay rebates to certain programs in order for their products to be covered and reimbursed. For example, the Medicaid Drug Rebate Program requires pharmaceutical manufacturers of covered outpatient drugs to enter into and have in effect a national rebate agreement with the federal government as a condition for coverage of the manufacturer's covered outpatient drug(s) by state Medicaid programs. The amount of the rebate for each product is based on a statutory formula and may be subject to an additional discount if certain pricing increases more than inflation. State Medicaid programs and Medicaid managed care plans can seek additional "supplemental" rebates from manufacturers in connection with states' establishment of preferred drug lists. A further requirement for Medicaid coverage is that manufacturers of single source and innovator multiple source drugs enter into a Master agreement and Federal Supply Schedule, or FSS, agreement with the Secretary for Veterans Affairs and charge no more than statutory ceiling prices to the Department of Veteran Affairs, the Department of Defense and certain other federal agencies.

Similarly, in order for a covered outpatient drug to receive federal reimbursement under the Medicare Part B and Medicaid programs, the manufacturer must extend discounts on the covered outpatient drug to entities that are enrolled and participating in the 340B drug pricing program, which is a federal program that requires manufacturers to provide discounts to certain statutorily-defined safety-net providers. The 340B discount for each product is calculated based on certain Medicaid Drug Rebate Program metrics that manufacturers are required to report to CMS.

Emflaza is also eligible for reimbursement under the Medicare Part D program. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities, which will provide coverage of outpatient prescription drugs. Part D prescription drug formularies are required to include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain, and payment of Medicare Coverage Gap discounts may further reduce realization on Part D drugs. Further, CMS is proposing to relax Part D coverage requirements to give plans more leverage in negotiating their formularies.

With respect to drugs eligible for reimbursement under Medicare Part B, on November 27, 2020, CMS issued an interim final rule implementing a Most Favored Nations payment model under which reimbursement for certain Medicare Part B drugs and biologicals will be based on a price that reflects the lowest per capita Gross Domestic Product-adjusted (GDP-adjusted) price of any non-U.S. member country of the Organisation for Economic Co-operation and Development (OECD) with a GDP per capita that is at least sixty percent of the U.S. GDP per capita. This rule now has been rescinded but other measures, including the Inflation Reduction Act of 2022, or IRA, have been enacted to address the costs of pharmaceuticals. The Inflation Reduction Act of 2022 requires manufacturers of selected drugs to negotiate discounted prices with the Secretary of the Department of Health and Human Services (HHS). Failure to reach an agreement can subject manufacturers to an excise tax or withdraw of all drug products from coverage under Medicare and Medicaid. Drug price negotiations and other program implementation measures could potentially be affected by the Executive Order, *Initial Rescissions of Harmful Executive Orders and Actions,* issued on January 20, 2025 and/or the anticipated change in leadership at Health and Human Services and the Centers for Medicare and Medicaid Services (CMS) under the new administration. Such rules and any additional healthcare reform measures could further constrain our business or limit the amounts that federal and state governments will pay for healthcare products and services, which could result in additional pricing pressures.

In addition, U.S. private health insurers often rely upon Medicare coverage policies and payment limitations in setting their own coverage and reimbursement policies. Any such coverage or payment limitations may result in a similar reduction in payments from non-governmental payors. Payment by private payors is also subject to payor-determined coverage and reimbursement policies that vary considerably and are subject to change without notice. We expect that coverage and reimbursement of Emflaza in the United States will vary from commercial payor to commercial payor. Many commercial payors, such as managed care plans, manage access to prescription drugs partly to control costs to their plans,

and may use drug formularies and medical policies to limit their exposure. Exclusion from policies can directly reduce product usage in the payor's patient population and may negatively impact utilization in other payor plans, as well.

There has been recent negative publicity and increasing legislative and public scrutiny around pharmaceutical drug pricing in the U.S., in particular with respect to orphan drugs and specifically with respect to Emflaza. Moreover, U.S. government authorities and third-party payors are increasingly attempting to limit or regulate drug prices and reimbursement, often with particular focus on orphan drugs. For example, certain drugs with an orphan designation may become subject to price negotiations under the IRA. These dynamics may give rise to heightened attention and potential negative reactions to pricing decisions for Emflaza and products for which we may receive regulatory approval in the future, possibly limiting our ability to generate revenue and attain profitability.

Moreover, in 2017, the U.S. Congress modified and amended certain provisions of the 2010 U.S. healthcare reform legislation (the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, known collectively as the Affordable Care Act), which could have an impact on coverage and reimbursement for healthcare items and services covered by the federal and state healthcare programs as well as plans in the private health insurance market. The so-called "individual mandate" was repealed as part of tax reform legislation adopted in December 2017. Legal challenges to the Affordable Care Act continue to arise and there may be future efforts to modify, repeal, or otherwise invalidate all, or certain provisions of the Affordable Care Act. We cannot assure that the Affordable Care Act, as currently enacted or as amended in the future, will not adversely affect our business and financial results and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

Additionally, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. Failure of the Joint Select Committee on Deficit Reduction to reach required deficit reduction goals triggered the legislation's automatic reduction to several government programs. This legislation resulted in aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031. However, pursuant to the CARES Act and subsequent legislation, these Medicare sequester reductions were suspended through the end of March 2022 and from April 2022 through June 2022, a 1% cut was in effect, with the full 2% cut remaining thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidates is prescribed or used.

In the EU, reference pricing systems and other measures may lead to cost containment and reduced prices with respect to Translarna for the treatment of nmDMD, Upstaza for the treatment of AADC deficiency and other product candidates that might receive marketing authorization in the future. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for our product or any of our product candidates that may receive marketing authorization, or a reduction in coverage for payment rates for our product or any such product candidates, could have a material adverse effect on our business, results of operations and financial condition. In addition, in the EU, an authorized trader, such as a wholesaler, can purchase a medicine in one EU member state and obtain a license to import the product into another EU member state. This process is called "parallel distribution". As a result, a purchaser in one EU member state may seek to import Translarna from another EU member state where Translarna is sold at a lower price. This could have a negative impact on our business, financial condition, results of operations and growth.

Similarly, sales of Emflaza or our other products in the United States could also be reduced if they, or products similar to them, are imported into the United States from lower-priced markets, whether legally or illegally. For example, in the United States, prices for pharmaceuticals are generally higher than in the bordering nations of Mexico and Canada. In October 2020, the Department of Health and Human Services, or HHS, and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. Certain states have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Florida received approval for its SIP from the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price

reduction is required by law. The rule also creates a safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. The effective date of the new safe harbors and the revision to the discount safe harbor was delayed by court order until January 1, 2023. Recent legislation further delayed implementation of the new safe harbors and the revision to the discount safe harbor until January 1, 2032.

There may be future changes in legal and regulatory requirements that may materially impact our results of operation.

Future changes in legal and regulatory requirements may introduce new risks into our operations and future prospects, which we are not able to currently anticipate. By example, changes taking place in the United States associated with a new federal administration, as well as changes in legal standards, including the reduced level of judicial deference due to administrative agencies following a 2024 Supreme Court decision, may introduce uncertainties with respect to our current and future operations and our future likelihood of success. It is possible that new federal or state laws or regulations may be passed, or laws and regulations may be enforced differently than they were before, which may expose us to additional legal and regulatory risk or uncertainty and require the expenditure of additional resources to ensure that we are able to comply. Such actions could also adversely restrict our business and operations. There could also be changes in the FDA's approval standards that could impact our ability to obtain product approval and market our product candidates within the currently anticipated timeframes or otherwise impact the competitive market for our product candidates. Such changes may necessitate the conduct of additional development work, including preclinical and clinical trials, and manufacturing development. By example, for products intended for rare and serious diseases with unmet medical needs, the FDA is authorized to exercise regulatory flexibility when making a medical risk-benefit judgment. It is possible that whether and how the FDA exercises any regulatory flexibility, including with respect to specialized pathways, such as accelerated approval, may change, which could impact our ability to obtain product approval. Further, legal and regulatory changes may impact how we may market and sell our products in the future, if they are approved, as well as how they are reimbursed. Moreover, there could be changes in the federal workforce and agency policies that may result in regulatory delays, including with respect to the FDA's review of marketing applications and other submissions, and that may impact the ability to communicate with and obtain guidance from the agencies. At this time, it is too early to predict the exact nature of any changes that may take place or whether and how they may impact our business and results of operation.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception and based on our current commercial, research and development plans, we expect to continue to incur significant operating expenses for the foreseeable future. We may never generate profits from operations or maintain profitability.

Since inception, we have incurred significant operating losses. As of December 31, 2024, we had an accumulated deficit of $3,646.9 million. We have financed our operations to date primarily through the private offerings of convertible senior notes, public and "at the market offerings" of common stock, proceeds from royalty purchase agreements, net proceeds from our borrowing under our credit agreement with Blackstone, private placements of our convertible preferred stock and common stock, collaborations, bank and institutional lender debt, other convertible debt, grant funding and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease area addressed by our product candidates. We have relied on revenue generated from net sales of Translarna for the treatment of nmDMD in territories outside of the United States since 2014, Emflaza for the treatment of DMD in the United States since 2017, and Upstaza for the treatment of AADC deficiency in the EEA since May 2022. We have also relied on revenue associated with milestone and royalty payments from Roche pursuant to the SMA License Agreement under our SMA program and revenue generated from net sales of Tegsedi and Waylivra in Latin America and the Caribbean. Based on our current commercial, research and development plans, we expect to continue to incur significant operating expenses for the foreseeable future, which we anticipate will be partially offset by revenues generated from the sale of our products and our collaboration and royalty revenues. We expect to continue to generate operating losses through 2025 and, while we anticipate that operating losses generated in future periods should decline versus prior periods, we may never generate profits from operations or maintain profitability. The net losses we incur may fluctuate significantly from period to period.

From time to time, we have engaged in strategic transactions to expand and diversify our product pipeline, including through the acquisition of assets or businesses. In connection with these acquisitions, we have entered into agreements

through which we have ongoing obligations, including obligations to make contingent payments upon the achievement of certain development, regulatory and net sales milestones or upon a percentage of net sales of certain products. See "Item 1. Business-Our Ongoing Acquisition-Related Obligations" for further information regarding our acquisitions and our ongoing obligations. We may engage in additional strategic transactions to expand and diversify our product pipeline, including through the acquisition of assets, businesses, or rights to products, product candidates or technologies or through strategic alliances or collaborations and we may incur expenses, including with respect to transaction costs, subsequent development costs or any upfront, milestone or other payments or other financial obligations associated with any such transaction.

Our current ability to generate revenue from sales of Translarna is dependent upon our ability to maintain our marketing authorizations in the EEA for Translarna for the treatment of nmDMD in ambulatory patients aged two years and older, in Russia for the treatment of nmDMD in patients aged two years and older and in Brazil for the treatment of nmDMD in ambulatory patients two years and older and for continued treatment of patients that become non-ambulatory, as well as in various other countries. The marketing authorization in the EEA is subject to annual review and renewal by the EC following reassessment by the EMA of the benefit-risk balance of the authorization. For example, in February 2023, we submitted an annual marketing authorization request to the EMA. In September 2023, the CHMP gave a negative opinion on the conversion of the conditional marketing authorization to the full marketing authorization of Translarna for the treatment of nmDMD and a negative opinion on the renewal of the existing conditional marketing authorization of Translarna. In January 2024, the CHMP issued a negative opinion for the renewal of the conditional marketing authorization following a re-examination procedure. In May 2024, the EC decided not to adopt the CHMP's negative opinion for the renewal of the conditional marketing authorization of Translarna and returned such opinion to the CHMP for re-evaluation. In June 2024, following the EC's request for re-review, the CHMP issued a negative opinion on the renewal of the conditional marketing authorization of Translarna for the treatment of nmDMD. On October 18, 2024, the CHMP maintained its negative opinion for the renewal of the conditional marketing authorization following the requested reexamination procedure. In accordance with EMA regulations, the EC has 67 days from the date of issuance to adopt the opinion. At this time, the EC has not yet adopted the negative opinion. If the EC adopts the negative opinion, Translarna would no longer have marketing authorization in the member states of the EEA. For more information regarding the risks associated with a potential EC adoption of the CHMP's negative opinion on Translarna's marketing authorization, see Item 1A. Risk Factors, "*We may be unable to continue to commercialize Translarna for nonsense mutation Duchenne muscular dystrophy in the European Economic Area if the European Commission nmDMD in the EEA if the EC adopts the negative opinion issued by the CHMP for the renewal of the existing conditional authorization for Translarna.*" We also expect that our efforts to advance Translarna for the treatment of nmDMD in the United States will be time-consuming and may be expensive. In October 2024, the FDA accepted for review the resubmission of the NDA for Translarna for the treatment of nmDMD. As this was an NDA resubmission following a CRL to the NDA which was filed over protest in 2016, the FDA is not obligated to follow the review timelines under PDUFA guidelines and an action date has not been provided.

We anticipate that we will continue to incur significant expenses in connection with our commercialization efforts in the United States, the EEA, Latin America and other territories, including expenses related to our commercial infrastructure and corresponding sales and marketing, legal and regulatory, and distribution and manufacturing undertakings as well as administrative and employee-based expenses. In addition to the foregoing, we expect to continue to incur significant costs in connection with ongoing, planned and potential future clinical trials and studies for sepiapterin and our splicing and inflammation and ferroptosis programs as well as studies in our products for maintaining authorizations, label extensions and additional indications. We continue to seek marketing authorization for Translarna for the treatment of nmDMD in territories that we do not currently have marketing authorization in and we are exploring other potential mechanisms by which we may provide Translarna to nmDMD patients in the EEA if the EC adopts the CHMP's negative opinion for Translarna. We also submitted an MAA to the EMA for sepiapterin for the treatment of PKU in March 2024, an NDA to the FDA for sepiapterin for the treatment of PKU in the third quarter of 2024, and an NDA to the FDA for vatiquinone for the treatment of FA in the fourth quarter of 2024. These efforts may significantly impact the timing and extent of our commercialization and manufacturing expenses.

In addition, the clinical and regulatory developments noted in this risk factor may exacerbate the risks related to our commercialization efforts set forth under the heading "Risks Related to the Development and Commercialization of our

Products and our Product Candidates," which could increase the costs associated with our commercial activities or have a negative impact on our revenues.

We may seek to continue to expand and diversify our product pipeline through opportunistically in-licensing or acquiring the rights to products, product candidates or technologies and we may incur expenses, including with respect to transaction costs, subsequent development costs or any upfront, milestone or other payments or other financial obligations associated with any such transaction, which would increase our future capital requirements.

With respect to our outstanding 1.50% convertible senior notes due September 15, 2026, or the 2026 Convertible Notes, cash interest payments are payable on a semi-annual basis in arrears, which will require total funding of $4.3 million annually.

We expect to make payments to the former Censa securityholders of $57.5 million in the aggregate in cash upon the potential achievement in 2025 of regulatory milestones relating to sepiapterin pursuant to the Censa Merger Agreement.

Upon the potential achievement in 2025 of certain regulatory milestones relating to vatiquinone, which milestones would be payable in 2026, we expect to make payments to BioElectron of $75.0 million in the aggregate, in cash or shares of our common stock, as determined by us.

In addition, our expenses will increase if and as we:

- seek to satisfy contractual and regulatory obligations that we assumed through our acquisitions and collaborations;
- execute our commercialization strategy for our products, including initial commercialization launches of our products, label extensions or entering new markets;
- are required to complete any additional clinical trials, non-clinical studies or Chemistry, Manufacturing and Controls, or CMC, assessments or analyses in order to advance our products or product candidates in the United States or elsewhere;
- are required to take other steps to maintain our current marketing authorization in the EEA, Brazil and Russia for Translarna for the treatment of nmDMD or to obtain further marketing authorizations for Translarna for the treatment of nmDMD or other indications;
- initiate or continue the research and development of sepiapterin and our splicing and inflammation and ferroptosis programs as well as studies in our products for maintaining authorizations, label extensions and additional indications;
- seek to discover and develop additional product candidates;
- seek to expand and diversify our product pipeline through strategic transactions;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts.

Our expenses may also increase as a result of economic conditions, such as potentially high inflation rates within the jurisdictions that we operate, sustained high interest rates, or unfavorable fluctuations in foreign currency exchange rates.

Our ability to generate profits from operations and become and remain profitable depends on our ability to successfully develop and commercialize drugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including:

- commercializing and marketing all of our products and products candidates;
- negotiating, securing, and maintaining adequate pricing, coverage and reimbursement terms, on a timely basis, with third-party payors for our products and product candidates;
- maintaining our marketing authorization for Translarna for the treatment of nmDMD in the EEA following the CHMP's negative opinion on the conditional marketing authorization and the EC's potential adoption of the negative opinion;

- advancing Translarna for the treatment of nmDMD in the United States;
- successfully completing any post-marketing requirements imposed by regulatory agencies with respect to our products;
- expanding the territories in which we are approved to market our products;
- successfully advancing our other programs and collaborations, including sepiapterin and our splicing and inflammation and ferroptosis programs as well as studies in our products for additional indications;
- maintaining a global commercial infrastructure, including the sales, marketing and distribution capabilities to effectively market and sell our products and product candidates throughout the world;
- implementing marketing and distribution relationships with third parties in territories where we do not pursue direct commercialization;
- identifying patients eligible for treatment with our products and product candidates;
- successfully developing or commercializing any product candidate or product that we may in-license or acquire;
- protecting our rights to our intellectual property portfolio related to Translarna and other products and product candidates; and
- contracting for the manufacture and distribution of commercial quantities of our products and product candidates.

We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to generate profits from operations. Even if we do generate profits from operations, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to generate profits from operations and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment in our company.

We may need additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

As noted in the prior risk factor, we expect to incur significant expenses related to our clinical, regulatory, commercial, legal, research and development, and other business efforts. We believe that our cash flows from product sales, together with existing cash and cash equivalents, and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next twelve months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

Our future capital requirements will depend on many factors, including:

- our ability to maintain our marketing authorization for Translarna for the treatment of nmDMD in the EEA following the CHMP's negative opinion on the conditional marketing authorization following a re-examination procedure and the EC's potential adoption of the negative opinion, or to identify other potential mechanisms in which we may provide Translarna to nmDMD patients in the EEA;
- our ability to maintain the marketing authorization for Translarna and our other products in territories outside of the EEA;
- our ability to commercialize and market our products and product candidates that may receive marketing authorization;
- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms, on a timely basis, with third-party payors for our products and products candidates;
- the amount of generic drug competition that we face for Emflaza following its loss of orphan drug exclusivity related to the treatment of DMD in patients five years and older;
- our ability to obtain marketing authorization for sepiapterin for the treatment of PKU in the United States and EEA;
- our ability to obtain marketing authorization for Translarna for the treatment of nmDMD in the United States;
- our ability to obtain marketing authorization for vatiquinone for the treatment of FA in the United States;
- unexpected decreases in revenue or increase in expenses resulting from potential widespread outbreaks of contagious disease;

- our ability to successfully complete all post-marketing requirements imposed by regulatory agencies with respect to our products;
- the progress and results of activities for sepiapterin and our splicing and inflammation and ferroptosis programs as well as studies in our products for maintaining authorizations, label extensions and additional indications;
- the scope, costs and timing of our commercialization activities, including product sales, marketing, legal, regulatory, distribution and manufacturing, for any of our products and for any of our other product candidates that may receive marketing authorization or any additional territories in which we receive authorization to market Translarna;
- the costs, timing and outcome of regulatory review of sepiapterin and our splicing and inflammation and ferroptosis programs and Translarna and Upstaza in other territories;
- our ability to satisfy our obligations under the indenture governing the 2026 Convertible Notes;
- the timing and scope of any potential future growth in our employee base;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates, including those in our splicing and inflammation and ferroptosis programs;
- revenue received from commercial sales of our products or any of our product candidates;
- our ability to obtain additional and maintain existing reimbursed named patient and cohort EAP programs for Translarna for the treatment of nmDMD on adequate terms, or at all;
- the ability and willingness of patients and healthcare professionals to access Translarna through alternative means if pricing and reimbursement negotiations in the applicable territory do not have a positive outcome;
- the costs of preparing, filing and prosecuting patent applications, maintaining, and protecting our intellectual property rights and defending against intellectual property-related claims;
- the extent to which we acquire or invest in other businesses, products, product candidates, and technologies, including the success of any acquisition, in-licensing or other strategic transaction we may pursue, and the costs of subsequent development requirements and commercialization efforts, including with respect to our acquisitions of Emflaza, Agilis, our inflammation and ferroptosis platform and Censa and our licensing of Tegsedi and Waylivra; and
- our ability to establish and maintain collaborations, including our collaborations with Roche, the SMA Foundation and our collaboration with Novartis, and our ability to obtain research funding and achieve milestones under these agreements.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales for certain product candidates or indications. In addition, our products and product candidates, if approved, may not achieve sustained commercial success. Likewise, if we fail to maintain our marketing authorization or lose non-patent market exclusivity for our products and product candidates, we will be unable to commercialize and generate revenue from the sales of those products.

Accordingly, we may need to continue to rely on additional financing in connection with our continuing operations and to achieve our business objectives. In addition, we may seek additional capital due to favorable market conditions or based on strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. Additional financing may not be available to us on acceptable terms or at all. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or our commercialization efforts.

We may engage in strategic transactions to acquire assets, businesses, or rights to products, product candidates or technologies or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt, or cause us to incur significant expense.

As part of our business strategy, we may engage in additional strategic transactions to expand and diversify our product pipeline, including through the acquisition of assets, businesses, or rights to products, product candidates or technologies or through strategic alliances or collaborations, similar to our acquisitions of Emflaza, Agilis, Censa and BioElectron's assets and the Tegsedi-Waylivra Agreement. We may not identify suitable strategic transactions, or complete such transactions in a timely manner, on a cost-effective basis, or at all. Moreover, we may devote resources to potential

opportunities that are never completed, or we may incorrectly judge the value or worth of such opportunities. Even if we successfully execute a strategic transaction, we may not be able to realize the anticipated benefits of such transaction, may incur additional debt or assume unknown or contingent liabilities in connection therewith, and may experience losses related to our investments in such transactions. Integration of an acquired company or assets into our existing business may not be successful and may disrupt ongoing operations, require the hiring of additional personnel and the implementation of additional internal systems and infrastructure, and require management resources that would otherwise focus on developing our existing business. Even if we are able to achieve the long-term benefits of a strategic transaction, our expenses and short-term costs may increase materially and adversely affect our liquidity. Any of the foregoing could have a detrimental effect on our business, results of operations and financial condition.

In addition, future strategic transactions may entail numerous operational, financial and legal risks, including:

- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- exposure to known and unknown liabilities, including possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- higher than expected acquisition and integration costs;
- difficulty in integrating operations and personnel of any acquired business;
- increased amortization expenses or, in the event that we write-down the value of acquired assets, impairment losses;
- impairment of relationships with key suppliers or customers of any acquired business due to changes in management and ownership;
- inability to retain personnel, customers, distributors, vendors and other business partners integral to an in-licensed or acquired product, product candidate or technology;
- potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges;
- entry into indications or markets in which we have no or limited direct prior development or commercial experience and where competitors in such markets have stronger market positions; and
- other challenges associated with managing an increasingly diversified business.

If we are unable to successfully manage any strategic transaction in which we may engage, our ability to develop new products and continue to expand and diversify our product pipeline may be limited.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate enough product revenues to cover our expenses, we expect to supplement our cash needs through a combination of equity offerings, debt financings, royalty sales, collaborations, strategic alliances, grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates; marketing, distribution, licensing or other arrangements.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Any debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, entering into agreements involving licenses to our intellectual property, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates; or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our ability to use our net operating losses and certain other tax attributes to offset potential taxable income and related income taxes that would otherwise be due is subject to limitation under the provisions of Sections 382 and 383 of the Internal Revenue Code as a result of ownership changes of the Company and could be subject to further annual limitations under such provisions. In addition, we may not generate sufficient future taxable income to use our net operating losses and certain other tax attributes.

If a corporation undergoes an "ownership change" within the meaning of Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or Sections 382 and 383, the corporation's ability to utilize any net operating losses, or NOLs, and certain tax credits and other tax attributes generated before such an ownership change, is limited. We believe that we have in the past experienced ownership changes within the meaning of Sections 382 and 383 that have resulted in limitations under Sections 382 and 383 (and similar state provisions) on the use of our NOLs and other tax attributes.

Sections 382 and 383 are extremely complex provisions with respect to which there are many uncertainties, and we have not requested a ruling from the United States Internal Revenue Service, or IRS, to confirm our analysis of the ownership change limitations related to the NOLs and other tax attributes generated by us. Therefore, we have not established whether the IRS would agree with our analysis regarding the application of Sections 382 and 383. We continue to fully evaluate the impact of a limitation on the use of our NOLs and other tax attributes under Sections 382 and 383.

Moreover, our ability to use these NOLs to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income. We generated taxable income that is subject to income tax in 2024, but continue to maintain NOLs from previous years that will be carried forward.

Changes in our effective income tax rates and future changes to U.S. and non-U.S. tax laws could adversely affect our results of operations.

We are subject to income taxes in the Unites States and various ex-U.S. jurisdictions. Taxes will be incurred as income is earned in these different jurisdictions. Various factors may have favorable or unfavorable effects on our effective income tax rate. These factors include, but are not limited to, interpretations of existing tax laws, changes in tax laws and rates, the accounting for stock options and other share-based compensation, changes in accounting standards, future levels of research and development spending, changes in the mix and level of pre-tax earnings by taxing jurisdiction, the outcome of examinations by the IRS and other taxing authorities, the accuracy of our estimates for unrecognized tax benefits, the realization of deferred tax assets, or changes to our ownership or capital structure. The impact on our income tax provision resulting from the above-mentioned factors and others may be significant and could adversely affect our results of operations.

Changes in tax laws or regulations, including further regulatory developments arising from U.S. tax reform legislation as well as multi-jurisdictional changes enacted in response to the action items provided by the Organization for Economic Cooperation and Development (OECD), may increase tax uncertainty and the amount of tax we pay.

On December 22, 2017, the United States government enacted the 2017 Tax Act, which significantly reformed the U.S. Internal Revenue Code of 1986, as amended, or the Code. The Tax Act, among other things, contained significant changes to corporate taxation. As part of Congress's response to the COVID-19 pandemic, economic relief legislation was enacted in 2020 and 2021. Such legislation contains numerous tax provisions. In addition, the IRA was signed into law in August 2022. The IRA introduced new tax provisions, including a 1% excise tax imposed on certain stock repurchases by publicly traded corporations. The 1% excise tax generally applies to any acquisition by the publicly traded corporation (or certain of its affiliates) of stock of the publicly traded corporation in exchange for money or other property (other than stock of the corporation itself), subject to a *de minimis* exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases.

Regulatory guidance under the 2017 Tax Act, the IRA, and such additional legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen the impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the 2017 Tax Act, the IRA, and additional tax legislation.

Although we monitor actual and potential changes to the tax laws in the United States and other jurisdictions, it is very difficult to assess to what extent these changes may impact the way in which we conduct our business or our effective tax rate due to the unpredictability and interdependency of these changes. Changes in tax laws and related regulations and practices could have a material adverse effect on our business operations, cash flows, effective tax rate, financial position and results of operations.

Risks Related to Regulatory Approval of our Products and our Product Candidates

We may not be able to obtain orphan drug exclusivity for our products or product candidates in either the United States or the EU.

Regulatory authorities in some jurisdictions, including the EU and the United States, may designate drugs for relatively small patient populations as orphan drugs. We have obtained orphan drug designations from the EMA and from the FDA for Translarna for the treatment of nmDMD, Upstaza/Kebilidi for the treatment of AADC, Evrysdi for the treatment of SMA, sepiapterin for the treatment of patients with hyperphenylalaninemia, including hyperphenylalaninemia caused by PKU and vatiquinone for the treatment of FA. The FDA has also granted an orphan drug designation to Emflaza for the treatment of DMD. We may also seek orphan drug designation and exclusivity for other product candidates, if we believe that the product candidate may qualify. We, however, may not be able to obtain orphan drug designation in the future for any of our other product candidates and, even if we obtain designation, we may ultimately not be able to obtain orphan drug exclusivity. Obtaining orphan drug exclusivity, both in the EU and in the United States, may be important to a product candidate's future success.

In the EU, if an orphan designated product subsequently receives the first marketing authorization for the indication for which it has received such a designation, the product is entitled to 10 years of market exclusivity, which, subject to certain exceptions, precludes the EMA from accepting another marketing application for a similar medicinal product, even if the new marketing application relies on independently generated data submitted as part of a full marketing authorization application dossier. The EU exclusivity period can be reduced to six years, at the end of the fifth year, if a drug no longer meets the criteria for orphan drug designation, including if the drug is sufficiently profitable so that market exclusivity is no longer justified. In addition, a competing similar medicinal product may in limited circumstances be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to the orphan product. In this context, a "similar medicinal product" is a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. Product candidates can also lose orphan designation, and the related benefits, prior to obtaining a marketing authorization if it is demonstrated that the orphan designation criteria are no longer met. The EC has conducted a review of the Orphan Drug Regulation together with the Paediatric Regulation. The outcome of this review is intended to guide future legislative changes and shape the EU's pharmaceutical strategy.

In the United States, under FDA's current policy, if a product with an orphan drug designation subsequently receives the first marketing authorization for the indication for which it has such designation, the product is entitled to seven years of market exclusivity which precludes the FDA from approving another marketing application for the "same drug" for the same orphan designated approved indication for that time period. When determining whether a drug is the "same drug" as an orphan designated product, the FDA looks to the products' molecular features and use. The specific sameness criteria, however, varies based on whether the product is composed of small or large molecules and if the product is a gene therapy. Moreover, for gene therapies, the sameness criteria are currently evolving. For example, the FDA issued a final guidance document specific to sameness determinations. Depending on product characteristics, sameness may be determined by the FDA on a case-by-case basis, making it difficult to predict when FDA may approve a product and whether periods of exclusivity will effectively block competitors seeking to market products that are the same or similar to ours for the same intended use. Moreover, following the Catalyst Pharms., Inc. v. Becerra and FDA's subsequent statement that it intends to continue to apply its regulations tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, as further described in this filing, the exact scope of orphan drug exclusivity may be an evolving space. Accordingly, whether any of our products or product candidates will be deemed to be the same as another product or product candidate is uncertain and the scope of any potential or received orphan drug exclusivity period, as well as any of our competitors that may block approval of one of our product candidates, may be subject to revision.

Obtaining orphan drug designation does not guarantee that we will be able to receive ultimate marketing approval. Orphan drug designation neither shortens the development time or regulatory review time of a product candidate nor gives the product candidate any advantage in the regulatory review or approval process. Moreover, the FDA may grant orphan drug designation to multiple products that are considered to be the "same drug" for the same indication. If a competitor obtains an orphan drug designation for and approval of a product with orphan drug exclusivity for the same indication as one of our product candidates before we do and if the competitor's product is the same drug, in the United States or a similar medicinal product, in the EU, as ours, we could be excluded from the market for a period of time.

We also may not be able to maintain any orphan drug designations or exclusivities. For instance, orphan drug designations may be revoked if the FDA finds that the request for designation contained an untrue statement of material fact or omitted material information, or if the FDA finds that the product candidate was not eligible for designation at the time of the submission of the request. Even if we are able to receive and maintain orphan drug designations, we may ultimately not receive any period of regulatory exclusivity if our product candidates are approved. For instance, we may not receive orphan product regulatory exclusivity if the indication for which we receive FDA approval is broader than the orphan drug designation. Orphan exclusivity may also be lost for the same reasons that designation may be lost. Orphan exclusivity may further be lost if we are unable to assure a sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Further, even if we do receive orphan drug exclusivity upon approval of a product candidate, this exclusivity is not absolute. For example, if a competitive product that is the same drug or a similar medicinal product as one of our approved products with orphan exclusivity is shown to be "clinically superior" to our product candidate as determined by the FDA or EMA, respectively, any orphan drug exclusivity we have obtained will not block the approval of such competitive product. Orphan exclusivity also would not block the FDA from approving a drug that is the same as our product candidates for different indications or products that are different from ours for the same indication. Moreover, marketing exclusivity would not prevent a provider from prescribing or using another drug off-label and third-party payors may reimburse for products off-label even if not indicated for the orphan condition.

For certain of our products, periods of orphan drug exclusivity are important. For instance, for Emflaza, we have previously relied on non-patent market exclusivity periods under the Orphan Drug Act to commercialize Emflaza in the United States. Emflaza's seven-year period of orphan drug exclusivity related to the treatment of DMD in patients five years and older expired in February 2024. We expect the expiration of this orphan drug exclusivity to have significant negative impact on Emflaza net product revenue, as we face competition from generic versions of Emflaza for this indication, which are generally priced less than Emflaza. Emflaza's orphan drug exclusivity related to the treatment of DMD in patients two years of age to less than five expires in June 2026. Healthcare providers may also substitute the generic version(s) of Emflaza for patients two years of age to five, despite the fact that the generic version(s) will not be approved for such indication until after June 2026.

The respective orphan designation and exclusivity frameworks in the United States and in the EU are subject to change, and any such changes may affect our ability to obtain, or the impact of obtaining, EU or United States orphan designations in the future.

All pharmaceutical products for which marketing authorization has been granted are subject to extensive and rigorous governmental regulation and could be subject to restrictions or withdrawal from the market. We may also be subject to penalties or other enforcement if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved, as well as our product candidates during development.

We, our products and product candidates, our operations, our facilities, our suppliers and our contract manufacturers, distributors, contract research organizations, clinical trial sites and contract testing laboratories are subject to extensive regulation by governmental authorities in the EEA, the United States, and other territories, with regulations differing from country to country.

We are not permitted to market our product candidates in the EEA, the United States, or other territories until we have received requisite regulatory approvals. In order to receive and maintain such approvals, and to be compliant with

regulatory authority requirements, we and our third-party service providers must comply on a continuous basis with a broad array of regulations and requirements. Depending on the stage of product development and whether a product is approved these requirements may relate to establishment registration and product listing, the payment of user fees, manufacturing processes, risk management measures, quality and pharmacovigilance systems (including reporting of manufacturing deviations and adverse events), pre- and post-approval clinical and pre-clinical data and study conduct, labeling, packaging, advertising, marketing and promotional activities (including product sampling), record keeping, distribution, storage, and import and export of pharmaceutical products. Any regulatory approval of any of our products or product candidates, once obtained, may be withdrawn. For example, our marketing authorization for Translarna for the treatment of nmDMD in the EEA is subject to annual review and renewal by the EC following reassessment by the EMA of the benefit-risk balance of the authorization, as well as the specific obligation to conduct and report the results of Study 041. In January 2024, the CHMP issued a negative opinion for the renewal of the conditional marketing authorization following a re-examination procedure. In May 2024, the EC decided not to adopt the CHMP's negative opinion for the renewal of the conditional marketing authorization of Translarna and returned such opinion to the CHMP for re-evaluation. In June 2024, following the EC's request for re-review, the CHMP issued a negative opinion on the renewal of the conditional marketing authorization of Translarna for the treatment of nmDMD. On October 18, 2024, the CHMP maintained its negative opinion for the renewal of the conditional marketing authorization following the requested reexamination procedure. In accordance with EMA regulations, the EC has 67 days from the date of issuance to adopt the opinion. At this time, the EC has not yet adopted the negative opinion. If the EC adopts the negative opinion, Translarna would no longer have marketing authorization in the member states of the EEA.

After approving a drug, the FDA may withdraw product approval if compliance with regulatory standards is not maintained or if safety problems occur after the product reaches the market. Requirements for additional clinical trials and studies to confirm safety and effectiveness may be imposed as a condition of marketing approval. In addition, the FDA requires surveillance programs to monitor approved products that have been commercialized, as well as REMS, and the agency has the power to require changes in labeling or to prevent further marketing and distribution of a product. For example, we were obligated to perform certain FDA post-marketing requirements in connection with our marketing authorization for Emflaza in the United States, including clinical safety studies. Additionally, our marketing authorizations for Translarna, Tegsedi and Waylivra in Brazil and our marketing authorization for Translarna in Russia are subject to renewal every five years. There is no guarantee that we will be able to complete our post-marketing obligations in accordance with the established timetables. Failure to complete the required studies in accordance with the established timetables or failure to provide the requisite periodic reports on the status of post-marketing studies in the absence of good cause could result in an enforcement action. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing and distribution.

Regulatory authorities conduct ongoing reviews and inspections or remote regulatory assessments of marketed products, as well as sponsors and manufacturing facilities. Regulatory authorities also conduct inspections of manufacturing facilities and clinical trial sites before approving a product, which can delay approval. If compliance issues are found, it could also result in refusal to approve marketing applications, disruption of production or distribution of a product or product candidate, disruption, cancellation, or suspension of a study, or require substantial resources to correct.

Even if marketing authorization of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed, the product may have labeling that includes significant restrictions, warnings, including black box warnings, and contraindications, the regulatory authorities may not approve label claims necessary for successful product marketing, or the approval may be subject to significant conditions of approval, including the requirement of a REMS. A regulatory authority also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. In addition, the competent authorities of each EU member state and the FDA closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling and regulatory requirements. Such regulatory authorities can and do impose stringent restrictions on our communications regarding off-label use and if we do not comply with the laws governing promotion of approved drugs, we may be subject to enforcement action for off-label promotion. For example, violations of the FDCA relating to the promotion of prescription drugs may lead to civil and criminal penalties, investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, both before and after product approval, may yield various results which could negatively affect our business, including:

- restrictions on such products, manufacturers or manufacturing processes;
- changes to or restrictions on the labeling or marketing of a product;
- modifications to promotional pieces;
- issuance of corrective information;
- clinical holds or termination of clinical trials;
- changes in the way a product is administered;
- liability for harm caused to patients or subjects;
- adverse publicity, reputational harm, or the product becoming less competitive;
- regulatory authority issuance of safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the product;
- restrictions on product distribution or use;
- requirements to implement a REMS;
- requirements to conduct post-marketing studies or clinical trials;
- warning, cyber or untitled letters;
- withdrawal of the products from the market or marketing suspensions;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing authorizations;
- refusal to permit the import or export of our products;
- product seizure or detention;
- injunctions;
- the imposition of civil or criminal penalties; or
- FDA debarment, suspension and debarment from government contracts, and refusal of orders under existing government contracts, exclusion from federal healthcare programs, consent decrees, or corporate integrity agreements.

Non-compliance with regulatory requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with regulatory requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Not only will we be responsible for our own conduct, but we will also be responsible for the conduct of our employees, independent contractors, consultants, commercial partners, manufacturers, investigators, and contract research organizations. To the extent that any of these third parties engage in intentional, reckless, negligent, or unintentional failures to comply applicable legal and regulatory requirements, we may be subject to regulatory enforcement action, legal actions and liability, and serious harm to our reputation. Moreover, it is possible for a whistleblower to pursue a False Claims Act case against us as a result of such third-party conduct, even if the government considers the claim unmeritorious and declines to intervene, which could require us to incur costs defending against such a claim.

Any of the above events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, or could substantially increase the costs and expenses of developing and commercializing such product, which in turn could delay or prevent us from generating significant revenues from its sale. Any of these events could further have other material and adverse effects on our operations and business and could adversely impact our stock price and could significantly harm our business, financial condition, results of operations, and prospects.

We may face competition from biosimilar, generic, and similar products approved through abbreviated pathways, as well as products approved pursuant to full applications.

Our approved products may face competition from products approved via abbreviated pathways as well as products approved pursuant to full applications. For example, our biologic products may face competition from biosimilar or interchangeable products. Sponsors seeking approval of biosimilar or interchangeable products to ours would reference our product in their applications. The applicable laws, however, establish certain protections for reference biologic products. For example, there is a complex and involved framework for sponsors to bring patent infringement actions and actions for declaratory judgment. Accordingly, we may need to pursue costly and time-consuming patent infringement actions, which may include certain statutorily specified regulatory steps before an infringement action may be brought. We may also need to spend time and money defending an action for declaratory judgement that is brought by the biosimilar product sponsor.

Another protection established for biologic products is a period of 12 years of exclusivity for reference products that begins on the date that the reference product was first licensed by the FDA. During this time, the FDA may not make the licensure of a biosimilar product effective. Biosimilar applications can, however, be submitted for FDA review beginning four years after the date of the reference product's first licensure. This exclusivity period, however, is subject to certain limitations. For example, certain changes and supplements to an approved BLA, and certain subsequent applications filed by the same sponsor, manufacturer, licensor, predecessor in interest, or other related entity do not qualify for the 12-year exclusivity period. Moreover, there have been legislative efforts to decrease this period of exclusivity to a shorter timeframe. Future proposed budgets, international trade agreements and other arrangements or proposals may affect periods of exclusivity. Further, there is a risk that the FDA will not consider our biologic products to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Additionally, this period of regulatory exclusivity does not apply to companies pursuing regulatory approval via their own traditional BLA, rather than via the abbreviated pathway. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet fully clear, and will depend on a number of marketplace and regulatory factors that are still developing. It is also possible that payers will give reimbursement preference to biosimilars, even over reference biologics, absent a determination of interchangeability. Similarly, in the EU, another company could gain approval for a competing product based on an MAA with a completely independent data package that includes pharmaceutical tests, preclinical tests and clinical trials.

For small molecule drug products, a pharmaceutical manufacturer may file an ANDA seeking approval of a generic copy of one of our approved products. A manufacturer could also submit an NDA under section 505(b)(2), referencing the FDA's finding of safety and efficacy for one of our drug products, while also conducting its own studies to support any product changes. Any ANDA or 505(b)(2) NDA products referencing our approved products would be required to submit patent certifications to the FDA. Unless the applicant does not seek approval until any of our Orange Book listed patents expire or, to the extent possible, carve out any of our Orange Book listed method of use patents, such an applicant would be required to submit what is known as a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. This would provide us with an opportunity to sue to enforce our patents, which would stay any FDA approval for 30 months from the patent or application owner's receipt of the notice of the paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent is favorably decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. While this would delay the approval of the generic or 505(b)(2) product, such actions would require significant time and cost.

Our small molecule drug products may also be eligible for certain periods of regulatory exclusivity (e.g., five years for new chemical entities and three years for changes to an approved drug requiring a new clinical study), which preclude FDA approval (or in some circumstances, FDA filing and review of) an ANDA or 505(b) (2) NDA relying on the FDA's finding of safety and effectiveness for the innovative drug. These exclusivities, however, are also subject to certain limitations. For instance, they would not block FDA acceptance and approval of full NDA applications.

Even with the various protections in place, we may not be successful in securing or maintaining proprietary patent protection for our products and product candidates necessary to prevail should we need to bring any challenges under the above FDA regulatory structures. We may also not receive any anticipated periods of regulatory exclusivity. Competition that our products may face from biosimilar, interchangeable, generic, or 505(b)(2) NDA products could materially and

adversely impact our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates. In the United States, this risk has increased in recent years as the FDA and the U.S. government have taken steps to encourage increased drug and biologic competition in the market, in an effort to bring down the cost of pharmaceutical products.

Commercialization of Translarna and Upstaza has been in, and is expected to continue to take place in, countries that tend to impose strict price controls, which may adversely affect our revenues. Failure to obtain and maintain acceptable pricing and reimbursement terms for Translarna for the treatment of nmDMD or Upstaza for the treatment of AADC deficiency in the EEA and other countries where Translarna is available would delay or prevent us from marketing our product in such regions, which would adversely affect our business, results of operations, and financial condition.

In some countries, particularly the member states of the EEA, the pricing of prescription pharmaceuticals is subject to strict governmental control. Each country in the EEA has its own pricing and reimbursement regulations and may have other regulations related to the marketing and sale of pharmaceutical products in the country. We generally will not be able to commence commercial sales of Translarna for the treatment of nmDMD or Upstaza for the treatment of AADC deficiency pursuant to the marketing authorization granted by the EC in any particular member state of the EEA until we conclude the applicable pricing and reimbursement negotiations and comply with any licensing, employment or related regulatory requirements in that country. In some countries we may be required to conduct additional clinical trials or other studies of our product, including trials that compare the cost-effectiveness of our product to other available therapies in order to obtain reimbursement or pricing approval. We may not be able to conclude pricing and reimbursement negotiations or comply with additional regulatory requirements in the countries in which we seek to commercialize Translarna or Upstaza on a timely basis, or at all.

The pricing and reimbursement process varies from country to country and can take a substantial amount of time from initiation to completion. Pricing negotiations may continue after reimbursement has been obtained. We cannot predict the timing of Translarna's or Upstaza's commercial launch in countries where we are awaiting pricing and reimbursement guidelines. While we have submitted pricing and reimbursement dossiers with respect to Translarna for the treatment of nmDMD and Upstaza for the treatment of AADC deficiency in many EEA countries, we have only received both pricing and reimbursement approval on terms that are acceptable to us in a limited number of countries.

The price that is approved by governmental authorities in any country pursuant to commercial pricing and reimbursement processes may be significantly lower than the price we are able to charge for sales under our reimbursed EAP programs and various forms of national "market access agreements" may need to be entered into to achieve reimbursement. In some instances, reimbursement may be subject to challenge, reduction or denial by the government and other payors.

For example, in France, EAP and commercial sales of a product can begin while pricing and reimbursement rates are under discussion with the applicable government health programs. In the event that the negotiated price of the product is lower than the amount reimbursed for sales made prior to the conclusion of price negotiations, we may become obligated to repay such excess amount to the applicable government health program. We will make such retroactive reimbursement, if any, following the conclusion of price negotiations with the applicable government health authority.

Further, based on unsustainable economics imposed by the arbitration board in Germany upon the conclusion of an arbitration process in 2016 with us and the German Federal Association of the Statutory Health Insurances, we delisted Translarna from the German pharmacy ordering system, effective April 1, 2016. While some patients and healthcare professionals in Germany have been able to access Translarna through a reimbursed importation pathway possible under German law, there can be no assurance that other patients or healthcare professionals in Germany will be successful doing so or, if initially successful, that any or all will continue to be successful. We were required to reimburse payors in Germany the difference between the commercial price of Translarna and the price established by the arbitration board in Germany for sales made in Germany after December 2015, other than sales made pursuant to the reimbursed importation pathway.

Political, economic and regulatory developments may further complicate pricing and reimbursement negotiations and there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. In addition, adverse clinical and regulatory developments may exacerbate these risks.

Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices and revenues. Publication of discounts by third-party payors or authorities may lead to further pressure on prices or reimbursement levels within the country of publication and other countries.

If we fail to successfully secure and maintain pricing and reimbursement coverage for Translarna or Upstaza or are significantly delayed in doing so or if burdensome conditions are imposed by private payers, government authorities or other third-party payors on such reimbursement, planned launches in the affected countries will be delayed and our business, results of operations and financial condition could be adversely affected.

Our relationships with customers, healthcare providers and professionals, patients, patient organizations, and third-party payors are or will be subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare professionals and third-party payors play a primary role in the recommendation and prescription of any products or product candidates. Our arrangements with customers, healthcare professionals and third-party payors may expose us to broadly applicable fraud and abuse, transparency and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing authorization. Failure to maintain a comprehensive and effective compliance program, and to integrate the operations of any acquired businesses into a combined comprehensive and effective compliance program on a timely basis, could result in business practices and operations that expose us to a range of regulatory actions that could adversely affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products.

There are numerous restrictions and reporting requirements under applicable U.S. federal and state healthcare laws and regulations, and equivalent laws and regulations in the EU and other countries in which we operate, as well as self-regulatory codes. Efforts to ensure that we and our business arrangements with third parties will comply with applicable healthcare laws, regulations, transparency requirements and self-regulatory codes have and will continue to involve substantial costs. We cannot guarantee that we, our employees, our consultants, our third-party contractors, or the healthcare professionals or entities with whom we expect to do business, are or will be in compliance with all federal, state and ex-U.S. regulations and codes. It is possible that governmental authorities could conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, and the curtailment or restructuring of our operations. Exclusion, suspension and debarment from government funded healthcare, procurement and non-procurement programs would adversely affect, perhaps materially, our ability to commercialize, sell or distribute any drug. Even if we were not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant time and resources and generate negative publicity, which could also have an adverse effect on our business, financial condition and results of operations.

Legislative and regulatory changes affecting the pharmaceutical industry or the healthcare system more broadly may increase the difficulty and cost for us to obtain or maintain marketing authorization of and commercialize our products and product candidates and affect the coverage and reimbursement we may obtain.

Our industry is highly regulated and changes in law may adversely impact our business, operations, or financial results. In the United States and some ex-U.S. jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing authorization of our products or product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products or product candidates for which we have obtained, or may obtain, marketing authorization.

Certain provisions of enacted or proposed legislative changes may negatively impact coverage and reimbursement of healthcare items and services. For example, in the United States, the Medicare Modernization Act requires manufacturers to calculate and report a drug's Average Sales Price used to reimburse providers for physician-administered drugs under

Medicare Part B and changed the way Medicare covers and pays for pharmaceutical products. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and reimbursement that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own policies. Therefore, any restrictions to coverage or reductions in reimbursement that result from the Medicare Modernization Act may result in a similar coverage restriction or reimbursement reduction from private payors. In addition, private payors may implement coverage restrictions or payment reductions independently from federal programs such as Medicare.

Similarly, in the United States, the Affordable Care Act contains provisions that may reduce the profitability of drug products. However, legal challenges to the Affordable Care Act may contribute to the uncertainty of the ongoing implementation and impact of the Affordable Care Act and also underscore the potential for additional reform going forward. We cannot assure that the Affordable Care Act, as currently enacted or as amended in the future, will not adversely affect our business and financial results.

Promulgated and proposed regulatory changes could also affect coverage or reimbursement of our products and in 2016, CMS issued a final rule regarding the Medicaid drug rebate program, which among other things, revises the manner in which the "average manufacturer price" is to be calculated by manufacturers participating in the program and implements certain amendments to the Medicaid rebate statute created under the ACA. More recently, Congress amended the Medicaid statute, effective October 1, 2019, to exclude prices paid by secondary manufacturers for an authorized generic drug (but not a product approved under the BLA process) from the NDA holder's AMP for the brand, thereby increasing the rebate amount and the 340B price for the brand. This was implemented by CMS in a final rule issued December 31, 2020. The rule also expanded the definition of products identified as "line extensions" and, in certain circumstances, required inclusion of patient copay assistance in Medicaid best price (effective January 1, 2023), thereby potentially increasing Medicaid rebates paid by manufacturers for such drugs. 340B program guidance regulations on civil monetary penalties for statutory violations, which had been finalized in early 2017 but deferred, recently also went into effect.

In 2020, the Trump administration issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

More recently, on August 16, 2022, the IRA was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (negotiated prices for the first 10 selected drugs effective beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D effective starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to

achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. Failure to participate in negotiations or to reach an agreement can result in a manufacturer being required to withdraw all drug products from coverage under Medicare and Medicaid. Drug price negotiations and other program implementation measures could potentially be affected by the Executive Order, *Initial Rescissions of Harmful Executive Orders and Actions,* issued on January 20, 2025 and/or the anticipated change in leadership at Health and Human Services (HHS) and the Centers for Medicare and Medicaid Services (CMS) under the new administration.

We anticipate that the U.S. Congress, administrative agencies, state legislatures and the private sector will continue to consider and may adopt healthcare policies intended to curb rising healthcare costs. These cost containment measures may include:

- controls on government funded reimbursement for drugs;
- caps or mandatory discounts under certain government sponsored programs;
- controls on healthcare providers;
- challenges to the pricing of drugs or limits on reimbursement of specific products through other means;
- reform of drug importation laws and policies;
- expansion of use of managed care systems in which the healthcare providers contract to provide comprehensive healthcare for a fixed cost per person; and
- requirements or restrictions related to direct-to-consumer advertising or drug marketing practices.

We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. In particular, we are unable to predict what changes the current administration will implement through the U.S. Congress or future executive orders and how these would impact us. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted, could significantly decrease the available coverage and the price we might establish for our products, which would have an adverse effect on our net revenues and operating results. Changes in FDA laws, regulations, and policies may also make it more difficult to obtain and maintain marketing authorizations.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize Translarna, Upstaza and our product candidates. 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. We cannot predict how future changes relating to healthcare reform in the EU, the United States, or other territories, will affect our business.

Legislative and regulatory proposals have also been made to expand post-approval requirements, limit regulatory exclusivity periods or the applicability of such exclusivity periods, restrict sales and promotional activities for pharmaceutical products and to otherwise encourage competition in the market and bring down drug prices, including proposals and regulatory actions related to drug importation. We cannot be sure whether additional legislative or regulatory changes will be enacted in any territory in which we are authorized, or become authorized, to market our products or product candidates, or whether applicable regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing authorizations of our products or product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process or by comparable ex-U.S. bodies overseeing regulatory authorities in other territories may significantly delay or prevent marketing authorization, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. We cannot predict how future changes relating to pre- and post-marketing approval and requirements will affect our business.

Risks Related to Our Business

We may expend our resources to pursue a particular product, product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We focus on products, research programs and product candidates for specific indications. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential.

For example, in connection with our acquisition of Censa, we paid to the Censa securityholders (i) cash consideration of $15.0 million, which consisted of an upfront payment of $10.4 million and an additional $4.6 million for the net assets on Censa's opening balance sheet as of the date of the acquisition, and (ii) 845,364 shares of our common stock. Censa securityholders may also be entitled to receive contingent consideration payments from us in the future. For example, we expect to make payments to the former Censa securityholders of $57.5 million in the aggregate in cash upon the potential achievement in 2025 of regulatory milestones relating to sepiapterin pursuant to the Censa Merger Agreement. We may never realize the anticipated benefits of the acquisition of Censa and by investing our resources in sepiapterin, we may be required to forgo or delay other opportunities.

In addition, we have previously commenced clinical trials that were not successful for a number of reasons, including inconsistent or negative data and difficulties identifying qualified patients. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

Notwithstanding our large investments to date and anticipated future expenditures in proprietary technologies for small-molecule drug discovery, to date we have been granted marketing authorization for a limited number of commercial products and have not achieved profitability. We may never realize a return on investment. We may not be able to successfully renew or satisfy the ongoing requirements of our current marketing authorizations for our current products and we may never successfully develop any other marketable drugs or indications using our scientific approach. As a result of pursuing the development of product candidates using our proprietary technologies, we may fail to develop product candidates or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development. For example, in November 2024, we announced that the global Phase 2 placebo-controlled CardinALS study of utreloxastat for the treatment of ALS did not meet its primary endpoint of slowing disease progression on the composite ALSFRS-R and mortality analysis. Due to the lack of efficacy and biomarker signal, further development of utreloxastat for the treatment of ALS is not planned at this time after previous investments in this product candidate.

If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We contract with third parties for the manufacture and distribution of our products and certain of our product candidates, which may increase the risk that we will not have sufficient quantities of our products or product candidates, such quantities may not meet the applicable regulatory quality standards, or such quantities at an acceptable cost, which could delay, prevent or impair our commercialization or development efforts.

We have limited personnel with experience in drug manufacturing and currently rely on third parties to manufacture our products and certain product candidates on a clinical or commercial scale. We currently rely on third parties for supply of the active pharmaceutical ingredients used in all of our products and product candidates. We outsource most of the manufacturing, packaging, labeling and distribution of our products and certain of our product candidates to third parties, including our commercial supply of Translarna, Emflaza, and Upstaza/Kebilidi.

We do not directly control manufacturing for our products and product candidates and we are dependent on and will continue to be dependent on, our contract manufacturers for compliance with cGMP or good distribution practice, or GDP, or similar regulatory requirements outside the EU and the United States for manufacture of both active drug substances and finished drug products. Should we or our contract manufacturers fail to comply with these requirements, we and they could face significant regulatory and commercial consequences. For example, regulatory authorities routinely inspect manufacturing and other drug/biologic facilities. Our manufacturers and manufacturing facilities must also be approved by such regulatory authorities pursuant to inspections that will be conducted after we submit our marketing applications and will be subject to continuing regulatory authority inspections should we receive marketing approval. If we or our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the EU member state regulatory authorities, FDA, or other ex-U.S. regulatory agencies, we and they will not be able to secure and/or maintain regulatory approval for the manufacturing facilities, and we would not be able to secure and/or maintain, or may be delayed in securing regulatory approval of marketing applications or supplements for the applicable products or product candidates. We may also have to repeat studies that used product that did not conform with applicable requirements. In addition, we or third-party manufacturers or distributors may not be able to comply with generally accepted worker safety standards, cGMP, GDP or similar regulatory requirements outside the EU and the United States. Our failure, or the failure of our third-party manufacturers or distributors, over whom we have no direct control, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, clinical holds or termination of clinical studies, warning or untitled letters, regulatory communications warning the public about safety issues with a product, import or export refusals, license revocation, seizures, detentions, or recalls of product candidates or products, operating restrictions, criminal prosecutions or debarment, suits under the civil False Claims act, corporate integrity agreements, or consent decrees, any of which could significantly and adversely affect our reputation and supplies of our products or product candidates and our business, results of operations and financial condition could be materially adversely affected.

In addition, we have no direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, all of our contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such other materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may generally affect the regulatory status of our contract manufacturers' facilities and our products or product candidates. If the FDA, EU member state regulatory authorities or a comparable ex-U.S. regulatory agency do not approve these or our facilities for the manufacture of our products or product candidates or if it withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would negatively impact our ability to develop, obtain regulatory approval for or market our products or product candidates, if approved. There is also no guarantee that we would be able to find alternative manufacturing facilities or enter into agreements with alternative manufacturers on favorable terms. There may be limited manufacturers who would have the ability to manufacture our products and product candidates, especially our gene therapy product candidates, particularly as the pharmaceutical manufacturing industry becomes increasingly more consolidated. Moreover, any alternative manufacturers would need to be approved by the relevant regulatory authority, which approval is not guaranteed. We, accordingly, may not be able to make alternative manufacturing arrangements, which could adversely affect our products, product candidates, and our business, results of operations and financial condition. See "Item 1. Business—Manufacturing" for additional information regarding the manufacturing of our products and product candidates.

Even if we are able to establish and maintain arrangements with third-party manufacturers, distributors and other third parties, reliance on such third parties entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the agreements by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possibility of commercial supplies of our products not being distributed to commercial vendors or end users in a timely manner, resulting in lost sales;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions;

- the possibility of third-party resources not being devoted in the manner necessary to satisfy our requirements within the expected time frame;
- the possibility of third parties not providing us with accurate or timely information regarding their inventories, the number of patients who are using our products, or serious adverse events and/or product complaints regarding our products;
- the possibility of third parties being unable to satisfy their financial obligations to us or to others; and
- the possible termination or nonrenewal of a critical agreement by the third party at a time that is costly or inconvenient to us.

Many additional factors could cause production or distribution interruptions with the manufacture and distribution of any of our products and product candidates, including human error, natural disasters, labor disputes, acts of terrorism or war, equipment malfunctions, contamination, supply chain disruption, including disruptions caused by outbreaks of contagious disease, any new tariffs imposed in the jurisdictions in which we operate, or raw material and component shortages. For example, we have previously experienced delays in receiving certain raw materials in connection with supply chain disruptions caused by the COVID-19 pandemic, however, these delays did not affect or delay our manufacturing given our inventories for such materials at the time. If future supply chain disruptions create prolonged delays, the supplies of our products or products candidates may be significantly and adversely affected and our business, results of operations and financial condition could be materially adversely affected.

Our products and product candidates and any other products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. In addition, changes in cGMP regulations could negatively impact our ability or the ability of our contract manufacturers to complete the manufacturing process of our products and our product candidates in a compliant manner on the schedule we require for commercial and clinical trial use, respectively.

If we or the third parties that we engage to manufacture product for our commercial sales, preclinical tests and clinical trials should, prior to the time that we have validated alternative providers, cease to continue to do so for any reason, we likely would experience delays in our ability to supply our products or product candidates to patients or in our ability to advance our clinical trials while we identify and qualify replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our products or product candidates or the drug substances used to manufacture them, we will lose commercial sales revenue and it will be more difficult for us to develop our product candidates and compete effectively.

In addition, to the extent that any contract manufactures that we engage develop proprietary manufacturing processes or procedures, should we need to change manufacturers, we may not be able to transfer know-how to a new manufacturer. In such a case, the new manufacturer would need to invest substantial time, money, and effort to develop its own processes and procedures, which would require regulatory authority approval.

Third parties might illegally distribute and sell counterfeit or unfit versions of our products that do not meet our rigorous manufacturing and testing standards. A patient who receives a counterfeit or unfit drug may be at risk for a number of dangerous health consequences. Our reputation and business could suffer harm as a result of counterfeit or unfit drugs sold under our brand name. In addition, thefts of inventory at warehouses, plants or while in-transit, which are not properly stored and which are sold through unauthorized channels, could adversely impact patient safety, our reputation and our business.

Our current and anticipated future dependence upon others for the manufacture and distribution of Translarna, Emflaza, Upstaza, Kebilidi, Tegsedi, Waylivra and our product candidates may adversely affect our business, financial condition, results of operations and limit our ability to grow including our ability to develop product candidates and commercialize our products that receive regulatory approval on a timely and competitive basis.

We rely on third parties to conduct our preclinical and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We do not independently conduct preclinical or clinical trials for our products or product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to perform this function. While we have agreements governing the activities of such third parties, we have limited influence and control over their actual performance and activities. For instance, our third-party service providers are not our employees, and except for remedies available to us under our agreements with such third parties we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, non-clinical, and preclinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements or for other reasons, our trials may be repeated, extended, delayed, or terminated, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates, we may not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates, or we or they may be subject to regulatory enforcement actions. 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 revenues could be delayed. To the extent we are unable to successfully identify and manage the performance of third-party service providers in the future, our business may be materially and adversely affected. Further, any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it will delay our product development activities.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. We are required to monitor the activities of these third parties but our monitoring may not be able to detect any existing or emerging issues. Moreover, the FDA requires us to comply with standards, commonly referred to as GCP for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. In addition, we will be required to report certain financial interests of our third-party investigators if these relationships exceed certain financial thresholds or meet other criteria. The FDA or comparable ex-U.S. regulatory authorities may question the integrity of the data from those clinical trials conducted by investigators who may have conflicts of interest. We must further ensure that our preclinical trials are conducted in accordance with good laboratory practices, or GLPs, as appropriate. Regulatory authorities enforce these requirements through periodic inspections or remote regulatory assessments of trial sponsors, clinical and preclinical investigators, and trial sites. Similar GCP and transparency requirements apply in the EU. Failure to comply with the applicable regulatory requirements, including with respect to clinical trials conducted outside the EU and United States, can also lead regulatory authorities to refuse to accept into account clinical trial data submitted as part of a marketing application, as well as other regulatory consequences, as further described above.

Furthermore, third parties that we rely on for our clinical development activities may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing authorizations for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Our product development costs will increase if we experience delays in testing or obtaining marketing authorizations.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing authorizations of our products or product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We currently depend, and expect to continue to depend, on collaborations with third parties for the development and commercialization of some of our products and product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these products and product candidates.

For each of our product candidates, we plan to evaluate the merits of retaining commercialization rights for ourselves or entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies, such as our collaborations with Roche and the SMA Foundation, for our SMA program, including Evrysdi. We have entered into arrangements with certain third parties to market or distribute Translarna for the treatment of nmDMD in certain countries and, as we continue to implement our commercialization plans for Translarna, we anticipate that we will engage additional third parties to perform these functions for us in other countries. We generally plan to seek collaborators for the development and commercialization of product candidates that have high anticipated development costs, are directed at indications for which a potential collaborator has a particular expertise, or involve markets that require a large sales and marketing organization to serve effectively. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements may include: large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and/or biotechnology companies.

We will have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates and our collaborators will be subject to the same product development and commercialization risks that we are subject to. Our ability to generate revenues from these arrangements will depend on our collaborators' desire and ability to successfully perform the functions assigned to them in these arrangements in a compliant manner. In particular, the commercial success of Evrysdi will depend on the success of Roche's commercialization program. Furthermore, the successful development of another product candidate from our spinal muscular atrophy program will depend on the success of our collaborations with the SMA Foundation and Roche, including whether Roche pursues clinical development of any other compounds identified under the collaborations.

Collaborations involving our products and product candidates, including our collaborations with the SMA Foundation and Roche, pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our products and product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that replace or compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may fail to comply with the applicable regulatory requirements, subjecting them or us to potential regulatory enforcement action;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborator and us as to the ownership of intellectual property arising during the collaboration;

- we may grant exclusive rights for our products or product candidates to our collaborators, which would prevent us from collaborating with others, or from using our products or product candidates ourselves;
- disputes may arise between the collaborators and us that result in the delay or termination of the collaboration, which may include ending research, development or commercialization activities for our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

We may rely on third parties to perform many essential services for any products that we commercialize, including services related to warehousing and inventory control, distribution, government price reporting, customer service, accounts receivable management, cash collection, and pharmacovigilance and adverse event reporting. If these third parties fail to perform as expected or to comply with legal and regulatory requirements, our ability to commercialize our product candidates will be significantly impacted and we may be subject to regulatory sanctions.

We may retain third-party service providers to perform a variety of functions related to the sale and distribution of our product candidates, key aspects of which will be out of our direct control. These service providers may provide key services related to warehousing and inventory control, distribution, customer service, accounts receivable management, and cash collection. If we retain a service provider, we will substantially rely on it as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical or natural damage at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired and we may be subject to regulatory enforcement action.

In addition, we may engage third parties to perform various other services for us relating to pharmacovigilance and adverse event reporting, safety database management, fulfillment of requests for medical information regarding our product candidates and related services. If the quality or accuracy of the data maintained by these service providers is insufficient, or these third parties otherwise fail to comply with regulatory requirements, we could be subject to regulatory sanctions.

Additionally, we may contract with a third party to calculate and report pricing information mandated by various government programs. If a third party fails to timely report or adjust prices as required, or makes errors in calculating government pricing information from transactional data in our financial records, it could impact our discount and rebate liability, and potentially subject us to regulatory sanctions or False Claims Act lawsuits.

Our business and operations would suffer in the event of computer system failures, cyber-attacks or a deficiency in our, or our collaborators' or third-party vendors', cyber-security.

We collect, store and transmit large amounts of confidential information, including personal information, operational and financial transactions and records, clinical trial data and information relating to intellectual property, on internal information systems and through the information systems of collaborators and third-party vendors with whom we contract. Despite our implementation of security measures, including implementing the National Institute of Standards and Technology cybersecurity framework, instituting a training and compliance program on cybersecurity for all employees and doing a yearly external audit and penetration test, these information systems are vulnerable to damage from computer viruses, malware, ransomware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet or other mechanisms, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. No such security measures can eliminate the possibility of the information systems' improper functioning or the improper access or disclosure of confidential or personally identifiable information such as in the event of cyber-attacks. Cybersecurity-related risks have generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. Additionally, outside parties may attempt to fraudulently induce employees, collaborators, or other third-party vendors to disclose sensitive information or take other actions, including making fraudulent payments or downloading malware, by using

"spoofing" and "phishing" emails or other types of attacks. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy, despite our having a security risk insurance policy and disaster recovery and incident response plans. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material legal claims and liability, damage to our reputation, suffer loss or harm to our intellectual property rights, face significant financial exposure, including incurring significant costs to remediate possible injury to the affected parties and the further research, development and commercial efforts of our products and product candidates could be delayed.

Product liability and other civil lawsuits against us could cause us to incur substantial liabilities and to limit clinical trials or commercialization of any current or future products. Our insurance program may not be extensive enough to adequately protect us against these risks.

We face an inherent risk of product liability exposure related to the commercialization of our products and the human clinical trials testing of our products and product candidates. If we cannot successfully defend ourselves against claims that our product candidates, products or gene therapy product materials caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for our products or any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- the inability to continue current clinical trials or begin planned clinical trials;
- withdrawal or reduced enrollment of clinical trial participants;
- significant costs to defend the related claims/litigation;
- increased insurance costs, or an inability to maintain appropriate insurance coverage;
- substantial monetary awards to trial participants, patients and/or their families;
- loss of revenue;
- the inability to commercialize or to continue commercializing any products or product candidates;
- initiation of investigations and enforcement actions by regulators; and
- the withdrawal of products from the market, product recalls, or the cessation of development or regulatory disapproval of product candidates or withdrawal of approvals, as well as labeling, marketing, or promotional restrictions.

We have a broad insurance program covering risks appropriate to our research and development activities and clinical programs and aggregate annual limits of $25.0 million covering our products and sales. We also have industry standard insurance policies covering other aspects of our business and operations based on our locations, activities and other relevant factors. With respect to all insurance matters, we are advised by our insurance brokers, and our insurance advisor who we retain and compensate on a non-commission basis. However, our insurance program may not adequately cover the risks that we face for a variety of reasons, including:

- certain risks and related losses, such as delays to our clinical and development programs, are too speculative or unquantifiable for us to adequately insure against;
- if we were to face multiple claims, renewing or replacing our insurance may become more expensive, the terms (including deductibles and limits) we receive may worsen, and we may even have difficulty securing any coverage at all;
- our insurance limits may not be adequate to cover all liabilities and defense costs that we may incur; and
- we may need to further increase our insurance coverage if we commercialize our current products in additional jurisdictions, our sales increase, or we commercialize new products.

The cost of insurance coverage is highly variable, based on a wide range of factors. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability or defense costs that may arise.

In addition, we could be subject to other costly civil litigation, including contractual claims with respect to our expected manufacturing of gene therapy product materials for potential external customers. If our customers believe that we have violated our contractual terms, they may seek reimbursement for the cost of our gene therapy product materials or other related losses, the cost of which could be significant.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures, manufacturing and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations currently, and may in the future, involve the use of hazardous and flammable materials, including chemicals and medical and biological materials, and produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and wastes, we cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials or disposal of hazardous wastes, we could be held liable for any resulting damages, and any liability could exceed our resources.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or manufacturing and distribution efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Dr. Matthew Klein, our Chief Executive Officer, and the other principal members of our executive, commercial and scientific teams. Although we have formal employment agreements with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain "key person" insurance on any of our executive officers. The loss of the services of any of these persons might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We experience competition for the hiring of scientific and clinical personnel from numerous pharmaceutical and biotechnology companies as well as universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Risks Related to our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection or other intellectual property rights with respect to our proprietary technology and products. One primary way that we seek to protect our proprietary position is by filing patent applications in the United States and in certain ex-U.S. jurisdictions related to our proprietary technology and products. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications. It is also possible that we will fail to file a patent application on patentable aspects of our research and development. Moreover, if we license technology or product candidates from third parties, these license agreements may not permit us to control the filing and prosecution of patent applications, or to maintain or

enforce the patents. These agreements could also give our licensors the right to enforce the licensed patents without our involvement, or to decide not to enforce the patents at all. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the commercial value of our patent rights is highly uncertain. Our pending and future patent applications may not result in patents being issued which prevent others from commercializing competitive technologies and products. Changes in patent laws or their interpretation in the United States and other countries may diminish the value of our patents.

The laws of ex-U.S. countries may not protect our rights to the same extent as the laws of the United States. For example, patent law in many countries restricts the patentability of methods of treatment of the human body more than U.S. law does. In addition, we may not pursue or obtain or be able to pursue or obtain patent protection in all major markets. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In addition, the Leahy-Smith America Invents Act of 2011, or the Act, which reformed certain patent laws in the U.S., may create additional uncertainty. The significant changes engendered by the Act include switching from a "first-to-invent" system to a "first-to-file" system, and the implementation of new procedures that permit competitors to challenge our patents in the USPTO after grant, including inter partes review and post grant review.

Moreover, we may be subject to a third-party prior art submissions in a patent office, or may become involved in patent office proceedings, including oppositions, derivation proceedings, reexamination, inter partes review, post grant review, interference proceedings, or litigation, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection or prevent competitors from competing with us. Our competitors may be able to circumvent our owned or licensed patents by developing alternative technologies or products in a non-infringing manner. Other companies may also attempt to circumvent any regulatory data protection or market exclusivity that we obtain under applicable legislation, which may require us to allocate significant resources to prevent such circumvention. Legal and regulatory developments in the European Union, or EU, and elsewhere may also result in clinical trial data and other information, that would ordinarily be treated as trade secret, submitted as part of a marketing authorization application becoming publicly available. The EMA Policy on publication of clinical data and other such information, as well as the current application of EU freedom of information regulations, could impact our proprietary information (comprising both clinical and non-clinical data and other information) that would normally be maintained by a regulatory body as commercially confidential. Such developments could enable other companies to circumvent our intellectual property rights and use our clinical trial data or other information to obtain marketing authorizations in the EU and in other jurisdictions where we have not been able to obtain any intellectual property or regulatory protection, resulting in loss of market share. Such developments may also require us to allocate significant resources or engage in litigation to prevent other companies from circumventing or violating our intellectual property rights. Our attempts to prevent third parties from circumventing or violating our intellectual property and other rights may ultimately be unsuccessful. We may also fail to take the required actions to maintain our patents.

For example, during 2015, we were notified by the EMA that it had received from another pharmaceutical company a request under Regulation (EC) No 1049/2001 seeking access to aspects of our marketing authorization for Translarna for the treatment of nmDMD. Following the decision of the EMA to release such documentation with only minimal redactions

we initiated litigation before the General Court of the EU to prevent disclosure of this information. In the first quarter of 2018, the Court ruled in favor of the EMA, allowing the EMA to release the documentation. We appealed the General Court's decision to the Court of Justice of the EU, or CJEU, but the CJEU dismissed our appeal in January 2020 and released the information to the requester.

An issued patent may be challenged, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our intellectual property. To counter infringement or unauthorized use, we may be required to file a lawsuit and claims for damages, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property or defenses, such that they do not infringe our intellectual property or that our intellectual property is invalid or unenforceable. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or may refuse to stop the other party from using the technology at issue.

Third parties may initiate legal proceedings alleging that our patents are invalid and unenforceable or that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our products and our product candidates and use our proprietary technologies without infringing the intellectual property and other proprietary rights of third parties. We may not be aware of all intellectual property rights potentially relating to our product and our product candidates. Typically, patent applications in the United States and other jurisdictions are not published until 18 months after filing, or in some cases not at all, and new patent applications are continuously publishing. Thus, we may not be aware of patents or patent applications relating to our product or our product candidates. There may be pending or future patent applications that, if issued, would block us from commercializing our products. Thus, we do not know with certainty whether any of our products or product candidates, or our commercialization thereof, would or would not infringe any third party's intellectual property.

We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights or other proprietary with respect to our products and technology. Third parties may assert infringement claims against us based on existing or future intellectual property rights. We may allege that a third-party patent we are alleged to infringe is invalid and/or we may be able to avail ourselves in the United States of the safe harbor exemption provided by the Hatch-Waxman Act as a basis for non-infringement. In order to successfully challenge the validity of a third party issued U.S. patent that we are alleged to infringe, we would need to overcome that patent's presumption of validity in district court or prove unpatentability by a preponderance of the evidence before the USPTO in a post grant proceeding. There is no assurance that a court or the USPTO would find these claims to be invalid or unpatentable, respectively.

If we are found to infringe a third party's intellectual property rights, or in order to avoid or settle litigation, we may seek to obtain a license to continue developing and marketing our products and technology. However, we may not be able to obtain any such license on commercially reasonable terms or at all. Also, any license obtained may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us, and could require us to make substantial payments. We could be forced, including by court order, to cease commercializing an alleged infringing technology or product. In addition, we could be found liable for monetary damages if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from commercializing our products or our

product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and could distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of such proceedings. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, sales, marketing or distribution activities. We may not have sufficient resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Without patent protection, our marketed products may face generic competition.

Certain of the products we market have no or limited patent protection and, as a result, potential competitors face fewer regulatory barriers in introducing competing products. Without patent protection or other regulatory exclusivity, we may not be able to exclude others from, among other things, selling or importing similar products in any jurisdiction. In some instances, we may rely on trade secrets and other unpatented proprietary information to protect our commercial position, although we may be unable to provide adequate protection for our commercial position via these means. In other instances, we may need to rely on regulatory exclusivity to protect our commercial position.

Furthermore, generic competition against a branded product often results in decreases in the prices at which the branded product can be sold, particularly when there is more than one generic product available in the marketplace. Third-party companies could also develop products that are similar, but not identical, to our marketed products, such as an alternative formulation of our product or an alternative formulation combined with a different delivery technology, and seek approval in the United States by referencing our products and relying, to some degree, on the FDA's finding that our products are safe and effective in their approved indications. In addition, legislation enacted in the United States allows for, and in a few instances, in the absence of specific instructions from the prescribing physician, mandates the dispensing of generic products rather than branded products where a generic version is available.

On February 9, 2017, the FDA approved the corticosteroid Emflaza for the treatment of patients 5 years and older with DMD. Although approved for other indications outside of the United States, this was the first approval for deflazacort in the United States and the first approval in the United States for the use of a corticosteroid to treat DMD. We have previously relied on an orphan exclusivity period to commercialize Emflaza in the United States. Emflaza's seven-year period of orphan drug exclusivity related to the treatment of DMD in patients five years and older expired in February 2024. We expect the expiration of this orphan drug exclusivity to have a significant negative impact on Emflaza net product revenue. Emflaza's orphan drug exclusivity related to the treatment of DMD in patients two years of age to less than five expires in June 2026.

We currently have no issued patents that could prevent a third-party company from seeking to introduce a generic Emflaza formulation in the United States for the treatment of DMD or another indication, and we do not expect to be able to obtain such patent protection. Such third-party companies may also obtain patents covering a new deflazacort formulation or method of use.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents and regulatory exclusivity for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. More particularly, we may rely on trade secrets and other unpatented proprietary information to protect our competitive position related to our products and product candidates, especially when patent protection is not obtainable. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors, partners and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets or that the agreements we have executed will provide adequate protection. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be obtained or independently developed by a competitor, our competitive position would be harmed. If our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, employees, consultants, advisors, partners and other third parties develop new inventions or processes related to our products independently, or jointly with us, that may be applicable to our products under development, disputes may arise about ownership or proprietary rights to those inventions and processes. Enforcing a claim that a third party illegally obtained and is using any of our inventions or trade secrets is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside of the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

We have not yet registered our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

Our trademark applications may be refused registration, or our registered trademarks may not be maintained or may be found to be unenforceable. During trademark examination proceedings, our trademark applications may be rejected. Although we are given an opportunity to respond to those rejections in most jurisdictions, we may not be able to successfully overcome them. In addition, in the U.S. Patent and Trademark Office and Trademark Offices in many other jurisdictions, third parties are given an opportunity to oppose pending trademark applications or to seek cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Further, if we do not secure registrations for our trademarks, we may encounter difficulty enforcing our trademark rights against third parties in the jurisdictions where we do not have registered rights.

If we are not able to obtain adequate trademark protection or regulatory approval for our brand names, we may be required to re-brand affected products, which could cause delays in getting such products to market and substantially increase our costs.

To protect our rights in any trademark we intend to use for our products or product candidates, we may seek to register such trademarks. Trademark registration is territory-specific and we must apply for trademark registration in the United States as well as any other country where we intend to commercialize our product or product candidates. Failure to obtain trademark registrations may place our use of the trademarks at risk or make them subject to legal challenges, which could force us to choose alternative names for our product or product candidates. In addition, the FDA, and other regulatory authorities outside the United States, conduct an independent review of proposed product names for pharmaceuticals, including an evaluation of the potential for confusion with other pharmaceutical product names for medications, which could result in medication errors in prescribing, dispensing and consumption. These regulatory authorities may also object to a proposed product name if they believe the name inappropriately makes or implies a therapeutic claim. If the FDA or other regulatory authorities outside the United States object to any of our proposed product names, we may be required to adopt alternative names for our product or product candidates. If we adopt alternative names, either because of our inability to obtain a trademark registration or because of objections from regulatory authorities, we would lose the benefit of our existing trademark applications and the rights attached thereto. Consequently, we may be required to expend significant additional resources in an effort to adopt a new product name that would be registrable under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA and other regulatory authorities, which could cause delays in getting our products to market and substantially increase our costs. Furthermore, in the United States and many other jurisdictions, a trademark registration may be cancelled through cancellation or forfeiture proceedings brought by a third party or from non-use of the trademark in that jurisdiction. We may not be able to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product or our product candidates.

Our rights to develop and commercialize Upstaza/Kebilidi are subject, in part, to the terms and conditions of licenses granted to us by others.

We depend upon the intellectual property rights granted to us under licenses from third parties that are important or necessary to the development of Upstaza/Kebilidi for the treatment of AADC deficiency. In particular, we have in-licensed certain intellectual property rights and know-how from National Taiwan University, or NTU, relevant to Upstaza/Kebilidi for the treatment of AADC deficiency. Any termination of these licenses could result in the loss of significant or all rights licensed to us and could harm or prevent our ability to commercialize Upstaza/Kebilidi for the treatment of AADC deficiency. Each of our existing gene therapy licensing agreements are exclusive but are limited to particular fields, such as AADC deficiency and are subject to certain retained rights.

Our current gene therapy license agreements, including our agreement with NTU pursuant to which we have in-licensed certain intellectual property rights and know-how relevant to Upstaza/Kebilidi for the treatment of AADC deficiency, impose various obligations, including certain payment obligations, including contingent payments to be made upon reaching certain development and regulatory milestones. If we fail to satisfy our obligations, the licensor may have the right to terminate the agreement. Disputes may arise between us and any of our licensors regarding intellectual property subject to such agreements and other issues. Such disputes over intellectual property that we have licensed or the terms of our license agreements, including with respect to Upstaza/Kebilidi for the treatment of AADC deficiency, may prevent or impair our ability to maintain our current arrangements on acceptable terms, or at all, or may impair the value of the arrangement to us. Any such dispute could have a material adverse effect on our business and our ability to realize the anticipated benefits of our acquisition of Agilis. If we cannot maintain a necessary license agreement, including with respect to Upstaza/Kebilidi for the treatment of AADC deficiency, or if the agreement is terminated, we may be unable to successfully develop and commercialize the affected product candidates.

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

We are a party to a number of license agreements and expect to enter into additional licenses in the future. Our existing licenses impose, and we expect that future licenses will impose, various diligence, milestone payment, royalty, insurance

and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by these agreements, which could materially adversely affect the value of the product candidate being developed under such license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms or cause us to lose rights in important intellectual property or technology.

We have also received grant funding for some of our development programs from philanthropic organizations and patient advocacy groups pursuant to agreements that impose development and commercialization diligence obligations on us. If we fail to comply with these obligations, the applicable organization could require us to grant to the organization exclusive rights under certain of our intellectual property, which could materially adversely affect the value to us of product candidates covered by that intellectual property even if we are entitled to a share of any consideration received by such organization in connection with any subsequent development or commercialization of the product candidates.

Some of our patented technology was developed with U.S. federal government funding. When new technologies are developed with U.S. government funding, the government obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise "march-in" rights to use or allow third parties to use our patented technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government and U.S. government funding must be disclosed in any resulting patent applications. Furthermore, our rights in such inventions are subject to government license rights and certain restrictions on manufacturing products outside the United States.

Risks Related to our Common Stock

Servicing the 2026 Convertible Notes requires a significant amount of cash. We may not have sufficient cash flow from our business to make payments on our debt, and we may not have the ability to raise the funds necessary to settle conversions of, or to repurchase, the 2026 Convertible Notes upon a fundamental change, which could adversely affect our business, financial condition and results of operations.

In September 2019, we incurred indebtedness in the amount of $287.5 million in aggregate principal with additional accrued interest under the 2026 Convertible Notes, for which interest is payable semi-annually in arrears on March 15 and September 15 of each year, beginning on March 15, 2020. Our ability to make scheduled payments of the principal of, to pay interest on or to refinance the 2026 Convertible Notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service our debt, including the 2026 Convertible Notes. If we are unable to generate cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be unfavorable to us or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at the time we seek to refinance such indebtedness. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

Upon conversion of the 2026 Convertible Notes, unless we elect to deliver solely shares of our common stock to settle such conversion (other than paying cash in lieu of delivering any fractional shares), we will be required to make cash payments in respect of the 2026 Convertible Notes being converted. However, we may not have enough available cash or be able to obtain financing at the time we are required to repurchase 2026 Convertible Notes, to pay the 2026 Convertible Notes at maturity or to pay cash upon conversions of 2026 Convertible Notes. In addition, our ability to repurchase 2026 Convertible Notes or to pay cash upon conversions of 2026 Convertible Notes may be limited by law, by regulatory authority or by agreements governing our future indebtedness. Our failure to repurchase 2026 Convertible Notes at a time when the repurchase is required by the indenture, to make interest payments on the 2026 Convertible Notes when due under the indenture or to pay any cash payable on future conversions of the 2026 Convertible Notes as required by the indenture would constitute a default under the indenture governing the 2026 Convertible Notes. An event of default under the indenture governing the 2026 Convertible Notes or the fundamental change itself could also lead to a default under

agreements governing our future indebtedness. If the repayment of any such related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness, repurchase the 2026 Convertible Notes, make interest payments on the 2026 Convertible Notes or make cash payments upon conversions of the 2026 Convertible Notes.

Even if holders of the 2026 Convertible Notes do not elect to convert their 2026 Convertible Notes, we could be required to reclassify all of the outstanding principal of the 2026 Convertible Notes as a current rather than long-term liability in accordance with applicable accounting rules, which would result in a material reduction of our net working capital. Any of these factors could materially and adversely affect our business, financial condition and results of operations.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- provide for a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock and lawsuits against us and our officers and directors.

Our stock price has been and will likely continue to be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased it. The market price for our common stock may be influenced by many factors, including:

- our ability to maintain our marketing authorization for Translarna for the treatment of nmDMD in the EEA following the CHMP's negative opinion on the conditional marketing authorization following a re-examination

procedure, and the EC's potential adoption of the negative opinion, or identify other potential mechanisms in which we may provide Translarna to nmDMD patients in the EEA;
- our ability to maintain the marketing authorization for Translarna and our other products in territories outside of the EEA;
- expectations with respect to sepiapterin for the treatment of PKU, including any potential regulatory submissions and potential approvals;
- expectations with respect to Upstaza/Kebilidi, including any potential regulatory submissions and potential approvals;
- expectations with respect to vatiquinone for the treatment of FA, including any potential regulatory submissions and potential approvals;
- any developments related to our ability or inability to execute our commercialization strategy for any of our products;
- our ability to resolve the matters set forth in the FDA's denial of our appeal to the CRL we received from the FDA in connection with our NDA for Translarna for the treatment of nmDMD;
- the commercialization of Evrysdi and the development of the SMA program with Roche and the SMA Foundation;
- results of clinical trials of any other product candidate that we develop;
- any additional clinical or non-clinical trial required by regulatory agencies for our products or product candidates;
- announcements by us or our competitors of significant acquisitions, licenses, strategic collaborations, joint ventures, collaborations or capital commitments;
- negative publicity around our products or product candidates;
- other developments concerning our regulatory submissions;
- the success of competitive products or technologies;
- results of clinical trials of product candidates of our competitors, including negative results that investors may associate with our product candidates;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- our ability to realize the benefits of our acquisitions or other business combinations;
- the recruitment or departure of key personnel;
- the loss of distributors, suppliers or manufacturers;
- the level of expenses related to any of our products, product candidates or clinical development programs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- announcements with respect to litigation;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including potentially high inflation rates and sustained high interest rates; and
- the other factors described in this "Risk Factors" section.

Companies that have experienced volatility in the market price of their stock have frequently been the subject of securities class action and shareholder derivative litigation. For example, in 2018 we settled a securities class action lawsuit initiated against us and certain of our current and former executive officers during 2016, as well as derivative lawsuits brought against us, as a nominal defendant, certain of our current and former executive officers and certain of our current and former directors during 2017. We could be the target of other such litigation in the future. Class action and derivative lawsuits, whether successful or not, could result in substantial costs, damage or settlement awards and a diversion of our management's resources and attention from running our business, which could materially harm our reputation, financial condition and results of operations.

Because we do not anticipate paying any cash dividends on our capital in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

The issuance of additional shares of our common stock or the sale of shares of our common stock by our stockholders could dilute our stockholders' ownership interest in the Company and could significantly reduce the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

We have issued a significant number of equity awards under our equity compensation plans or as inducement grants to new hire employees pursuant to Nasdaq rules. The shares underlying these awards are registered on a Form S-8 registration statement. As a result, upon vesting these shares can be freely exercised and sold in the public market upon issuance, subject to volume limitations applicable to affiliates. The exercise of options and the subsequent sale of the underlying common stock or the sale of restricted stock upon vesting could cause a decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

Certain of our employees, executive officers and directors have entered or may enter into Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the employee, director or officer when entering into the plan, without further direction from the employee, officer or director. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers and directors may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Additionally, certain shares that we issued in connection with our acquisitions or other strategic transactions have not yet been sold and are currently restricted as a result of securities laws. These shares may be freely sold in the public market subject to any requirements and restrictions, including any applicable volume limitations, imposed by Rule 144 under the Securities Act. The sale or resale of these shares in the public market, or the market's expectation of such sales, may result in an immediate and substantial decline in our stock price. Such a decline will adversely affect our investors and also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

Sales of substantial amounts of shares of our common stock or other securities by our stockholders or by us, including sales made under our At the Market Offering Sales Agreement with Cantor Fitzgerald and RBC Capital Markets, LLC, pursuant to which we may offer and sell shares of our common stock having an aggregate offering price of up to $125 million from time to time, through the Sales Agent by any method that is deemed to be an "at the market" offering as defined in Rule 415(a)(4) promulgated under the Securities Act, or the issuance of shares of our common stock upon conversion of our outstanding 2026 Convertible Notes or any future securities convertible or exchangeable into our common stock or in connection with a strategic transaction or otherwise, could dilute our stockholders, lower the market price of our common stock and impair our ability to raise capital through the sale of equity securities.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Cybersecurity Risk Management and Strategy

As is the case for most companies, we are regularly subject to cyber-attacks and other cyber incidents and, therefore, cybersecurity is an important element of our overall enterprise risk management program. As part of our ordinary course of business, we collect, store and transmit large amounts of confidential information, including personal information, operational and financial transactions and records, clinical trial data and information relating to intellectual property, on internal information systems and through the information systems of collaborators and third-party vendors with whom we contract. We have a multilayered approach for assessing, identifying and managing cybersecurity risks, that is designed to help protect such information from internal and external cyber threats by understanding and seeking to mitigate risk while ensuring business resiliency. Our cybersecurity prevention methods include implementing the National Institute of Standards and Technology cybersecurity framework, instituting a training and compliance program on cybersecurity for all employees, completing a yearly external audit and penetration test, conducting vulnerability scans and remediations and monitoring threat intelligence feeds. As part of our overall risk management strategy, we also maintain cyber insurance coverage; however, such insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches. We also conduct security assessments of all third-party providers before engagement and maintain ongoing monitoring to ensure compliance with our cybersecurity standards. This process involves third-party providers responding to cybersecurity questionnaires and information technology, or IT, security team meetings to review and assess the third-party providers security posture to confirm that the provider is ensuring the security, integrity, and availability of processed data.

We have also established a global incident response management standard operating procedure, or GIRM. Our GIRM provides step-by-step instructions for managing any global incident which is disruptive of or interferes with the delivery and operation of our IT services and systems that are in use. Specifically, our GIRM provides direction as to how information with respect to a cybersecurity incident is communicated internally, including with our executive committee leadership team. As regulatory disclosure requirements regarding cybersecurity incidents and data privacy matters have become more prevalent, we have developed an incident workflow designed to monitor and evaluate if such disclosure requirements are triggered by an incident through the inclusion of members of our legal, data privacy and executive teams in the incident response process.

We engage third parties, including independent privacy assessors, computer security firms and risk management and governance experts to enhance our cybersecurity oversight. For example, on an annual basis we run a penetration test of our systems, performed by a different external third party each year. We also regularly consult with these third parties on emerging industry trends.

Based on an assessment using the previously described enterprise risk management program, we do not believe that there are currently any risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have material affected or are reasonably likely to materially affect us, including our business strategy, results of operations or financial conditions. See "*Our business and operations would suffer in the event of computer system failures, cyber-attacks or a deficiency in our, or our collaborators' or third-party vendors', cyber-security"* in Part I, Item 1A. "Risk Factors" for additional information.

Cybersecurity Governance and Oversight

Our Board of Directors administers its cybersecurity risk oversight function primarily through the Audit Committee of the Board of Directors. In accordance with our Audit Committee Charter, our Chief Information Officer, or CIO, provides periodic updates to our Audit Committee regarding the Company's cybersecurity and other technology risks, internal controls and procedures, including the Company's plan to mitigate cybersecurity risk and respond to data breaches. The Audit Committee is also responsible for reviewing any related periodic public filing disclosures. The Board of Directors receives regular reports from the Audit Committee. Our CIO also presents directly to our Board of Directors on an annual basis on these matters. Our IT team is responsible for maintaining daily operations and ensuring the confidentiality, integrity and availability of data. Our CIO oversees a cybersecurity team that has over 15 years' experience in cybersecurity along with advanced and undergrad degrees in cybersecurity, and industry recognized security certifications such as CISSP (Certified Information Systems Security Professional) and CISM (Certified Information Security Manager). Our CIO reports directly to our Chief Legal Officer, both of whom are members of our executive committee leadership team. Cybersecurity incident status updates are provided as necessary to the executive committee as set forth in our GIRM. In the event of a cybersecurity incident, our IT team is trained to follow our GIRM.

In an effort to deter and detect cyber threats, we periodically provide all employees, including part-time and temporary employees, with data protection, cybersecurity and incident response and prevention training as part of our overall IT compliance program, which covers timely and relevant topics. Past topics have included social engineering, phishing, password protection, confidential data protection, asset use and mobile security. This training functions to educate employees on the importance of reporting all incidents immediately. We also use technology-based tools to mitigate cybersecurity risks and to bolster our employee-based cybersecurity programs.

For more information regarding the risks associated our cybersecurity program, see Item 1A. Risk Factors, "Our business and operations would suffer in the event of computer system failures, cyber-attacks or a deficiency in our, or our collaborators' or third-party vendors', cyber-security."

Item 2. Properties

Our principal facility consists of approximately 180,000 square feet of office space and shell condition, modifiable space located at 500 Warren Corporate Center Drive in Warren, New Jersey, that we occupy under a lease that expires in 2039. The rental term for such facility commenced on June 1, 2022, with an initial term of seventeen years followed by three consecutive five-year renewal periods at our option. Additionally, we lease 103,000 square feet of laboratory and office space in Bridgewater, New Jersey. The rental term for such facility commenced on May 1, 2020 with an initial term of seven years and two consecutive five year renewal periods at our option. We lease approximately 11,500 square feet of office space in Dublin, Ireland, that we occupy under a lease that expires in 2034. Additionally, we lease approximately 5,000 square feet of office space in Sao Paulo, Brazil, that we occupy under a lease that expires in 2028. We also lease additional laboratory and office space in the U.S. and other countries to support our operations as a global organization, but these leases are not material to us.

Item 3. Legal Proceedings

From time to time in the ordinary course of our business, we are subject to claims, legal proceedings and disputes. We are not currently aware of any material legal proceedings which we are a party to or of which any of our property is the subject.

Item 4. Mine Safety Disclosures

None.

PART II

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

Market Information

Our common stock has been publicly traded on the Nasdaq Global Select Market under the symbol "PTCT" since June 20, 2013. Prior to that time, there was no public market for our common stock.

Holders

As of February 25, 2025, there were 78 holders of record of our common stock. This number does not include beneficial owners whose shares are held in street name.

Recent Sales of Unregistered Securities

We did not sell any of our equity securities or any options, warrants, or rights to purchase our equity securities during the period covered by this Annual Report on Form 10-K that were not registered under the Securities Act of 1933, as amended, or the Securities Act, and that have not otherwise been described in a Current Report on Form 8-K or a Quarterly Report on Form 10-Q.

Purchase of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. [Reserved]

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

The following discussion and analysis is meant to provide material information relevant to an assessment of the financial condition and results of operations of our company, including an evaluation of the amounts and certainty of cash flows from operations and from outside resources, so as to allow investors to better view our company from management's perspective. The following discussion of our financial condition and results of operations should be read in conjunction with our financial statements and the notes to those financial statements appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth in Part I, Item 1A. Risk Factors, of this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in these forward-looking statements.

We are a global biopharmaceutical company that discovers, develops and commercializes clinically differentiated medicines that provide benefits to children and adults living with rare disorders. Our ability to innovate to identify new therapies and to globally commercialize products is the foundation that drives investment in a robust and diversified pipeline of transformative medicines. Our mission is to provide access to best-in-class treatments for patients who have little to no treatment options. Our strategy is to leverage our strong scientific and clinical expertise and global commercial infrastructure to bring therapies to patients. We believe that this allows us to maximize value for all of our stakeholders. We have a diversified therapeutic portfolio that includes several commercial products and product candidates in various stages of development, including clinical, pre-clinical and research and discovery stages, focused on the development of new treatments for multiple therapeutic areas for rare diseases relating to neurology and metabolism.

We have two products, Translarna™ (ataluren) and Emflaza® (deflazacort), for the treatment of Duchenne muscular dystrophy, or DMD, a rare, life threatening disorder. Translarna currently has conditional marketing authorization in the European Economic Area, or EEA, for the treatment of nonsense mutation Duchenne muscular dystrophy, or nmDMD, in ambulatory patients aged two years and older. Translarna also has marketing authorization in Russia for the treatment of

nmDMD in patients aged two years and older, and in Brazil for the treatment of nmDMD in ambulatory patients two years and older and for continued treatment of patients that become non-ambulatory, as well as in various other countries. During the year ended December 31, 2024, we recognized $339.9 million in sales of Translarna. We hold worldwide commercialization rights to Translarna for all indications in all territories. Emflaza is approved in the United States for the treatment of DMD in patients two years and older. During the year ended December 31, 2024, Emflaza achieved net sales of $207.2 million.

Our marketing authorization for Translarna in the EEA is subject to annual review and renewal by the European Commission, or EC, following reassessment by the European Medicines Agency, or EMA, of the benefit-risk balance of the authorization, which we refer to as the annual EMA reassessment. In September 2022, we submitted a Type II variation to the EMA to support conversion of the conditional marketing authorization for Translarna to a standard marketing authorization, which included a report on the placebo-controlled trial of Study 041 and data from the open-label extension as further described below. Study 041 was an 18-month, placebo-controlled trial, followed by an 18-month open-label extension of Translarna in the treatment of ambulatory patients with nmDMD aged five years or older. In February 2023, we also submitted an annual marketing authorization renewal request to the EMA. In September 2023, the Committee for Medicinal Products for Human Use, or CHMP, gave a negative opinion on the conversion of the conditional marketing authorization to full marketing authorization of Translarna for the treatment of nmDMD and a negative opinion on the renewal of the existing conditional marketing authorization of Translarna for the treatment of nmDMD. In January 2024, the CHMP issued a negative opinion for the renewal of the conditional marketing authorization following a re-examination procedure. In May 2024, the EC decided not to adopt the CHMP's negative opinion for the renewal of the conditional marketing authorization of Translarna and returned such opinion to the CHMP for re-evaluation. In June 2024, following the EC's request for re-review, the CHMP issued a negative opinion on the renewal of the conditional marketing authorization of Translarna for the treatment of nmDMD. On October 18, 2024, the CHMP maintained its negative opinion for the renewal of the conditional marketing authorization following the requested reexamination procedure. In accordance with EMA regulations, the EC has 67 days from the date of issuance to adopt the opinion. At this time, the EC has not yet adopted the negative opinion. If the EC adopts the negative opinion, Translarna would no longer have marketing authorization in the member states of the EEA. The marketing authorization for Translarna remains in effect, pending the EC's potential adoption of the negative opinion.

Each country, including each member state of the EEA, has its own pricing and reimbursement regulations. In order to commence commercial sale of product pursuant to our Translarna marketing authorization in any particular country in the EEA, we must finalize pricing and reimbursement negotiations with the applicable government body in such country. As a result, our commercial launch will continue to be on a country-by-country basis. We also have made, and expect to continue to make, product available under early access programs, or EAP programs, or similar styled programs both in countries in the EEA and other territories. Our ability to negotiate, secure and maintain reimbursement for product under commercial and EAP programs can be subject to challenge in any particular country and can also be affected by political, economic and regulatory developments in such country.

There is substantial risk that if the EC adopts the CHMP's negative opinion, or we are otherwise unable to renew our EEA marketing authorization during any annual renewal cycle, or we are unable to identify other potential mechanisms in which we may provide Translarna to nmDMD patients in the EEA should the EC adopts the CHMP's negative opinion or our product label is materially restricted, we would lose all, or a significant portion of, our ability to generate revenue from sales of Translarna in the EEA and other territories. For more information regarding the risks associated with a potential EC adoption of the CHMP's negative opinion on Translarna's marketing authorization, see Item 1A. Risk Factors, "*We may be unable to continue to commercialize Translarna for nmDMD in the EEA if the EC adopts the negative opinion issued by the CHMP for the renewal of the existing conditional authorization for Translarna.*"

Translarna is an investigational new drug in the United States. During the first quarter of 2017, we filed a New Drug Application, or NDA, for Translarna for the treatment of nmDMD over protest with the United States Food and Drug Administration, or FDA. In October 2017, the Office of Drug Evaluation I of the FDA issued a Complete Response Letter, or CRL, for the NDA, stating that it was unable to approve the application in its current form. In response, we filed a formal dispute resolution request with the Office of New Drugs of the FDA. In February 2018, the Office of New Drugs of the FDA denied our appeal of the CRL. In its response, the Office of New Drugs recommended a possible path forward for the ataluren NDA submission based on the accelerated approval pathway. This would involve a re-submission of an

NDA containing the current data on effectiveness of ataluren with new data to be generated on dystrophin production in nmDMD patients' muscles. We followed the FDA's recommendation and collected, using newer technologies via procedures and methods that we designed, such dystrophin data in a new study, Study 045, and announced the results of Study 045 in February 2021. Study 045 did not meet its pre-specified primary endpoint. In June 2022, we announced top-line results from the placebo-controlled trial of Study 041. Following this announcement, we submitted a meeting request to the FDA to gain clarity on the regulatory pathway for a potential re-submission of an NDA for Translarna. The FDA provided initial written feedback that Study 041 does not provide substantial evidence of effectiveness to support NDA re-submission. We held a Type C meeting with the FDA in the fourth quarter of 2023 to discuss the totality of Translarna data. Based on feedback from the FDA, we re-submitted the NDA in July 2024, based on the results from Study 041 and from our international drug registry study for nmDMD patients receiving Translarna. In October 2024, the FDA accepted for review the resubmission of the NDA for Translarna for the treatment of nmDMD. As this was an NDA resubmission following a complete response letter to the NDA which was filed over protest in 2016, the FDA is not obligated to follow the review timelines under PDUFA guidelines and an action date has not been provided.

We have previously relied on Emflaza's seven-year marketing exclusivity period in the United States for its approved indications under the provisions of the Orphan Drug Act of 1983, or the Orphan Drug Act, when commercializing Emflaza. Emflaza's seven-year period of orphan drug exclusivity related to the treatment of DMD in patients five years and older expired in February 2024. We expect the expiration of this orphan drug exclusivity to have a significant negative impact on Emflaza net product revenue. Emflaza's orphan drug exclusivity related to the treatment of DMD in patients two years of age to less than five expires in June 2026.

Upstaza is a gene therapy for the treatment of Aromatic L Amino Decarboxylase, or AADC, deficiency, a rare central nervous system, or CNS, disorder arising from reductions in the enzyme AADC that results from mutations in the dopa decarboxylase gene. In July 2022, the EC approved Upstaza for the treatment of AADC deficiency for patients 18 months and older within the EEA. In November 2022, the Medicines and Healthcare Products Regulatory Agency approved Upstaza for the treatment of AADC deficiency for patients 18 months and older within the United Kingdom. In November 2024, the FDA granted accelerated approval of our gene therapy for the treatment of children and adults with AADC deficiency, which is marketed with the brand name Kebilidi in the United States.

We hold the rights for the commercialization of Tegsedi and Waylivra for the treatment of rare diseases in countries in Latin America and the Caribbean pursuant to a Collaboration and License Agreement, or the Tegsedi-Waylivra Agreement, dated August 1, 2018, by and between us and Akcea Therapeutics, Inc., or Akcea, a subsidiary of Ionis Pharmaceuticals, Inc. Tegsedi has received marketing authorization in the United States, European Union, or EU, and Brazil for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis, or hATTR amyloidosis. In August 2021, ANVISA, the Brazilian health regulatory authority, approved Waylivra as the first treatment for familial chylomicronemia syndrome, or FCS, in Brazil. In December 2022, ANVISA approved Waylivra for the treatment of familial partial lipodystrophy, or FPL. Waylivra has also received marketing authorization in the EU for the treatment of FCS.

We also have a spinal muscular atrophy, or SMA, collaboration with F. Hoffman La Roche Ltd. and Hoffman La Roche inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or SMA Foundation. The SMA program has one approved product, Evrysdi® (risdiplam), which was approved by the FDA in August 2020 for the treatment of SMA in adults and children two months and older and by the EC in March 2021 for the treatment of 5q SMA in patients two months and older with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies. Evrysdi has also received marketing authorization for the treatment of SMA in over 100 countries. In May 2022, the FDA approved a label expansion for Evrysdi to include infants under two months old with SMA. In August 2023, the EC approved an extension of the Evrysdi marketing authorization to include infants under two months old in the EU.

One of our most advanced clinical stage molecules is sepiapterin. Sepiapterin is our product candidate for the treatment of phenylketonuria, or PKU. In May 2023, we announced that the primary endpoint was achieved in our registration-directed Phase 3 trial for sepiapterin for phenylketonuria, or PKU. The primary endpoint of the study was the achievement of statistically-significant reduction in blood Phe level. The primary analysis population included those patients who have a greater than 30% reduction in blood Phe levels during the Part 1 run-in phase of the trial. Sepiapterin demonstrated Phe

level reduction of approximately 63% in the overall primary analysis population and Phe level reduction of approximately 69% in the subset for classical PKU patients. Additionally, sepiapterin was well tolerated with no serious adverse events. Following the placebo-controlled study, patients were eligible to enroll in a long-term open-label study, which is still ongoing and will evaluate long-term safety, durability and Phe tolerance. In March 2024, we submitted a marketing authorization application, or MAA, to the EMA for sepiapterin for the treatment of PKU in the EEA, which was validated and accepted for review by the EMA in May 2024. We expect an opinion from the CHMP in the second quarter of 2025. In July 2024, we submitted an NDA to the FDA for sepiapterin for the treatment of pediatric and adult patients with PKU, including the full spectrum of ages and disease subtypes, in the United States. In September 2024, the FDA accepted for filing the NDA, with a target regulatory action date of July 29, 2025. We also made regulatory submissions for sepiapterin for the treatment of PKU in Brazil in the third quarter of 2024, and in Japan in the fourth quarter of 2024, with a regulatory decision in Japan expected in the fourth quarter of 2025.

In addition to our SMA program, our splicing platform also includes PTC518, which is being developed for the treatment of Huntington's disease, or HD. We announced the results from our Phase 1 study of PTC518 in healthy volunteers in September 2021 demonstrating dose-dependent lowering of huntingtin messenger ribonucleic acid and protein levels, that PTC518 efficiently crosses blood brain barrier at significant levels and that PTC518 was well tolerated. We initiated a Phase 2 study of PTC518 for the treatment of HD in the first quarter of 2022, which consists of an initial 12-week placebo-controlled phase focused on safety, pharmacology and pharmacodynamic effects followed by a nine-month placebo-controlled phase focused on PTC518 biomarker effect. In June 2023, we announced interim data from the 12-week placebo-controlled phase of the Phase 2 study of PTC518. The study demonstrated dose-dependent lowering of huntingtin, or HTT, protein levels in peripheral blood cells, reaching an approximate mean 30% reduction in mutant HTT levels at the 10mg dose level. In addition, PTC518 exposure in the cerebrospinal fluid was consistent with or higher than plasma unbound drug levels. Furthermore, PTC518 was well tolerated with no treatment-related serious adverse events. In June 2024, we announced interim results from the full Phase 2 study of PTC518. In September 2024, the FDA granted Fast Track designation to the PTC518 program for the treatment of HD. In December 2024, we held a Type C meeting with the FDA to discuss whether huntingtin protein lowering could be considered a surrogate endpoint for accelerated approval of PTC518. The FDA was aligned on the scientific rationale and asked to see additional data supportive of an association between huntingtin protein lowering and changes in clinical outcome scores. We expect to provide results from the Phase 2 study of PTC518 for the treatment of HD in the second quarter of 2025. In November 2024, we entered into the Novartis Agreement with Novartis Pharmaceuticals Corporation, or Novartis, relating to our PTC518 program. This transaction closed in January 2025. Pursuant to the Novartis Agreement, we will continue to conduct the ongoing Phase 2A Clinical Trial and the ongoing OLE Clinical Trial pursuant to its existing development plan, with the goal of transitioning the ongoing OLE Clinical Trial to Novartis within 12 months after the effective date of the Novartis Agreement. Novartis will be responsible for all other development of licensed compounds and licensed products and the manufacture and commercialization of licensed compounds and licensed products worldwide.

Our inflammation and ferroptosis platform consists of small molecule compounds that target oxidoreductase enzymes that regulate oxidative stress and inflammatory pathways central to the pathology of a number of CNS diseases. The most advanced molecule in our inflammation and ferroptosis platform is vatiquinone. We announced topline results from a registration-directed Phase 3 trial of vatiquinone in children and young adults with FA, called MOVE-FA, in May 2023. While the study did not meet its primary endpoint of statistically significant change in modified Friedreich Ataxia Rating Scale, or mFARS, score at 72 weeks in the primary analysis population, vatiquinone treatment did demonstrate significant benefit on key disease subscales and secondary endpoints. In addition, in the population of subjects that completed the study protocol, significance was reached in the mFARS endpoint and several secondary endpoints, including the upright stability subscale. Furthermore, vatiquinone was well tolerated. In October 2024, we announced that the pre-specified endpoint for two different FA long-term extension studies was met, with statistically significant evidence of durable treatment benefit on disease progression. In December 2024, we submitted an NDA to the FDA for vatiquinone for the treatment of children and adults living with FA. In February 2025, the FDA accepted for filing the NDA and granted priority review with a target regulatory action date of August 19, 2025.

In addition, we have a pipeline of product candidates and discovery programs that are in early clinical, pre-clinical and research and development stages focused on the development of new treatments for multiple therapeutic areas for rare diseases.

Overview—Funding

The success of our products and any other product candidates we may develop depends largely on obtaining and maintaining reimbursement from governments and third-party insurers. During 2024, our revenues were primarily generated from sales of Translarna for the treatment of nmDMD in countries where we were able to obtain acceptable commercial pricing and reimbursement terms and in select countries where we are permitted to distribute Translarna under our EAP programs or through similar styled programs, and from sales of Emflaza for the treatment of DMD in the United States. We also generated revenue from sales of Upstaza for the treatment of AADC deficiency in the EEA and have recognized revenue associated with milestone and royalty payments from Roche pursuant to a License and Collaboration Agreement, or the SMA License Agreement, by and among us, Roche and, for the limited purposes set forth therein, the SMA Foundation, under our SMA program.

See "Item 1. Business—Commercial Matters—Market Access Considerations" for additional information and "Item 1A. Risk Factors—*Commercialization of Translarna and Upstaza has been in, and is expected to continue to take place in, countries that tend to impose strict price controls, which may adversely affect our revenues. Failure to obtain and maintain acceptable pricing and reimbursement terms for Translarna for the treatment of nmDMD or Upstaza for the treatment of AADC deficiency in the EEA and other countries where Translarna is available would delay or prevent us from marketing our product in such regions, which would adversely affect our business, results of operations, and financial condition.*"

In August 2019, we entered into an At the Market Offering Sales Agreement, or the Sales Agreement, with Cantor Fitzgerald and RBC Capital Markets, LLC, or together, the Sales Agents, pursuant to which, we may offer and sell shares of our common stock, having an aggregate offering price of up to $125.0 million from time to time through the Sales Agents by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. We did not issue or sell any shares of common stock pursuant to the Sales Agreement during the years ended December 31, 2024, 2023 and 2022. The remaining shares of our common stock available to be issued and sold, under the Sales Agreement, have an aggregate offering price of up to $93.0 million as of December 31, 2024.

In September 2019, we issued $287.5 million aggregate principal amount of 1.50% convertible senior notes due September 15, 2026, or the 2026 Convertible Notes, which included an option to purchase up to an additional $37.5 million in aggregate principal amount of the 2026 Convertible Notes, which was exercised in full by the initial purchasers. We received net proceeds of $279.3 million after deducting the initial purchasers' discounts and commissions and the offering expenses payable by us. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and capital resources—Sources of Liquidity" for additional information.

In July 2020, we entered into a Royalty Purchase Agreement, or the Original Royalty Purchase Agreement, with RPI Intermediate Finance Trust, or RPI, and, for the limited purposes set forth in the agreement, Royalty Pharma plc. Pursuant to the Original Royalty Purchase Agreement, we sold to RPI 42.933%, or the Original Assigned Royalty Rights, of the Royalty (as defined below) for $650.0 million. At that time, we retained a 57.067% interest in the Royalty and all economic rights to receive the remaining potential regulatory and sales milestone payments under the SMA License Agreement.

In June 2021, we filed a Certificate of Amendment to our Restated Certificate of Incorporation, which increased the number of authorized shares of our common stock from 125,000,000 to 250,000,000 shares.

In October 2022, we entered into the Credit Agreement, dated October 27, 2022, by and among us and certain of our subsidiaries from time to time party thereto, as guarantors, or, collectively with us, the Loan Parties, funds and other affiliated entities advised or managed by Blackstone Life Sciences and Blackstone Credit, or collectively, Blackstone, as lenders, together with their permitted assignees, the Lenders, and Wilmington Trust, National Association, as the administrative agent for the Lenders, or the Blackstone Credit Agreement. The Blackstone Credit Agreement provided for fundings of up to $950.0 million consisting of a committed loan facility consisting of a senior secured term loan facility funded on October 27, 2022, or the Closing Date, in the aggregate principal amount of $300.0 million, and a delayed draw term loan facility of up to $150.0 million to be funded at our request within 18 months of the Closing Date subject to specified conditions, and further contemplating the potential for up to $500.0 million of additional financing, to the extent

that we requested such additional financing and subject to the Lenders' agreement to provide such additional financing and to mutual agreement on terms. In October 2023, we terminated the Blackstone Credit Agreement. In connection with the termination of the Blackstone Credit Agreement, we repaid outstanding principal of $300.0 million, accrued interest of $2.1 million, an additional $82.0 million in prepayment premiums, exit fees, and creditor expenses, and $0.2 million in legal fees. We recorded a loss on the extinguishment of debt of $92.7 million which is included on the statement of operations for the period ended December 31, 2023. The loss on extinguishment of debt consisted of $82.0 million in prepayment premiums, exit fees, and creditor expenses and debt issuance costs of $10.7 million. All liens and security interests securing the loans made pursuant to the Blackstone Credit Agreement were released upon termination.

In June 2024, we entered into an amendment with Royalty Pharma Investments 2019 ICAV, or Royalty Pharma, and Royalty Pharma plc, to the Amended and Restated Royalty Purchase Agreement, dated October 18, 2023, or the A&R Royalty Purchase Agreement, which amends and restated in its entirety the Original Royalty Purchase Agreement, and we exercised our first put option in exchange for $241.8 million in cash consideration. To date, Royalty Pharma has paid to us cash consideration of $1.9 billion (less Royalty payments received by us with respect to assigned Royalties, or the Assigned Royalty Rights) in exchange for 90.49% of the Royalty, which will be reduced to 83.33% after Royalty Pharma receives $1.3 billion in aggregate payments, or the Assigned Royalty Cap, from the Royalty assigned under the Original Royalty Purchase Agreement. We currently retain 9.51% of the Royalty, which increases to 16.67% after the Assigned Royalty Cap has been met. We have the option to sell our retained portions of the Royalty to Royalty Pharma in up to three tranches for the following payments: (1) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the Assigned Royalty Cap has been met, (2) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the Assigned Royalty Cap has been met, and (3) $50.0 million in exchange for 1.90% of the Royalty, which increases to 3.33% after the Assigned Royalty Cap has been met, in each case less Royalty payments received by us with respect to the Assigned Royalty Rights. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and capital resources—Sources of Liquidity" for additional information.

In November 2024, we entered into the Novartis Agreement relating to our PTC518 HD program which includes related molecules. Pursuant to the Novartis Agreement, we will continue to conduct the ongoing Phase 2A Clinical Trial and the ongoing OLE Clinical Trial pursuant to its existing development plan, with the goal of transitioning the ongoing OLE Clinical Trial to Novartis within 12 months after the effective date. Novartis will be responsible for all other development of licensed compounds and licensed products and the manufacture and commercialization of licensed compounds and licensed products worldwide. Under the Novartis Agreement, and upon the closing of the transaction contemplated by the Novartis Agreement in January 2025, we received an upfront payment of $1.0 billion on the effective date and can receive up to $1.9 billion in development, regulatory and sales milestones, a 40% share of U.S. profits and losses, and tiered double-digit royalties on ex-U.S. sales See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and capital resources—Sources of Liquidity" for additional information.

We have financed our operations to date primarily through the private offerings of convertible senior notes, public and "at the market offerings" of common stock, proceeds from royalty purchase agreements, net proceeds from our borrowings under our credit agreement with Blackstone, private placements of our convertible preferred stock and common stock, collaborations, bank and institutional lender debt, other convertible debt, grant funding and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease area addressed by our product candidates. We have relied on revenue generated from net sales of Translarna for the treatment of nmDMD in territories outside of the United States since 2014, Emflaza for the treatment of DMD in the United States since 2017 and Upstaza for the treatment of AADC deficiency in the EEA since 2022. We have also relied on revenue associated with milestone and royalty payments from Roche pursuant to the SMA License Agreement under our SMA program and revenue generated from net sales of Tegsedi and Waylivra in Latin America and the Caribbean.

As of December 31, 2024, we had an accumulated deficit of $3,646.9 million. We had a net loss of $363.3 million, $626.6 million, and $559.0 million for the fiscal years ended December 31, 2024, 2023 and 2022, respectively.

We anticipate that we will continue to incur significant expenses in connection with our commercialization efforts in the United States, the EEA, Latin America and other territories, including expenses related to our commercial infrastructure and corresponding sales and marketing, legal and regulatory, and distribution and manufacturing undertakings as well as

administrative and employee-based expenses. In addition to the foregoing, we expect to continue to incur significant costs in connection with ongoing, planned and potential future clinical trials and studies for sepiapterin and our splicing and inflammation and ferroptosis programs as well as studies in our products for maintaining authorizations, label extensions and additional indications. We continue to seek marketing authorization for Translarna for the treatment of nmDMD in territories that we do not currently have marketing authorization in and we are exploring other potential mechanisms by which we may provide Translarna to nmDMD patients in the EEA if the EC adopts the CHMP's negative opinion for Translarna following a re-examination procedure. We also submitted an MAA to the EMA for sepiapterin for the treatment of PKU in March 2024, an NDA to the FDA for sepiapterin for the treatment of PKU in the third quarter of 2024, and an NDA to the FDA for vatiquinione for the treatment of FA in the fourth quarter of 2024. These efforts may significantly impact the timing and extent of our commercialization and manufacturing expenses.

We may seek to expand and diversify our product pipeline through opportunistically in-licensing or acquiring the rights to products, product candidates or technologies and we may incur expenses, including with respect to transaction costs, subsequent development costs or any upfront, milestone or other payments or other financial obligations associated with any such transaction, which would increase our future capital requirements.

With respect to our outstanding 2026 Convertible Notes, cash interest payments are payable on a semi-annual basis in arrears, which will require total funding of $4.3 million annually. Borrowings under the Blackstone Credit Agreement, which was terminated in October 2023, bore interest at a variable rate equal to, at our option, either an adjusted Term SOFR rate plus seven and a quarter percent (7.25%) or the Base Rate plus six and a quarter percent (6.25%), subject to a floor of one percent (1%) and two percent (2%) with respect to Term SOFR rate and Base Rate (each as defined in the Blackstone Credit Agreement), respectively.

In May 2024, we announced the validation and acceptance for review of an MMA for sepiapterin by the EMA for the treatment of PKU. In connection with this event and pursuant to the Censa Merger Agreement, we paid a $15.0 million regulatory milestone to the former Censa securityholders. In July 2024, we announced the submission of an NDA to the FDA for sepiapterin for the treatment of pediatric and adult patients with PKU, including the full spectrum of ages and disease subtypes. Pursuant to the Censa Merger Agreement, the decision to submit the NDA triggered a $25.0 million regulatory milestone payment to the former Censa securityholders. In September 2024, we announced the FDA acceptance for filing of the NDA. In connection with this event and pursuant to the Censa Merger Agreement, we paid a $25.0 million regulatory milestone to the former Censa securityholders.

We expect to make additional payments to the former Censa securityholders of $57.5 million in the aggregate in cash upon the potential achievement in 2025 of certain regulatory milestones relating to sepiapterin.

Upon the potential achievement in 2025 of certain regulatory milestones relating to vatiquinone, which milestones would be payable in 2026, we expect to make payments to BioElectron of $75.0 million in the aggregate, in cash or shares of our common stock, as determined by us.

We have never been profitable and we will need to generate significant revenues to achieve and sustain profitability, and we may never do so. Accordingly, we may need to obtain substantial additional funding in connection with our continuing operations. Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or our commercialization efforts.

Financial operations overview

Revenues

To date, our net product revenues have consisted primarily of sales of Translarna for the treatment of nmDMD in territories outside of the United States, and sales of Emflaza for the treatment of DMD in the United States. Our process for recognizing revenue is described below under "Critical accounting policies and significant judgments and estimates—Revenue recognition".

Roche and the SMA Foundation Collaboration. In November 2011, we entered into the SMA License Agreement pursuant to which we are collaborating with Roche and the SMA Foundation to further develop and commercialize compounds identified under our SMA program with the SMA Foundation. The research component of this agreement terminated effective December 31, 2014. We are eligible to receive additional payments from Roche if specified events are achieved with respect to each licensed product, including up to $135.0 million in research and development event milestones, up to $325.0 million in sales milestones upon achievement of specified sales events, and up to double digit royalties on worldwide annual net sales of a commercial product. As of December 31, 2024, we had recognized a total of $310.0 million in milestone payments and $545.6 million royalties on net sales pursuant to the SMA License Agreement. As of December 31, 2024, there are no remaining research and development event milestones that we can receive. The remaining potential sales milestones as of December 31, 2024 are $150.0 million upon achievement of certain sales events.

In June 2024, we entered into an amendment to the A&R Royalty Purchase Agreement, and we exercised our first put option in exchange for $241.8 million in cash consideration. Pursuant to the A&R Royalty Purchase Agreement, Royalty Pharma has paid to us aggregate cash consideration of $1.9 billion (less Royalty payments received by us with respect to the Assigned Royalty Rights) in exchange for 90.49% of the Royalty, which will be reduced to 83.33% of the Royalty after Royalty Pharma receives $1.3 billion in aggregate payments from the Royalty assigned at the closing of the Original Purchase Agreement. We currently retain 9.51% of the Royalty, which increases to 16.67% after the Assigned Royalty Cap has been met, and all economic rights to receive the remaining potential regulatory and sales milestone payments under the SMA License Agreement.

We have the option to sell our retained portions of the Royalty to Royalty Pharma in up to three tranches for the following payments: (1) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the Assigned Royalty Cap has been met, (2) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the Assigned Royalty Cap has been met, and (3) $50.0 million in exchange for 1.90% of the Royalty, which increases to 3.33% after the Assigned Royalty Cap has been met, in each case less Royalty payments received by us with respect to the Assigned Royalty Rights. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and capital resources—Sources of Liquidity" for additional information.

On November 27, 2024, we and Novartis entered into the Novartis Agreement relating to our PTC518 HD program which includes related molecules. Under the Novartis Agreement, and upon the closing of the transaction contemplated by the Novartis Agreement in January 2025, we received an upfront payment of $1.0 billion on the effective date and can receive up to $1.9 billion in development, regulatory and sales milestones, a 40% share of U.S. profits and losses, and tiered double-digit royalties on ex-U.S. sales. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and capital resources—Sources of Liquidity" for additional information.

Research and development expense

Research and development expenses consist of the costs associated with our research activities, as well as the costs associated with our drug discovery efforts, conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings. Our research and development expenses consist of:

- external research and development expenses incurred under agreements with third-party contract research organizations and investigative sites, third-party manufacturing organizations and consultants;
- employee-related expenses, which include salaries and benefits, including share-based compensation, for the personnel involved in our drug discovery and development activities; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, IT, human resources, and other support functions, depreciation of leasehold improvements and equipment, and laboratory and other supplies.

We use our employee and infrastructure resources across multiple research projects, including our drug development programs. We track expenses related to our clinical programs and certain preclinical programs on a per project basis.

We expect our research and development expenses to fluctuate in connection with our ongoing activities, particularly in connection with our activities for sepiapterin and our splicing and inflammation and ferroptosis programs and

performance of any post-marketing requirements imposed by regulatory agencies with respect to our products. The timing and amount of these expenses will depend upon the outcome of our ongoing clinical trials and the costs associated with our planned clinical trials. The timing and amount of these expenses will also depend on the costs associated with potential future clinical trials of our products or product candidates and the related expansion of our research and development organization, regulatory requirements, advancement of our preclinical programs, and product and product candidate manufacturing costs. In 2023, as part of our strategic pipeline prioritizations, we decided to discontinue our preclinical and early research programs for our gene therapy and oncology platforms, reducing research and development expenses in these areas.

The following table provides research and development expense for our most advanced principal product development programs, for the years ended December 31, 2024, 2023, and 2022.

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Development	$ 219,594	$ 281,134	$ 304,116
Research	63,375	99,286	115,159
Milestones	65,000	30,000	—
Payroll, benefits, and share-based stock compensation	147,052	205,359	188,751
Facilities and other	39,459	50,784	43,470
Total research and development	$ 534,480	$ 666,563	$ 651,496

Development. Consists of costs incurred for product candidates following initiation of a clinical trial.

For the year ended December 31, 2024, compared to the years ended December 31, 2023 and 2022, the decrease in development expenses primarily reflected the decrease in program spend related to our strategic pipeline prioritization in 2023 as we continued to focus our resources on our differentiated, high potential research and development programs.

Research. Consists of costs incurred for product candidates before initiation of a clinical trial.

For the year ended December 31, 2024, compared to the years ended December 31, 2023 and 2022, the decrease in research expenses was primarily related to our strategic pipeline prioritization in 2023 where we discontinued several preclinical and early research programs.

Milestones. Consists of development and regulatory milestone expenses incurred in connection with our collaborative arrangements.

For the year ended December 31, 2024, compared to the years ended December 31, 2023 and 2022, the increase in milestone expenses primarily related to the achievement of a $15.0 million success-based regulatory milestone for the validation and acceptance of an MMA for sepiapterin for PKU in May 2024, the achievement of a $25.0 million regulatory milestone for the decision to submit an NDA to the FDA for sepiapterin for PKU in July 2024, and the achievement of a $25.0 million regulatory milestone for the acceptance of an NDA to the FDA for sepiapterin for PKU in September 2024, as compared to the achievement of a $30.0 million success-based development milestone for the completion of enrollment of a Phase 3 clinical trial for sepiapterin for PKU in February 2023, and no milestones achieved in the year ended December 31, 2022.

Payroll, benefits, and share-based stock compensation. Consists of costs incurred for salaries and wages, bonus, payroll taxes, benefits and stock-based compensation associated with employees involved in research and development activities. Stock-based compensation may fluctuate from period to period based on factors that are not within our control, such as our stock price on the dates stock-based grants are issued.

For the year ended December 31, 2024, compared to the years ended December 31, 2023 and 2022, the change in payroll, benefits, and share-based stock compensation expenses primarily relates to our reduction in workforce in

connection with our strategic pipeline prioritization in 2023 and discontinuation of our preclinical and early research programs in our gene therapy platform.

Facilities and other. Consists of indirect costs incurred for the benefit of multiple programs, including information technology, and other facility-based expenses, such as rent expense.

For the year ended December 31, 2024, compared to the years ended December 31, 2023 and 2022, the change in facilities and other expenses primarily related to decreases in facility-based expenses at our facility in Hopewell Township, New Jersey as a result of an amendment and restatement of our lease for such facility.

The successful development of our products and product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our clinical trials and other research and development activities;
- the potential benefits of our products and product candidates over other therapies;
- our ability to market, commercialize and achieve market acceptance for our products or any of our product candidates that we are developing or may develop in the future, including our ability to negotiate pricing and reimbursement terms acceptable to us;
- clinical trial results;
- the terms and timing of regulatory approvals; and
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of our products or product candidates could mean a significant change in the costs and timing associated with the development of those products or product candidates. For example, if the EMA or the FDA or other regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate will be required for the completion of clinical development of any of our products or product candidates or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Selling, general and administrative expense

Selling, general and administrative expenses consist primarily of salaries and other related costs for personnel, including share-based compensation expenses, in our executive, legal, business development, commercial, finance, accounting, information technology and human resource functions. Other selling, general and administrative expenses include facility-related costs not otherwise included in research and development expense; advertising and promotional expenses; costs associated with industry and trade shows; and professional fees for legal services, including patent-related expenses, accounting services and miscellaneous selling costs.

We expect that we will continue to incur significant selling, general and administrative expenses in future periods in connection with our continued efforts to commercialize our products, including increased payroll, expanded infrastructure, commercial operations, increased consulting, legal, accounting and investor relations expenses.

Interest expense, net

Interest expense, net consists of interest expense from the liability for the sale of future royalties related to the Original Royalty Purchase Agreement, the A&R Royalty Purchase Agreement, the 2026 Convertible Notes outstanding, the Blackstone Credit Agreement that we repaid and terminated in October 2023, the 3.00% convertible senior notes due 2022, or the 2022 Convertible Notes, that we repaid in August 2022, offset by interest income earned on investments.

Critical accounting policies and significant judgments and estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States. The

preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. Actual results may differ from these estimates under different assumptions or conditions.

Of our policies, revenue recognition related to net product revenue is considered critical to an understanding of our consolidated financial statements as it requires the application of the most subjective and complex judgment, involving critical accounting estimates and assumptions impacting our consolidated financial statements.

Revenue recognition related to net product revenue

Net product revenues. Our net product revenue primarily consists of sales of Translarna in territories outside of the U.S. and sales of Emflaza in the U.S., both for the treatment of DMD. We recognize revenue when performance obligations with customers have been satisfied. Our performance obligations are to provide products based on customer orders from distributors, hospitals, specialty pharmacies or retail pharmacies. The performance obligations are satisfied at a point in time when our customer obtains control of the product, which is typically upon delivery. We invoice customers after the products have been delivered and invoice payments are generally due within 30 to 90 days of invoice date. We determine the transaction price based on fixed consideration in its contractual agreements. Contract liabilities arise in certain circumstances when consideration is due for goods not yet provided. As we have identified only one distinct performance obligation, the transaction price is allocated entirely to the product sale. In determining the transaction price, a significant financing component does not exist since the timing from when we deliver product to when the customers pay for the product is typically less than one year. Customers in certain countries pay in advance of product delivery. In those instances, payment and delivery typically occur in the same month.

We record product sales net of any variable consideration, which includes discounts, allowances, rebates related to Medicaid and other government pricing programs, and distribution fees. We use the expected value or most likely amount method when estimating variable consideration, unless discount or rebate terms are specified within contracts. The identified variable consideration is recorded as a reduction of revenue at the time revenues from product sales are recognized. These estimates for variable consideration are adjusted to reflect known changes in factors and may impact such estimates in the quarter those changes are known. Revenue recognized does not include amounts of variable consideration that are constrained.

During the years ended December 31, 2024, 2023, and 2022, net product sales in the United States were $207.2 million, $255.1 million, and $218.3 million, respectively, consisting solely of sales of Emflaza, and net product sales outside of the United States were $393.8 million, $406.1 million, and $316.9 million, respectively, consisting of sales of Translarna, Tegsedi, Waylivra, and Upstaza. Translarna net product revenues made up $339.9 million, $355.8 million, and $288.6 million of the net product sales outside the United States for the years ended December 31, 2024, 2023 and 2022, respectively. During the year ended December 31, 2024, three countries, the United States, Russia, and Brazil, accounted for at least 10% of our net product sales, representing $207.2 million, $105.4 million, and $72.1 million of net product sales, respectively. During the years ended December 31, 2023 and 2022, two countries, the United States and Russia, accounted for at least 10% of our net product sales, representing $255.1 million and $86.0 million, and $218.3 million and $59.7 million, respectively.

In relation to customer contracts, we incur costs to fulfill a contract but do not incur costs to obtain a contract. These costs to fulfill a contract do not meet the criteria for capitalization and are expensed as incurred. We consider any shipping and handling costs that are incurred after the customer has obtained control of the product as a cost to fulfill a promise. Shipping and handling costs associated with finished goods delivered to customers are recorded as a selling expense.

For a description of our significant accounting policies, see note 2 to our consolidated financial statements.

Year ended December 31, 2024 compared to year ended December 31, 2023

The following table summarizes revenues and selected expense and other income data for the year ended December 31, 2024 and 2023:

(in thousands)	Year ended December 31, 2024	2023	Change 2024 vs. 2023
Net product revenue	$ 600,951	$ 661,249	$ (60,298)
Collaboration revenue	304	100,030	$ (99,726)
Royalty revenue	203,864	168,856	$ 35,008
Manufacturing revenue	1,661	7,687	$ (6,026)
Cost of product sales, excluding amortization of acquired intangible assets	57,398	65,486	$ (8,088)
Amortization of acquired intangible assets	60,738	222,635	$ (161,897)
Research and development expense	534,480	666,563	$ (132,083)
Selling, general and administrative expense	300,911	332,540	$ (31,629)
Change in the fair value of contingent consideration	(4,475)	(127,700)	$ 123,225
Intangible asset impairment	159,548	217,800	$ (58,252)
Tangible asset impairment and losses (gains) on transactions, net	750	—	$ 750
Interest expense, net	(166,993)	(129,180)	$ (37,813)
Other income, net	6,544	10,130	$ (3,586)
Gain on sale of priority review voucher	99,900	—	$ 99,900
Loss on extinguishment of debt	—	(137,558)	$ 137,558
Income tax (expense) benefit	(176)	69,506	$ (69,682)

Net product revenue. Net product revenue was $601.0 million for the year ended December 31, 2024, a decrease of $60.3 million, or 9%, from net product revenue of $661.2 million for the year ended December 31, 2023. Translarna net product revenues were $339.9 million for the year ended December 31, 2024, a decrease of $15.9 million, or 4%, compared to $355.8 million for the year ended December 31, 2023. These results were due to the timing of bulk patient orders, as well as the residual impact from the CHMP negative opinion in September 2023. Emflaza net product revenues were $207.2 million for the year ended December 31, 2024, a decrease of $47.9 million, or 19%, compared to $255.1 million for the year ended December 31, 2023. These results were driven by the expiration of Emflaza's orphan drug exclusivity in February 2024. The remaining change of $3.5 million was due to an increase of $5.4 million in net product sales relating to Tegsedi and Waylivra, and a decrease in net product sales of $1.9 million relating to Upstaza.

Collaboration revenue. Collaboration revenue was $0.3 million for the year ended December 31, 2024, a decrease of $99.7 million, or 100%, from collaboration revenue of $100.0 million for the year ended December 31, 2023. The decrease relates to sales milestone of $100.0 million that was recognized for the achievement of $1.5 billion in worldwide annual net sales from Evrysdi in the year ended December 31, 2023.

Royalty revenue. Royalty revenue was $203.9 million for the year ended December 31, 2024, an increase of $35.0 million, or 21%, from $168.9 million for the year ended December 31, 2023. The increase in royalty revenue was due to higher Evrysdi sales in the year ended December 31, 2024, compared to the year ended December 31, 2023. In accordance with the SMA License Agreement, we are entitled to royalties on worldwide annual net sales of the product.

Manufacturing revenue. Manufacturing revenues were $1.7 million for the year ended December 31, 2024, a decrease of $6.0 million, or 78%, from $7.7 million for the year ended December 31, 2023. The decrease was due to the completion of all manufacturing services related to the production of plasmid DNA and AAV vectors for gene therapy applications for external customers. In June 2024, we sold our gene therapy manufacturing business in Hopewell Township, New Jersey. Accordingly, we do not expect to have manufacturing revenue going forward.

Cost of product sales, excluding amortization of acquired intangible asset. Cost of product sales, excluding amortization of acquired intangible asset, was $57.4 million for the year ended December 31, 2024, a decrease of $8.1

million, or 12%, from $65.5 million for the year ended December 31, 2023. Cost of product sales excluding amortization of acquired intangible asset consisted primarily of royalty payments associated with Emflaza, Translarna, and Upstaza net product sales, costs associated with Emflaza, Translarna, and Upstaza products sold during the period, and royalty expense related to royalty revenues and collaboration milestone revenues. The decrease in cost of product sales, excluding amortization of acquired intangible asset, was primarily due to decreases in costs related to royalty and collaboration revenues, partially offset by increases in royalty costs driven by Emflaza.

Amortization of acquired intangible asset. Amortization of acquired intangible asset was $60.7 million for the year ended December 31, 2024, a decrease of $161.9 million, or 73%, from $222.6 million for the year ended December 31, 2023. These amounts are related to the Emflaza rights acquisition, as well as the Waylivra, Tegsedi, and Upstaza/Kebilidi intangible assets, which are all being amortized on a straight-line basis over their estimated useful lives. The amortization decrease was driven by the Emflaza rights intangible asset being fully amortized as of February 2024, therefore, milestones are recorded on the consolidated statement of operations within cost of product sales, excluding amortization of acquired intangible assets from February 2024 onward.

Research and development expense. Research and development expense was $534.5 million for the year ended December 31, 2024, a decrease of $132.1 million, or 20%, compared to $666.6 million for the year ended December 31, 2023. The decrease in research and development expenses related to decreases in program spend related to our strategic portfolio prioritization as we continued to focus our resources on our differentiated, high potential research and development programs. Research and development expense also included a total of $65.0 million regulatory success-based milestones paid to the former Censa securityholders for the year ended December 31, 2024, as compared to a $30.0 million success-based development milestone paid to the former Censa securityholders for the year ended December 31, 2023.

Selling, general and administrative expense. Selling, general and administrative expense was $300.9 million for the year ended December 31, 2024, a decrease of $31.6 million, or 10%, from $332.5 million for the year ended December 31, 2023. The decrease reflected lower employee costs as a result of the reduction in workforce in 2023.

Change in the fair value of contingent consideration. Change in the fair value of contingent consideration was a gain of $4.5 million for the year ended December 31, 2024, a decrease of $123.2 million, or 96%, from a gain of $127.7 million for the year ended December 31, 2023. The decrease is primarily related to our strategic portfolio prioritization in 2023 and decision to discontinue our preclinical and early research programs in our gene therapy platform in May 2023, which included programs for FA and Angelman syndrome. As a result, we fully impaired the FA and Angelman syndrome intangible assets and determined that the fair value for all of the contingent consideration payable related to FA and Angelman syndrome was $0. As a result, we recorded a fair value change of $128.4 million for the year ended December 31, 2023 for the contingent consideration related to FA and Angelman syndrome.

Intangible asset impairment. Intangible asset impairment was $159.5 million for the year ended December 31, 2024, a decrease of $58.3 million, or 27%, from intangible asset impairment of $217.8 million for the year ended December 31, 2023. During the year ended December 31, 2024, as a result of our annual impairment test for our PTC-AADC indefinite lived intangible asset, we impaired $159.5 million due to a decrease in projected cash flows due to refinements in current market assumptions and the timing of patient treatments. During the year ended December 31, 2023, as a result of our strategic portfolio prioritization in 2023 and decision to discontinue our preclinical and early research programs in our gene therapy platform, which included programs for FA and Angelman syndrome, we fully impaired the FA and Angelman syndrome intangible assets and recorded impairment expense of $217.8 million.

Tangible asset impairment and losses (gains) on transactions, net. Tangible asset impairment and losses (gains) on transactions, net was $0.8 million for the year ended December 31, 2024, an increase of $0.8 million, or 100%, from impairment of tangible assets of $0.0 million for the year ended December 31, 2023. The increase in tangible asset impairment and losses (gains) on transactions, net, was due to a $4.4 million loss primarily related to the sale of certain assets for gene therapy manufacturing, and a $4.1 million loss primarily related to fixed asset impairments in connection with the South Plainfield, New Jersey office closure and Warren, New Jersey lease modification. These amounts were partially offset by a gain of $2.2 million on lease terminations, and a gain of $5.5 million on lease modifications.

Interest expense, net. Interest expense, net was $167.0 million for the year ended December 31, 2024, an increase of $37.8 million, or 29%, from interest expense, net of $129.2 million for the year ended December 31, 2023. The increase in interest expense, net was primarily due to interest expense recorded from the liability for the sale of future royalties related to the A&R Royalty Purchase Agreement and the Original Royalty Purchase Agreement, offset by a decrease in interest expense due to the termination of our Blackstone Credit Agreement.

Other income, net. Other income, net was $6.5 million for the year ended December 31, 2024, a decrease of $3.6 million, or 35%, from other income, net of $10.1 million for the year ended December 31, 2023. The decrease in other income, net resulted primarily from a decrease in unrealized and realized foreign exchange gains of $8.0 million for the year ended December 31, 2024 as compared to the year ended December 31, 2023. In addition, we had unrealized gains on our ClearPoint equity investments of $7.7 million and unrealized and realized losses on our ClearPoint convertible debt security of $2.6 million for the year ended December 31, 2024, as compared to unrealized and realized losses on our ClearPoint equity investments and ClearPoint convertible debt security of $2.3 million and $2.7 million, respectively, for the year ended December 31, 2023. For the years ended December 31, 2024 and 2023, we had net realized gains of $0.1 million on marketable securities – available for sale and $4.8 million on marketable securities – equity investments, respectively.

Gain on sale of priority review voucher. Gain on sale of priority review voucher was $99.9 million for the year ended December 31, 2024, an increase of $99.9 million, or 100%, from gain on sale of priority review voucher of $0.0 million for the year ended December 31, 2023. In connection with our FDA approval of Kebilidi, we received a Priority Review Voucher, or PRV, and sold the PRV for aggregate net proceeds of $148.0 million. We had previously recorded an indefinite lived intangible asset for the PRV of $48.1 million in connection with the acquisition of Agilis in 2018, which was included as part of the book balance of our PTC-AADC indefinite lived intangible asset balance. Accordingly, we derecognized the book value of the PRV and recorded a gain of $99.9 million upon the sale.

Loss on extinguishment of debt. Loss on extinguishment of debt was $0.0 million for the year ended December 31, 2024, a decrease of $137.6 million, or 100%, from loss on extinguishment of debt of $137.6 million for the year ended December 31, 2023. The decrease was primarily due to the early termination of our Blackstone Credit Agreement in 2023, with no similar event occurring in 2024. We recorded a loss on the extinguishment of debt of $92.7 million for the period ended December 31, 2023. The loss on extinguishment of debt consisted of $82.0 million in prepayment premiums, exit fees, and creditor expenses and debt issuance costs of $10.7 million. In addition, we recorded $44.9 million on the loss of extinguishment of debt relating to the A&R Royalty Purchase Agreement.

Income tax (expense) benefit. Income tax expense was $0.2 million for the year ended December 31, 2024, a change of $69.7 million, or over 100%, from income tax benefit of $69.5 million for the year ended December 31, 2023. The change in income tax (expense) benefit was attributable to an increase of current federal and state tax expense driven by the recognition of previously deferred revenue from the A&R Royalty Purchase Agreement.

Year ended December 31, 2023 compared to year ended December 31, 2022

The following table summarizes revenues and selected expense and other income data for the years ended December 31, 2023 and 2022:

(in thousands)	Year ended December 31, 2023	2022	Change 2023 vs. 2022
Net product revenue	$ 661,249	$ 535,228	$ 126,021
Collaboration revenue	100,030	50,052	$ 49,978
Royalty revenue	168,856	113,521	$ 55,335
Manufacturing revenue	7,687	—	$ 7,687
Cost of product sales, excluding amortization of acquired intangible assets	65,486	44,678	$ 20,808
Amortization of acquired intangible assets	222,635	116,554	$ 106,081
Research and development expense	666,563	651,496	$ 15,067
Selling, general and administrative expense	332,540	325,998	$ 6,542
Change in the fair value of contingent consideration	(127,700)	(25,900)	$ (101,800)
Intangible asset impairment	217,800	33,384	$ 184,416
Interest expense, net	(129,180)	(90,871)	$ (38,309)
Other income (expense), net	10,130	(49,207)	$ 59,337
Loss on extinguishment of debt	(137,558)	—	$ (137,558)
Income tax benefit	69,506	28,470	$ 41,036

Net product revenue. Net product revenue was $661.2 million for the year ended December 31, 2023, an increase of $126.0 million, or 24%, from net product revenue of $535.2 million for the year ended December 31, 2022. Translarna net product revenues were $355.8 million for the year ended December 31, 2023, an increase of $67.2 million, or 23%, compared to $288.6 million for the year ended December 31, 2022. These results were driven by treatment of new patients in existing geographies and continued geographic expansion. Emflaza net product revenues were $255.1 million for the year ended December 31, 2023, an increase of $36.8 million, or 17%, compared to $218.3 million for the year ended December 31, 2022. These results were driven by new patient starts and high compliance. The remaining increase of $22.0 million was due to an increase in net product sales of Tegsedi, Waylivra, and Upstaza.

Collaboration revenue. Collaboration revenue was $100.0 million for the year ended December 31, 2023, an increase of $50.0 million, or 100%, from collaboration revenue of $50.1 million for the year ended December 31, 2022. The increase is due to an increase in actual milestones that were achieved in the year ended December 31, 2023 compared to the year ended December 31, 2022, respectively. A sales milestone of $100.0 million was recognized for the achievement of $1.5 billion in worldwide annual net sales from Evrysdi in the year ended December 31, 2023. A sales milestone of $50.0 million was recognized for the achievement of $750.0 million in worldwide annual net sales from Evrysdi in the year ended December 31, 2022.

Royalty revenue. Royalty revenue was $168.9 million for the year ended December 31, 2023, an increase of $55.3 million, or 49%, from $113.5 million for the year ended December 31, 2022. The increase in royalty revenue was due to higher Evrysdi sales in the year ended December 31, 2023 compared to the year ended December 31, 2022. In accordance with the SMA License Agreement, we are entitled to royalties on worldwide annual net sales of the product.

Manufacturing revenue. Manufacturing revenues were $7.7 million for the year ended December 31, 2023, an increase of $7.7 million, or over 100%, from $0.0 million for the year ended December 31, 2022. The increase in manufacturing revenue was due to the manufacturing services related to the production of plasmid DNA and AAV vectors for gene therapy applications for external customers.

Cost of product sales, excluding amortization of acquired intangible asset. Cost of product sales, excluding amortization of acquired intangible asset, was $65.5 million for the year ended December 31, 2023, an increase of $20.8

million, or 47%, from $44.7 million for the year ended December 31, 2022. Cost of product sales excluding amortization of acquired intangible asset, consisted primarily of royalty payments associated with Emflaza, Translarna and Upstaza net product sales, excluding contingent payments to Marathon, costs associated with Emflaza, Translarna and Upstaza product sold during the period, inventory reserves, and royalty expense related to royalty revenues and collaboration milestone revenues. The increase in cost of product sales, excluding amortization of acquired intangible asset, was primarily due to the increases in net product revenue, Upstaza inventory reserves, royalty revenues, and collaboration milestone revenue.

Amortization of acquired intangible asset. Amortization of acquired intangible asset was $222.6 million for the year ended December 31, 2023, an increase of $106.1 million, or 91%, from $116.6 million for the year ended December 31, 2022. These amounts were related to the Emflaza rights acquisition, as well as the Waylivra, Tegsedi, and Upstaza intangible assets, which are all being amortized on a straight-line basis over their estimated useful lives. The amortization increase was primarily related to additional Marathon contingent payments for Emflaza.

Research and development expense. Research and development expense was $666.6 million for the year ended December 31, 2023, an increase of $15.1 million, or 2%, compared to $651.5 million for the year ended December 31, 2022. The increase in research and development expenses included the achievement of a $30.0 million success-based development milestone for the completion of enrollment of a Phase 3 clinical trial for sepiapterin for PKU. The increase also included restructuring costs from a reduction in workforce in connection with our strategic pipeline prioritization and discontinuation of our preclinical and early research programs in our gene therapy platform in the year ended December 31, 2023. These increases were partially offset by decreases in program spend related to our strategic portfolio prioritization as we continued to focus our resources on our differentiated, high potential research and development programs.

Selling, general and administrative expense. Selling, general and administrative expense was $332.5 million for the year ended December 31, 2023, an increase of $6.5 million, or 2%, from $326.0 million for the year ended December 31, 2022. The increase reflected our continued investment to support our commercial activities including our expanding commercial portfolio. The increase also includes restructuring costs from a reduction in workforce in connection with our strategic pipeline prioritization and discontinuation of our preclinical and early research programs in our gene therapy platform in the year ended December 31, 2023.

Change in the fair value of contingent consideration. Change in the fair value of contingent consideration was a gain of $127.7 million for the year ended December 31, 2023, a change of $101.8 million, or over 100%, from a gain of $25.9 million for the year ended December 31, 2022. The change was primarily related to our strategic portfolio prioritization and decision to discontinue our preclinical and early research programs in our gene therapy platform, which included programs for FA and Angelman syndrome, which was announced in May 2023. As a result, we fully impaired the FA and Angelman syndrome intangible assets and determined that the fair value for all of the contingent consideration payable related to FA and Angelman syndrome was $0. As a result, we recorded a fair value change of $128.4 million for the year ended December 31, 2023 for the contingent consideration related to FA and Angelman syndrome

Intangible asset impairment. Intangible asset impairment was $217.8 million for the year ended December 31, 2023, an increase of $184.4 million, or over 100%, from intangible asset impairment of $33.4 million for the year ended December 31, 2022. The change was due to our strategic portfolio prioritization and decision to discontinue our preclinical and early research programs in our gene therapy platform, which included programs for FA and Angelman syndrome, which was announced in May 2023. As a result, we fully impaired the FA and Angelman syndrome intangible assets and recorded impairment expense of $217.8 million during the year ended December 31, 2023. During the year ended December 31, 2022, a partial impairment of $33.4 million was recorded due to a decrease in projected cash flows for the Upstaza indefinite lived intangible asset due to refinements in market assumptions.

Interest expense, net. Interest expense, net was $129.2 million for the year ended December 31, 2023, an increase of $38.3 million, or 42%, from interest expense, net of $90.9 million for the year ended December 31, 2022. The increase in interest expense, net was primarily due to interest expense recorded from the liability for the sale of future royalties related to the A&R Royalty Purchase Agreement and the Original Royalty Purchase Agreement.

Other income (expense), net. Other income, net was $10.1 million for the year ended December 31, 2023, a change of $59.3 million, or over 100%, from other expense, net of $49.2 million for the year ended December 31, 2022. The change in other income (expense), net resulted primarily from unrealized foreign exchange gains of $11.7 million and realized foreign currency exchanges losses of $2.7 million, for the year ended December 31, 2023, as compared to unrealized foreign exchange losses of $14.4 million and a non cash foreign currency remeasurement loss of $16.9 million from the remeasurement of our intercompany loan for the year ended December 31, 2022. In addition, we had unrealized and realized losses on our equity investments and convertible debt security in ClearPoint of $2.3 million and $2.7 million, respectively, for the year ended December 31, 2023, as compared to unrealized losses on our equity investments and convertible debt security in ClearPoint, of $3.5 million and $5.8 million, respectively, for the year ended December 31, 2022.

Loss on extinguishment of debt. Loss on extinguishment of debt was $137.6 million for the year ended December 31, 2023, an increase of $137.6 million, or 100%, from loss on extinguishment of debt of $0.0 million for the year ended December 31, 2022. The increase was primarily due to the early termination of our Blackstone Credit Agreement. We recorded a loss on the extinguishment of debt of $92.7 million for the period ended December 31, 2023. The loss on extinguishment of debt consisted of $82.0 million in prepayment premiums, exit fees, and creditor expenses and debt issuance costs of $10.7 million. In addition, we recorded $44.9 million on the loss of extinguishment of debt relating to the A&R Royalty Purchase Agreement.

Income tax benefit. Income tax benefit was $69.5 million for the year ended December 31, 2023, an increase of $41.0 million, or over 100%, from income tax benefit of $28.5 million for the year ended December 31, 2022. The increase in income tax benefit was attributable to the receipt of an outstanding state tax refund received during the year ended December 31, 2023, and the subsequent release of the associated ASC 740 income tax reserve, as well as the reversal of the deferred tax liability recognized in conjunction with the discontinuation of our preclinical and early research programs in our gene therapy platform, which included programs for FA and Angelman syndrome, during the year ended December 31, 2023.

Liquidity and capital resources

Sources of liquidity

Since inception, we have incurred significant operating losses.

As a growing commercial-stage biopharmaceutical company, we are engaging in significant commercialization efforts for our products while also devoting a substantial portion of our efforts on research and development related to our products, product candidates and other programs. To date, our product revenue has primarily consisted of sales of Translarna for the treatment of nmDMD in territories outside of the United States and from Emflaza for the treatment of DMD in the United States. Our ongoing ability to generate revenue from sales of Translarna for the treatment of nmDMD is dependent upon our ability to maintain our marketing authorizations in Brazil, Russia and in the EEA and secure market access through commercial programs following the conclusion of pricing and reimbursement terms at sustainable levels in the member states of the EEA or through EAP programs or similar styled programs in the EEA and other territories. In January 2024, the CHMP issued a negative opinion for the renewal of the conditional marketing authorization following a re-examination procedure. In May 2024, the EC decided not to adopt the CHMP's negative opinion for the renewal of the conditional marketing authorization of Translarna and returned such opinion to the CHMP for re-evaluation. In June 2024, following the EC's request for re-review, the CHMP issued a negative opinion on the renewal of the conditional marketing authorization of Translarna for the treatment of nmDMD. On October 18, 2024, the CHMP maintained its negative opinion for the renewal of the conditional marketing authorization following the requested reexamination procedure. In accordance with EMA regulations, the EC has 67 days from the date of issuance to adopt the opinion. At this time, the EC has not yet adopted the negative opinion. If the EC adopts the negative opinion, Translarna would no longer have marketing authorization in the member states of the EEA. The marketing authorization for Translarna remains in effect, pending the EC's potential adoption of the negative opinion. We are exploring other potential mechanisms by which we may provide Translarna to nmDMD patients in the EEA if the negative opinion is adopted by the EC. Emflaza is approved in the United States for the treatment of DMD in patients two years and older. Our ability to generate product revenue from Emflaza will largely depend on the coverage and reimbursement levels set by governmental authorities,

private health insurers and other third-party payors. Additionally, Emflaza's seven-year period of orphan drug exclusivity related to the treatment of DMD in patients five years and older expired in February 2024. We have previously relied on this exclusivity period to commercialize Emflaza in the United States. We expect the expiration of this orphan drug exclusivity to have a significant negative impact on Emflaza net product revenue. Emflaza's orphan drug exclusivity related to the treatment of DMD in patients two years of age to less than five expires in June 2026.

We have financed our operations to date primarily through private offerings of convertible senior notes, public and "at the market offerings" of common stock, proceeds from royalty purchase agreements, net proceeds from our borrowings under our credit agreement with Blackstone, private placements of our convertible preferred stock and common stock, collaborations, bank and institutional lender debt, other convertible debt, grant funding and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease area addressed by our product candidates. We expect to continue to incur significant expenses and operating losses for at least the next fiscal year. The net losses we incur may fluctuate significantly from quarter to quarter.

In August 2019, we entered into the Sales Agreement, pursuant to which, we may offer and sell shares of our common stock, having an aggregate offering price of up to $125.0 million from time to time through the Sales Agents by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Overview—Funding" for additional information.

In September 2019, we issued $287.5 million aggregate principal amount of 2026 Convertible Notes, which included an option to purchase up to an additional $37.5 million in aggregate principal amount of the 2026 Convertible Notes, which was exercised in full by the initial purchasers. The 2026 Convertible Notes bear cash interest at a rate of 1.50% per year, payable semi-annually on March 15 and September 15 of each year, beginning on March 15, 2020. The 2026 Convertible Notes will mature on September 15, 2026, unless earlier repurchased or converted. We received net proceeds of $279.3 million after deducting the initial purchasers' discounts and commissions and the offering expenses payable by us.

Holders may convert their 2026 Convertible Notes at their option at any time prior to the close of business on the business day immediately preceding March 15, 2026 only under the following circumstances: (1) during any calendar quarter commencing on or after December 31, 2019 (and only during such calendar quarter), if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; (2) during the five business day period after any five consecutive trading day period, or the measurement period, in which the trading price (as defined in the 2026 Convertible Notes Indenture) per $1,000 principal amount of 2026 Convertible Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our common stock and the conversion rate on each such trading day; (3) during any period after we have issued notice of redemption until the close of business on the scheduled trading day immediately preceding the relevant redemption date; or (4) upon the occurrence of specified corporate events. On or after March 15, 2026, until the close of business on the business day immediately preceding the maturity date, holders may convert their 2026 Convertible Notes at any time, regardless of the foregoing circumstances. Upon conversion, we will pay or deliver, as the case may be, cash, shares of our common stock or any combination thereof at our election.

The conversion rate for the 2026 Convertible Notes was initially, and remains, 19.0404 shares of our common stock per $1,000 principal amount of the 2026 Convertible Notes, which is equivalent to an initial conversion price of approximately $52.52 per share of our common stock. The conversion rate may be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest.

We were not permitted to redeem the 2026 Convertible Notes prior to September 20, 2023. We may redeem for cash all or any portion of the 2026 Convertible Notes, at our option, if the last reported sale price of our common stock has been at least 130% of the conversion price then in effect on the last trading day of, and for at least 19 other trading days (whether or not consecutive) during, any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption, at a redemption price equal to 100% of the principal amount

of the 2026 Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. No sinking fund is provided for the 2026 Convertible Notes, which means that we are not required to redeem or retire the 2026 Convertible Notes periodically.

If we undergo a "fundamental change" (as defined in the 2026 Convertible Notes Indenture), subject to certain conditions, holders of the 2026 Convertible Notes may require us to repurchase for cash all or part of their 2026 Convertible Notes at a repurchase price equal to 100% of the principal amount of the 2026 Convertible Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

The 2026 Convertible Notes represent senior unsecured obligations and will rank senior in right of payment to our future indebtedness that is expressly subordinated in right of payment to the notes, equal in right of payment to our existing and future unsecured indebtedness that is not so subordinated, effectively junior in right of payment to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness, and structurally subordinated to all existing and future indebtedness and other liabilities (including trade payables) incurred by our subsidiaries. The 2026 Convertible Notes Indenture contains customary events of default with respect to the 2026 Convertible Notes, including that upon certain events of default (including our failure to make any payment of principal or interest on the 2026 Convertible Notes when due and payable) occurring and continuing, the 2026 Convertible Notes Trustee by notice to us, or the holders of at least 25% in principal amount of the outstanding 2026 Convertible Notes by notice to us and the Convertible Notes Trustee, may, and the 2026 Convertible Notes Trustee at the request of such holders (subject to the provisions of the 2026 Convertible Notes Indenture) will, declare 100% of the principal of and accrued and unpaid interest, if any, on all the 2026 Convertible Notes to be due and payable. In case of certain events of bankruptcy, insolvency or reorganization, involving us or a significant subsidiary, 100% of the principal of and accrued and unpaid interest on the 2026 Convertible Notes will automatically become due and payable. Upon such a declaration of acceleration, such principal and accrued and unpaid interest, if any, will be due and payable immediately.

In October 2022, we entered into the Blackstone Credit Agreement for fundings of up to $950.0 million consisting of a committed loan facility consisting of a senior secured term loan facility funded on the Closing Date, in the aggregate principal amount of $300.0 million, and a delayed draw term loan facility of up to $150.0 million to be funded at our request within 18 months of the Closing Date subject to specified conditions, and further contemplating the potential for up to $500.0 million of additional financing, to the extent that we request such additional financing and subject to the Lenders' agreement to provide such additional financing and to mutual agreement on terms. In October 2023, we terminated the Blackstone Credit Agreement. We recorded a loss on the extinguishment of debt of $92.7 million which is included on the statement of operations for the period ended December 31, 2023. The loss on extinguishment of debt consisted of $82.0 million in prepayment premiums, exit fees, and creditor expenses and debt issuance costs of $10.7 million. All liens and security interests securing the loans made pursuant to the Blackstone Credit Agreement were released upon termination.

We have received fundings from Royalty Pharma under the A&R Royalty Purchase Agreement in July 2020, October 2023 and June 2024 totaling $1.9 billion (less Royalty payments received by us with respect to the Assigned Royalty Rights). In exchange for these fundings, we sold Royalty Pharma 90.49% of the Royalty, which will be reduced to 83.33% after Royalty Pharma receives $1.3 billion in aggregate payments, or the Assigned Royalty Cap, from the Royalty assigned under the Original Royalty Purchase Agreement. We currently retain 9.51% of the Royalty, which increases to 16.67% after the Assigned Royalty Cap has been met. We have the option to sell our retained portions of the Royalty to Royalty Pharma in up to three tranches for the following payments: (1) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the Assigned Royalty Cap has been met, (2) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the Assigned Royalty Cap has been met, and (3) $50.0 million in exchange for 1.90% of the Royalty, which increases to 3.33% after the Assigned Royalty Cap has been met, in each case less Royalty payments received by us with respect to the Assigned Royalty Rights

In November 2024, we and Novartis entered into the Novartis Agreement relating to our PTC518 HD program which includes related molecules. Pursuant to the Novartis Agreement, we will continue to conduct the ongoing Phase 2A Clinical Trial and the ongoing OLE Clinical Trial pursuant to its existing development plan, with the goal of transitioning the ongoing OLE Clinical Trial to Novartis within 12 months after the effective date. Novartis will be responsible for all other development of licensed compounds and licensed products and the manufacture and commercialization of licensed

compounds and licensed products worldwide. Under the Novartis Agreement, and upon the closing of the transaction contemplated by the Novartis Agreement in January 2025, we received an upfront payment of $1.0 billion on the effective date and can receive up to $1.9 billion in development, regulatory and sales milestones, a 40% share of U.S. profits and losses, and tiered double-digit royalties on ex-U.S. sales.

Cash flows

As of December 31, 2024, we had cash and cash equivalents and marketable securities of $1,139.7 million.

The following table provides information regarding our cash flows and our capital expenditures for the periods indicated.

	Years ended December 31,		
(in thousands)	**2024**	**2023**	**2022**
Cash (used in) provided by:			
Operating activities	$ (107,688)	$ (158,418)	$ (356,654)
Investing activities	$ 44,182	$ (176,737)	$ 290,181
Financing activities	$ 255,866	$ 646,400	$ 167,952

Net cash used in operating activities was $107.7 million, $158.4 million, and $356.7 million for the years ended December 31, 2024, 2023, and 2022, respectively. The net cash used in operating activities primarily related to supporting clinical development and commercial activities for the years ended December 31, 2024, 2023, and 2022.

Net cash provided by investing activities was $44.2 million for the year ended December 31, 2024. Net cash used in investing activities was $176.7 million for the year ended December 31, 2023. Net cash provided by investing activities was $290.2 million for the year ended December 31, 2022. The cash provided by investing activities for the year ended December 31, 2024 was primarily attributable to the sale and redemption of marketable securities – available for sale, sale and redemption of marketable securities – equity investments, proceeds from sales of fixed assets, proceeds from the sale of the PRV, and proceeds from settlement of the ClearPoint convertible debt security, offset by the acquisition of product rights, purchases of marketable securities – available for sale, purchases of fixed assets, and purchases of marketable securities –equity investments. The cash used in investing activities for the year ended December 31, 2023 is primarily attributable to the purchases of marketable securities – available for sale, purchases of marketable securities – equity investments, purchases of fixed assets, and the acquisition of product rights, offset by the sale and redemption of marketable securities – available for sale, sale and redemption of marketable securities – equity investments, and the sale and redemption of ClearPoint Equity Investments. The cash provided by investing activities for the years ended December 31, 2022 was primarily related to net sales and redemptions of marketable securities – available for sale and net sales and redemptions of marketable securities – equity investments, partially offset by purchases of marketable securities – available for sale, purchases of marketable securities – equity investments, purchases of fixed assets, and the acquisition of product rights.

Net cash provided by financing activities was $255.9 million, $646.4 million, and $168.0 million for the years ended December 31, 2024, 2023 and 2022, respectively. The cash provided by financing activities for the year ended December 31, 2024 was primarily attributable to the proceeds received from the A&R Royalty Purchase Agreement, exercise of options, issuance of stock under our Employee Stock Purchase Plan, or ESPP, offset by payments on contingent consideration obligation, and payments on our finance lease principal. The cash provided by financing activities for the year ended December 31, 2023 was primarily attributable to the proceeds received from the A&R Royalty Purchase Agreement, exercise of options, issuance of stock under our ESPP, offset by the repayment of the senior secured term loan, debt issuance costs, debt extinguishment costs related to senior secured term loan, and payments on our finance lease principal. The cash provided by financing activities for the year ended December 31, 2022 was primarily attributable to the proceeds from the issuance of the senior secured term loan under the Blackstone Credit Agreement, the stock purchase agreement entered into in connection with the execution of the Blackstone Credit Agreement, the exercise of options, and issuance of stock under our ESPP, offset by the repayment of the 2022 Convertible Notes, payments on contingent consideration obligation, and payments on our finance lease principal.

Funding requirements

We anticipate that we will continue to incur significant expenses in connection with our commercialization efforts in the United States, the EEA, Latin America and other territories, including expenses related to our commercial infrastructure and corresponding sales and marketing, legal and regulatory, and distribution and manufacturing undertakings as well as administrative and employee-based expenses. In addition to the foregoing, we expect to continue to incur significant costs in connection with ongoing, planned and potential future clinical trials and studies for sepiapterin and our splicing and inflammation and ferroptosis programs as well as studies in our products for maintaining authorizations, label extensions and additional indications. We continue to seek marketing authorization for Translarna for the treatment of nmDMD in territories that we do not currently have marketing authorization in and we are exploring other potential mechanisms by which we may provide Translarna to nmDMD patients in the EEA if the EC adopts the CHMP's negative opinion for Translarna. In July 2024, we re-submitted the NDA to the FDA for Translarna for the treatment of nmDMD. In October 2024, the FDA accepted for review the resubmission of the NDA for Translarna for the treatment of nmDMD. As this was an NDA resubmission following a complete response letter to the NDA which was filed over protest in 2016, the FDA is not obligated to follow the review timelines under PDUFA guidelines and an action date has not been provided. In March 2024, we submitted an MAA to the EMA for sepiapterin for the treatment of PKU in the EEA, which was validated and accepted for review by the EMA in May 2024. We expect an opinion from the CHMP in the second quarter of 2025. In July 2024, we submitted an NDA to the FDA for sepiapterin for the treatment of pediatric and adult patients with PKU, including the full spectrum of ages and disease subtypes, in the United States. In September 2024, the FDA accepted for filing the NDA, with a target regulatory action date of July 29, 2025. We also made regulatory submissions for sepiapterin for the treatment of PKU in Brazil in the third quarter of 2024 and in Japan in the fourth quarter of 2024, with a regulatory decision in Japan expected in the fourth quarter of 2025 In December 2024, we submitted an NDA to the FDA for vatiquinone for the treatment of children and adults living with FA. In February 2025, the FDA accepted for filing the NDA and granted priority review with a target regulatory action date of August 19, 2025. These efforts may significantly impact the timing and extent of our commercialization and manufacturing expenses.

In addition, our expenses will increase if and as we:

- seek to satisfy contractual and regulatory obligations that we assumed through our acquisitions and collaborations;
- execute our commercialization strategy for our products, including initial commercialization launches of our products, label extensions or entering new markets;
- are required to complete any additional clinical trials, non-clinical studies or Chemistry, Manufacturing and Controls, or CMC, assessments or analyses in order to advance our products or product candidates in the United States or elsewhere;
- are required to take other steps to maintain our current marketing authorization in the EEA, Brazil and Russia for Translarna for the treatment of nmDMD or to obtain further marketing authorizations for Translarna for the treatment of nmDMD or other indications;
- initiate or continue the research and development of sepiapterin and our splicing and inflammation and ferroptosis programs as well as studies in our products for maintaining authorizations, label extensions and additional indications;
- seek to discover and develop additional product candidates;
- seek to expand and diversify our product pipeline through strategic transactions;
- maintain, expand and protect our intellectual property portfolio; and

- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts.

We believe that our cash flows from product sales, together with existing cash and cash equivalents, and marketable securities, will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next twelve months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

Our future capital requirements will depend on many factors, including:

- our ability to maintain our marketing authorization for Translarna for the treatment of nmDMD in the EEA following the CHMP's negative opinion on the conditional marketing authorization procedure, and the EC's potential adoption of the negative opinion, or identify other potential mechanisms in which we may provide Translarna to nmDMD patients in the EEA;

- our ability to maintain the marketing authorization for Translarna and our other products in territories outside of the EEA;

- our ability to commercialize and market our products and product candidates that may receive marketing authorization;

- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms, on a timely basis, with third-party payors for our products and products candidates;

- the amount of generic drug competition that we face for Emflaza for the treatment of DMD in patients five years and older;

- our ability to obtain marketing authorization for sepiapterin for the treatment of PKU in the United States and EEA;

- our ability to obtain marketing authorization for Translarna for the treatment of nmDMD in the United States;

- our ability to obtain marketing authorization for vatiquinone for the treatment of FA in the United States;

- our ability to successfully complete all post-marketing requirements imposed by regulatory agencies with respect to our products;

- the progress and results of activities for sepiapterin and our splicing and inflammation and ferroptosis programs as well as studies in our products for maintaining authorizations, label extensions and additional indications;

- the scope, costs and timing of our commercialization activities, including product sales, marketing, legal, regulatory, distribution and manufacturing, for any of our products and for any of our other product candidates that may receive marketing authorization or any additional territories in which we receive authorization to market Translarna;

- the costs, timing and outcome of regulatory review of sepiapterin and our splicing and inflammation and ferroptosis programs and Translarna and Upstaza/Kebilidi in other territories;

- our ability to satisfy our obligations under the indenture governing the 2026 Convertible Notes;

- the timing and scope of any potential future growth in our employee base;

- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates, including those in our splicing and inflammation and ferroptosis programs;

- revenue received from commercial sales of our products or any of our product candidates;

- our ability to obtain additional and maintain existing reimbursed named patient and cohort EAP programs for Translarna for the treatment of nmDMD on adequate terms, or at all;

- the ability and willingness of patients and healthcare professionals to access Translarna through alternative means if pricing and reimbursement negotiations in the applicable territory do not have a positive outcome;

- the costs of preparing, filing and prosecuting patent applications, maintaining, and protecting our intellectual property rights and defending against intellectual property-related claims;

- the extent to which we acquire or invest in other businesses, products, product candidates, and technologies, including the success of any acquisition, in-licensing or other strategic transaction we may pursue, and the costs of subsequent development requirements and commercialization efforts, including with respect to our acquisitions of Emflaza, Agilis, our inflammation and ferroptosis platform and Censa and our licensing of Tegsedi and Waylivra; and

- our ability to establish and maintain collaborations, including our collaborations with Roche and the SMA Foundation, and our ability to obtain research funding and achieve milestones under these agreements.

- the progress and results of activities for our PTC518 program, including our right to receive any development, regulatory and sales milestones, profit sharing and royalty payments from Novartis; and

- unexpected decreases in revenue or increase in expenses resulting from potential widespread outbreaks of contagious disease.

With respect to our outstanding 2026 Convertible Notes, cash interest payments are payable on a semi-annual basis in arrears, which will require total funding of $4.3 million annually.

In May 2024, the MAA submission for sepiapterin for the treatment of PKU was validated and accepted by the EMA. Pursuant to the Censa Merger Agreement, the acceptance triggered a $15.0 million regulatory milestone to the former Censa securityholders. In July 2024, we announced the submission of an NDA to the FDA for sepiapterin for the treatment of pediatric and adult patients with PKU, including the full spectrum of ages and disease subtypes. Pursuant to the Censa Merger Agreement, the decision to submit the NDA triggered a $25.0 million regulatory milestone to the former Censa securityholders. In September 2024, we announced the FDA acceptance for filing of the NDA. Pursuant to the Censa Merger Agreement, the acceptance triggered a $25.0 million regulatory milestone to the former Censa securityholders. Together, the $65.0 million of regulatory milestones were paid and recorded in research and development expense on our consolidated statements of operations for the year ended December 31, 2024.

In March 2024, we submitted a BLA to the FDA for our gene therapy for the treatment of AADC deficiency in the United States, which the FDA accepted in May 2024. As a result of the acceptance, we paid a $20.0 million milestone payment to former equity holders of Agilis, during the year ended December 31, 2024. On November 13, 2024, our BLA for our gene therapy treatment of AADC deficiency was approved by the FDA. In connection with the approval, we were granted a rare disease PRV. The FDA approval of the BLA and the PRV triggered $11.0 million in regulatory milestones, which were recorded in accounts payable and accrued expenses on the balance sheet as of December 31, 2024. As of December 31, 2024, there are no remaining regulatory milestones. As of December 31, 2024, the remaining potential sales milestone related to Upstaza/Kebilidi is $50.0 million.

We also have certain significant contractual obligations and commercial commitments that require funding. We lease office and shell condition, modifiable space for our principal office in Warren, New Jersey and we occupy under leases

that expire in 2039, with three consecutive five-year renewal options to renew the leases at our option. Additionally, we entered into a lease agreement for approximately 103,000 square feet of laboratory and office space in Bridgewater, New Jersey. The rental term for such facility commenced on May 1, 2020 with an initial term of seven years and two consecutive five year renewal periods at our option. In addition, we lease office space, vehicles and equipment in various other locations in the U.S. and other countries for our employees and operations. We have a total of $127.7 million in obligations that stem from our operating leases.

We have a total of $24.0 million in obligations that stem from a commercial manufacturing services agreement entered into with MassBio on June 19, 2020, for a term of 12.5 years. Pursuant to the terms of the agreement, MassBio agreed to provide us with four dedicated rooms for our Upstaza/Kebilidi program.

Under an Exclusive License and Supply Agreement, or the Faes Agreement, with Faes Farma, S.A., or Faes, we are required to pay royalties as a percentage of or as a fixed payment with respect to net product sales by us allocable to the Emflaza oral suspension product. We are required to pay Faes an annual royalty during the first twelve calendar years from the FDA approval date of the Emflaza oral suspension product.

Under various agreements, including the sponsored research agreement with the SMA Foundation discussed below, we will be required to pay royalties and milestone payments upon the successful development and commercialization of products.

We have entered into a sponsored research agreement with the SMA Foundation in connection with our SMA program. We may become obligated to pay the SMA Foundation single-digit royalties on worldwide net product sales of any collaboration product that we successfully develop and subsequently commercialize or, with respect to collaboration products we outlicense, including Evrysdi, a specified percentage of certain payments we receive from our licensee. We are not obligated to make such payments unless and until annual sales of a collaboration product exceed a designated threshold. Since inception, the SMA Foundation has earned $52.5 million, all of which was paid as of December 31, 2024. We have reached our obligation to make such payments to the SMA Foundation of an aggregate of $52.5 million as of December 31, 2024. Refer to “Ongoing Acquisition- Related Obligations” in Item 1. Business.

Additionally, we have employment agreements with certain employees which require the funding of a specific level of payments, if certain events, such as a change in control or termination without cause, occur.

We have never been profitable and we will need to generate significant revenues to achieve and sustain profitability, and we may never do so. We may need to obtain substantial additional funding in connection with our continuing operations. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs primarily through a combination of equity offerings, debt financings, collaborations, strategic alliances, grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product and product candidates and marketing, distribution or licensing arrangements. Adequate additional financing may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

If we are unable to raise additional funds through equity, debt or other financings when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. At any time, sharp changes in interest rates can affect the fair value of the investment portfolio and its interest earnings. There were no investments classified as long-term at December 31, 2024. At December 31, 2024, we held $1,139.7 million in cash and cash equivalents and marketable securities. After a review of our marketable investment securities, we believe that in the event of a hypothetical ten percent increase in interest rates, the resulting decrease in fair value of our marketable investment securities would be insignificant to the consolidated financial statements.

Currently, we do not hedge these interest rate exposures. We maintain an investment portfolio in accordance with our investment policy. The primary objectives of our investment policy are to preserve principal, maintain proper liquidity and to meet operating needs. Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investment. Our investments are also subject to interest rate risk and will decrease in value if market interest rates increase. However, due to the conservative nature of our investments and relatively short duration, interest rate risk is mitigated. We do not own derivative financial instruments. Accordingly, we do not believe that there is any material market risk exposure with respect to derivative or other financial instruments.

As a result of our ex-U.S. operations, we face exposure to movements in foreign currency exchange rates, including the British Pound, Euro, Brazilian Real, and Swiss Franc against the U.S. dollar. The current exposures arise primarily from cash, accounts receivable, intercompany receivables and payables, intercompany loans and product sales denominated in foreign currencies. Both positive and negative impacts to our international product sales from movements in foreign currency exchange rates may be partially mitigated by the natural, opposite impact that foreign currency exchange rates have on our international operating expenses. For the year ended December 31, 2024, we recognized realized foreign currency transaction losses, net, of $6.8 million, which is recorded within other income, net on the Statement of Operations. A hypothetical ten percent increase or decrease in the exchange rate between the U.S. dollar and the British Pound, Euro, Brazilian Real, or Swiss Franc from the December 31, 2024 rate would not have a significant impact on our cash flows. We are not currently engaged in any foreign currency hedging activities. We will evaluate the use of derivative financial instruments to hedge our exposure as the needs and risks should arise.

In September 2019, we issued $287.5 million of 1.50% convertible senior notes due September 15, 2026, or the 2026 Convertible Notes. We do not have economic interest rate exposure on the 2026 Convertible Notes as they have a fixed annual interest rate of 1.50%. However, the fair value of the 2026 Convertible Notes is exposed to interest rate risk. We do not carry the 2026 Convertible Notes at fair value on our balance sheet but present the fair value of the principal amount for disclosure purposes. Generally, the fair value of the 2026 Convertible Notes will increase as interest rates fall and decrease as interest rates rise. The 2026 Convertible Notes are also affected by the price and volatility of our common stock and will generally increase or decrease as the market price of our common stock changes. The estimated fair value of the 2026 Convertible Notes was approximately $321.3 million as of December 31, 2024.

Item 8. Financial Statements and Supplementary Data

Index to consolidated financial statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of PTC Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of PTC Therapeutics, Inc. (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations, comprehensive loss, stockholders' equity/(deficit) and cash flows for each of the three years in the period ended December 31, 2024, 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 at December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, 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, 2024, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 27, 2025 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 Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates 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 matter 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 matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Variable consideration in contracts with customers

Description of the Matter

As discussed in Note 2 of the consolidated financial statements, the Company's revenues for product sold to its customers within the United States reflect discounts mandated by the Medicaid Drug Rebate Program. The Company includes an estimate of this variable consideration in its transaction price at the time of sale when control of the product transfers to the customer. The Company uses the expected value or most likely amount method when estimating variable consideration, unless discount or rebate terms are specified within contracts. The estimates for variable consideration are adjusted to reflect known changes.

Auditing the amount of consideration to be paid under the Medicaid Drug Rebate Program (Medicaid) was complex and highly judgmental due to the interpretation of government rules, regulations, policy, and guidance under the government program. Management is responsible for complying with these rules and regulations. Governmental pricing calculations are complex as a result of interpretation of regulations and management's policy impacting the average manufacturer price, which would result in an impact to the best price and the unit rebate amount. The reductions to gross product revenues are sensitive to these significant estimates and calculations.

How We Addressed the Matter in Our Audit

We identified, evaluated and tested controls over management's review of the calculated reductions to gross product prices related to Medicaid and the significant assumptions and data inputs utilized in the calculations.

To test the revenue adjustments related to Medicaid our audit procedures included, among others, evaluating the methodology used as well as testing the significant estimates discussed above and the underlying assumptions and data used by the Company in its analysis. We evaluated pricing adjustments recorded in the current period and assessed the historical accuracy of management's estimates against actual results. In addition, we involved an internal governmental pricing specialist to assist with our evaluation of management's methodology and the calculations made to measure the estimated Medicaid rebates.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2010.

Iselin, New Jersey

February 27, 2025

PTC Therapeutics, Inc.

Consolidated Balance Sheets

In thousands, except shares

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 779,709	$ 594,001
Marketable securities	359,987	282,738
Trade and royalty receivables, net	158,554	160,822
Inventory, net	23,194	30,577
Prepaid expenses and other current assets	44,087	150,491
Total current assets	1,365,531	1,218,629
Fixed assets, net	60,970	87,089
Intangible assets, net	118,794	379,497
Goodwill	82,341	82,341
Operating lease ROU assets	56,685	91,896
Deposits and other assets	20,703	36,246
Total assets	$ 1,705,024	$ 1,895,698
Liabilities and stockholders' deficit		
Current liabilities:		
Accounts payable and accrued expenses	$ 304,292	$ 391,983
Deferred revenue	5,505	801
Operating lease liabilities- current	10,363	13,002
Finance lease liabilities- current	3,000	3,000
Liability for sale of future royalties- current	257,821	194,314
Total current liabilities	580,981	603,100
Long-term debt	285,412	284,213
Contingent consideration payable	800	36,300
Deferred tax liability	—	55,905
Operating lease liabilities- noncurrent	74,947	97,627
Finance lease liabilities- noncurrent	15,574	17,184
Liability for sale of future royalties- noncurrent	1,823,955	1,619,783
Other long-term liabilities	21,426	141
Total liabilities	2,803,095	2,714,253
Stockholders' deficit:		
Common stock, $0.001 par value. Authorized 250,000,000 shares; issued and outstanding 77,704,188 shares at December 31, 2024. Authorized 250,000,000 shares; issued and outstanding 75,708,889 shares at December 31, 2023.	77	75
Additional paid-in capital	2,574,611	2,466,233
Accumulated other comprehensive loss	(25,886)	(1,285)
Accumulated deficit	(3,646,873)	(3,283,578)
Total stockholders' deficit	(1,098,071)	(818,555)
Total liabilities and stockholders' deficit	$ 1,705,024	$ 1,895,698

See accompanying consolidated notes.

PTC Therapeutics, Inc.

Consolidated Statements of Operations

In thousands, except shares and per share data

	Year ended December 31,		
	2024	2023	2022
Revenues:			
Net product revenue	$ 600,951	$ 661,249	$ 535,228
Collaboration revenue	304	100,030	50,052
Royalty revenue	203,864	168,856	113,521
Manufacturing revenue	1,661	7,687	—
Total revenues	806,780	937,822	698,801
Operating expenses:			
Cost of product sales, excluding amortization of acquired intangible assets	57,398	65,486	44,678
Amortization of acquired intangible assets	60,738	222,635	116,554
Research and development	534,480	666,563	651,496
Selling, general and administrative	300,911	332,540	325,998
Change in the fair value of contingent consideration	(4,475)	(127,700)	(25,900)
Intangible asset impairment	159,548	217,800	33,384
Tangible asset impairment and losses (gains) on transactions, net	750	—	—
Total operating expenses	1,109,350	1,377,324	1,146,210
Loss from operations	(302,570)	(439,502)	(447,409)
Interest expense, net	(166,993)	(129,180)	(90,871)
Other income (expense), net	6,544	10,130	(49,207)
Gain on sale of priority review voucher	99,900	—	—
Loss on extinguishment of debt	—	(137,558)	—
Loss before income tax (expense) benefit	(363,119)	(696,110)	(587,487)
Income tax (expense) benefit	(176)	69,506	28,470
Net loss attributable to common stockholders	$ (363,295)	$ (626,604)	$ (559,017)
Weighted-average shares outstanding:			
Basic and diluted (in shares)	76,845,055	74,838,392	71,728,634
Net loss per share—basic and diluted (in dollars per share)	$ (4.73)	$ (8.37)	$ (7.79)

See accompanying consolidated notes.

PTC Therapeutics, Inc.

Consolidated Statements of Comprehensive Loss

In thousands

	Year ended December 31,		
	2024	2023	2022
Net loss	$ (363,295)	$ (626,604)	$ (559,017)
Other comprehensive (loss) income:			
Unrealized (loss) gain on marketable securities, net of tax	(57)	820	108
Foreign currency translation (loss) gain, net of tax	(24,544)	(6,901)	28,970
Comprehensive loss	$ (387,896)	$ (632,685)	$ (529,939)

See accompanying consolidated notes.

PTC Therapeutics, Inc.

Consolidated Statements of Stockholders' Equity/ (Deficit)

In thousands, except shares

	Common stock		Additional paid-in capital	Accumulated other comprehensive (loss) income	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount				
Balance, December 31, 2021	70,828,226	$ 71	$ 2,123,606	$ (24,282)	$ (2,097,957)	$ 1,438
Issuance of common stock related to stock purchase agreement	1,095,290	1	49,999	—	—	50,000
Exercise of options	496,863	—	14,632	—	—	14,632
Restricted stock vesting and issuance, net	490,008	—	—	—	—	—
Issuance of common stock in connection with an employee stock purchase plan	194,305	—	6,450	—	—	6,450
Share-based compensation expense	—	—	110,333	—	—	110,333
Net loss	—	—	—	—	(559,017)	(559,017)
Comprehensive income	—	—	—	29,078	—	29,078
Balance, December 31, 2022	73,104,692	$ 72	$ 2,305,020	$ 4,796	$ (2,656,974)	$ (347,086)
Issuance of common stock in connection with a milestone payable	657,462	1	29,569	—	—	29,570
Exercise of options	822,482	1	24,039	—	—	24,040
Restricted stock vesting and issuance, net	915,203	1	—	—	—	1
Issuance of common stock in connection with an employee stock purchase plan	209,050	—	5,954	—	—	5,954
Share-based compensation expense	—	—	101,636	—	—	101,636
Receivable from investor	—	—	15	—	—	15
Net loss	—	—	—	—	(626,604)	(626,604)
Comprehensive loss	—	—	—	(6,081)	—	(6,081)
Balance, December 31, 2023	75,708,889	$ 75	$ 2,466,233	$ (1,285)	$ (3,283,578)	$ (818,555)
Retired Shares	(20)	—	—	—	—	—
Exercise of options	824,813	1	28,564	—	—	28,565
Restricted stock vesting and issuance, net	963,543	1	—	—	—	1
Issuance of common stock in connection with an employee stock purchase plan	206,963	—	5,199	—	—	5,199
Share-based compensation expense	—	—	74,615	—	—	74,615
Net loss	—	—	—	—	(363,295)	(363,295)
Comprehensive loss	—	—	—	(24,601)	—	(24,601)
Balance, December 31, 2024	77,704,188	$ 77	$ 2,574,611	$ (25,886)	$ (3,646,873)	$ (1,098,071)

See accompanying consolidated notes.

PTC Therapeutics, Inc.

Consolidated Statements of Cash Flows

In thousands

	Year ended December 31,		
	2024	2023	2022
Cash flows from operating activities			
Net loss	$ (363,295)	$ (626,604)	$ (559,017)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	75,663	236,590	128,836
Non-cash operating lease expense	7,752	9,827	9,884
Non-cash royalty revenue related to sale of future royalties	(181,507)	(93,460)	(48,738)
Non-cash interest expense on liability related to sale of future royalties	207,394	104,790	72,639
Intangible asset impairment	159,548	217,800	33,384
Change in valuation of contingent consideration	(4,475)	(127,700)	(25,900)
Tangible asset impairment	4,095	—	—
Loss on sale of fixed assets	4,298	—	—
Gain on lease terminations	(2,179)	—	—
Gain on lease modification	(5,464)	—	—
Gain on sale of priority review voucher	(99,900)	—	—
Unrealized (gain) loss on ClearPoint Equity Investments	(7,685)	1,515	3,560
Unrealized loss on ClearPoint convertible debt security	1,931	2,678	5,740
Realized loss for the sale of ClearPoint Equity Investment	—	782	—
Realized loss on ClearPoint convertible debt security	622	—	—
Realized gain on redemption of marketable securities - equity investments	—	(4,383)	—
Unrealized (gain) loss on marketable securities - equity investments	(2,572)	(2,517)	7,992
Non-cash stock consideration, milestone payment	—	29,570	—
Disposal of asset	345	806	80
Deferred income taxes	(55,912)	(46,930)	(34,276)
Amortization of (discounts) premiums on investments, net	(12,529)	(2,200)	1,713
Amortization of debt issuance costs	1,198	1,873	1,901
Loss on extinguishment of debt	—	55,625	—
Share-based compensation expense	74,615	101,636	110,333
Unrealized foreign currency transaction (gains) losses, net	(10,374)	(14,113)	13,263
Non-cash foreign currency remeasurement loss on intercompany loan	—	—	16,887
Changes in operating assets and liabilities:			
Inventory, net	6,164	(8,183)	(6,668)
Prepaid expenses and other current assets	98,763	(44,992)	(51,621)
Trade and royalty receivables, net	1,732	(1,539)	(48,468)
Deposits and other assets	12,459	5,222	(2,913)
Accounts payable and accrued expenses	(33,322)	48,346	27,542
Other liabilities	11,830	(2,307)	(4,558)
Deferred revenue	4,917	(550)	1,351
Payments on contingent consideration	(1,800)	—	(9,600)
Net cash used in operating activities	(107,688)	(158,418)	(356,654)
Cash flows from investing activities			
Purchases of fixed assets	(6,502)	(28,438)	(32,016)
Proceeds from sale of fixed assets	28,056	—	—
Proceeds from sale of priority review voucher	150,000	—	—
Purchases of marketable securities- available for sale	(607,984)	(174,086)	(52,764)
Purchases of marketable securities- equity investments	(59,377)	(38,398)	(22,787)
Sale and redemption of marketable securities- available for sale	549,609	21,544	405,234
Sale and redemption of marketable securities- equity investments	48,127	132,228	112,958
Sale and redemption of ClearPoint Equity Investments	—	2,594	—
Proceeds from settlement of Clearpoint convertible debt security	10,000	—	—
Acquisition of product rights and licenses	(67,747)	(92,181)	(120,444)
Net cash provided by (used in) investing activities	44,182	(176,737)	290,181
Cash flows from financing activities			
Proceeds from exercise of options	28,565	24,040	14,632
Repayment of senior secured term loan	—	(300,000)	—
Debt extinguishment costs related to senior secured term loan	—	(81,933)	—
Cash consideration received from A&R Royalty Purchase Agreement	241,792	1,000,000	—
Debt issuance costs related to senior secured term loan	—	(282)	(11,454)
Proceeds from issuance of senior secured term loan	—	—	300,000
Repayment of Convertible Notes	—	—	(150,000)
Payments on contingent consideration obligation	(18,200)	—	(40,400)
Proceeds from employee stock purchase plan	5,199	5,954	6,450
Payment of finance lease principal	(1,490)	(1,379)	(1,276)
Proceeds from stock purchase agreement	—	—	50,000

Net cash provided by financing activities	255,866	646,400	167,952
Effect of exchange rate changes on cash	(7,328)	3,114	(2,772)
Net increase in cash and cash equivalents	185,032	314,359	98,707
Cash and cash equivalents, and restricted cash beginning of period	610,284	295,925	197,218
Cash and cash equivalents, and restricted cash end of period	$ 795,316	$ 610,284	$ 295,925
Supplemental disclosure of cash information			
Cash paid for interest	$ 5,823	$ 36,131	$ 18,463
Cash paid for income taxes	$ 17,550	$ 14,155	$ 4,922
Supplemental disclosure of non-cash investing and financing activity			
Unrealized (loss) gain on marketable securities, net of tax	$ (57)	$ 820	$ 108
Right-of-use assets obtained in exchange for operating lease obligations	$ 6,462	$ —	$ 35,817
Acquisition of product rights and licenses	$ 420	$ 54,618	$ 33,239
Fixed asset additions through tenant improvement allowance	$ 18,848	$ —	$ —
Accrued brokerage fees in connection with sale of priority review voucher	$ 2,000	$ —	$ —
Milestone payable	$ 11,025	$ 2,500	$ —
Debt issuance costs related to senior secured term loan	$ —	$ —	$ 159
Capital expenditures unpaid at the end of the period	$ 70	$ —	$ 308

See accompanying consolidated notes.

1. The Company

PTC Therapeutics, Inc. (the "Company" or "PTC") is a global biopharmaceutical company that discovers, develops and commercializes clinically differentiated medicines that provide benefits to children and adults living with rare disorders. PTC's ability to innovate to identify new therapies and to globally commercialize products is the foundation that drives investment in a robust and diversified pipeline of transformative medicines. PTC's mission is to provide access to best-in-class treatments for patients who have little to no treatment options. PTC's strategy is to leverage its strong scientific and clinical expertise and global commercial infrastructure to bring therapies to patients. PTC believes that this allows it to maximize value for all of its stakeholders.

The Company has two products, Translarna™ (ataluren) and Emflaza® (deflazacort), for the treatment of Duchenne muscular dystrophy ("DMD"), a rare, life-threatening disorder. Translarna has marketing authorization in the European Economic Area (the "EEA") for the treatment of nonsense mutation Duchenne muscular dystrophy ("nmDMD") in ambulatory patients aged two years and older. In July 2020, the European Commission ("EC") approved the removal of the statement "efficacy has not been demonstrated in non-ambulatory patients" from the indication statement for Translarna. Translarna also has marketing authorization in Russia for the treatment of nmDMD in patients aged two years and older, and in Brazil for the treatment of nmDMD in ambulatory patients two years and older and for continued treatment of patients that become non-ambulatory, as well as in various other countries. Emflaza is approved in the United States for the treatment of DMD in patients two years and older.

The Company's marketing authorization for Translarna in the EEA is subject to annual review and renewal by the EC following reassessment by the European Medicines Agency ("EMA") of the benefit-risk balance of the authorization, which the Company refers to as the annual EMA reassessment. In September 2022, the Company submitted a Type II variation to the EMA to support conversion of the conditional marketing authorization for Translarna to a standard marketing authorization, which included a report on the placebo-controlled trial of Study 041 and data from the open-label extension. In February 2023, the Company also submitted an annual marketing authorization renewal request to the EMA. In September 2023, the Committee for Medicinal Products for Human Use ("CHMP'), gave a negative opinion on the conversion of the conditional marketing authorization to full marketing authorization of Translarna for the treatment of nmDMD and a negative opinion on the renewal of the existing conditional marketing authorization of Translarna for the treatment of nmDMD. In January 2024, the CHMP issued a negative opinion for the renewal of the conditional marketing authorization following a re-examination procedure. In May 2024, the EC decided not to adopt the CHMP's negative opinion for the renewal of the conditional marketing authorization of Translarna and returned such opinion to the CHMP for re-evaluation. In June 2024, following the EC's request for re-review, the CHMP issued a negative opinion on the renewal of the conditional marketing authorization of Translarna for the treatment of nmDMD. On October 18, 2024, the CHMP maintained its negative opinion for the renewal of the conditional marketing authorization following the requested reexamination procedure. In accordance with EMA regulations, the EC has 67 days from the date of issuance to adopt the opinion. At this time, the EC has not yet adopted the negative opinion. The marketing authorization for Translarna remains in effect, pending the EC's potential adoption of the negative opinion. The Company is exploring other potential mechanisms by which it may provide Translarna to nmDMD patients in the EEA if the negative opinion is adopted by the EC.

Translarna is an investigational new drug in the United States. Following the Company's announcement of top-line results from the placebo-controlled trial of Study 041 in June 2022, the Company submitted a meeting request to the U.S. Food and Drug Administration ("FDA") to gain clarity on the regulatory pathway for a potential re-submission of a New Drug Application ("NDA") for Translarna. The FDA provided initial written feedback that Study 041 does not provide substantial evidence of effectiveness to support NDA re-submission. The Company held a Type C meeting with the FDA

in the fourth quarter of 2023 to discuss the totality of Translarna data. Based on feedback from the FDA, the Company re-submitted the NDA in July 2024, based on the results from Study 041 and from the Company's international drug registry study for nmDMD patients receiving Translarna. In October 2024, the FDA accepted for review the resubmission of the NDA for Translarna for the treatment of nmDMD. As this was an NDA resubmission following a complete response letter to the NDA which was filed over protest in 2016, the FDA is not obligated to follow the review timelines under Prescription Drug User Fee Act guidelines and an action date has not been provided.

The Company has developed Upstaza (eladocagene exuparvovec), a gene therapy used for the treatment of Aromatic L-Amino Acid Decarboxylase ("AADC") deficiency ("AADC deficiency"), a rare central nervous system ("CNS") disorder arising from reductions in the enzyme AADC that results from mutations in the dopa decarboxylase gene. In July 2022, the EC approved Upstaza for the treatment of AADC deficiency for patients 18 months and older within the EEA. In November 2022, the Medicines and Healthcare Products Regulatory Agency approved Upstaza for the treatment of AADC deficiency for patients 18 months and older within the United Kingdom. On November 13, 2024, the Company's biologics license application ("BLA") for its gene therapy treatment of AADC deficiency was approved by the FDA. This gene therapy is marketed under the brand name Kebilidi in the United States.

The Company holds the rights for the commercialization of Tegsedi® (inotersen) and Waylivra® (volanesorsen) for the treatment of rare diseases in countries in Latin America and the Caribbean pursuant to the Collaboration and License Agreement (the "Tegsedi-Waylivra Agreement"), dated August 1, 2018, by and between the Company and Akcea Therapeutics, Inc. ("Akcea"), a subsidiary of Ionis Pharmaceuticals, Inc. Tegsedi has received marketing authorization in the United States, the European Union (the "EU") and Brazil for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis ("hATTR amyloidosis"). In August 2021, ANVISA, the Brazilian health regulatory authority, approved Waylivra as the first treatment for familial chylomicronemia syndrome ("FCS") in Brazil. In December 2022, ANVISA approved Waylivra for the treatment of familial partial lipodystrophy ("FPL"). Waylivra has also received marketing authorization in the EU for the treatment of FCS.

The Company also has a spinal muscular atrophy ("SMA") collaboration with F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc. (referred to collectively as "Roche") and the Spinal Muscular Atrophy Foundation ("SMA Foundation"). The SMA program has one approved product, Evrysdi® (risdiplam), which was approved by the FDA in August 2020 for the treatment of SMA in adults and children two months and older and by the EC in March 2021 for the treatment of 5q SMA in patients two months and older with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies. Evrysdi has also received marketing authorization for the treatment of SMA in over 100 countries. In May 2022, the FDA approved a label expansion for Evrysdi to include infants under two months old with SMA. In August 2023, the EC approved an extension of the Evrysdi marketing authorization to include infants under two months old in the EU.

One of the Company's most advanced clinical stage molecules is sepiapterin. Sepiapterin is the Company's product candidate for the treatment of phenylketonuria ("PKU"). In May 2023, the Company announced that the primary endpoint was achieved in its registration-directed Phase 3 trial for sepiapterin for phenylketonuria ("PKU"). The primary endpoint of the study was the achievement of statistically-significant reduction in blood Phe level. In March 2024, the Company submitted a marketing authorization application ("MAA") to the EMA for sepiapterin for the treatment of PKU in the EEA, which was validated and accepted for review by the EMA in May 2024. The Company expects an opinion from the CHMP in the second quarter of 2025. In July 2024 the Company submitted an NDA to the FDA for sepiapterin for the treatment of pediatric and adult patients with PKU, including the full spectrum of ages and disease subtypes, in the United States. In September 2024, the FDA accepted for filing the NDA, with a target regulatory action date of July 29, 2025. The Company also made a regulatory submission for sepiapterin for the treatment of PKU in Brazil in the third quarter of 2024, and in Japan in the fourth quarter of 2024, with a regulatory decision in Japan expected in the fourth quarter of 2025.

In addition to the Company's SMA program, the Company's splicing platform also includes PTC518, which is being developed for the treatment of Huntington's disease ("HD"). The Company initiated a Phase 2 study of PTC518 for the treatment of HD in the first quarter of 2022, which consists of an initial 12-week placebo-controlled phase focused on safety, pharmacology and pharmacodynamic effects followed by a nine-month placebo-controlled phase focused on PTC518 biomarker effect. In June 2023, the Company announced interim data from the 12-week placebo-controlled phase of the Phase 2 study of PTC518. In June 2024, the Company announced interim results from the full Phase 2 study of PTC518. At month 12, PTC518 treatment demonstrated durable dose-dependent lowering of mutant HTT ("mHTT") protein in the blood and dose-dependent lowering of mHTT protein in the cerebrospinal fluid in the interim cohort of stage 2 patients. In addition, favorable trends were demonstrated on several relevant HD clinical assessments. Furthermore, following 12 months of treatment, PTC518 continued to be well tolerated. In September 2024, the FDA granted Fast Track designation to the PTC518 program for the treatment of HD. In December 2024, the Company held a Type C meeting with the FDA to discuss whether huntingtin protein lowering could be considered a surrogate endpoint for accelerated approval of PTC518. The FDA was aligned on the scientific rationale and asked to see additional data supportive of an association between huntingtin protein lowering and changes in clinical outcome scores. The Company expects to provide results from the Phase 2 study of PTC518 for the treatment of HD in the second quarter of 2025. In November 2024, the Company entered into a License and Collaboration Agreement (the "Novartis Agreement") with Novartis Pharmaceuticals Corporation ("Novartis"), relating to its PTC518 HD program which included related molecules. This transaction closed on January 11, 2025, and triggered a $1.0 billion upfront cash payment to the Company. See Note 18. Subsequent Events for additional information.

The Company's inflammation and ferroptosis platform consists of small molecule compounds that target oxidoreductase enzymes that regulate oxidative stress and inflammatory pathways central to the pathology of a number of CNS diseases. The most advanced molecule in the Company's inflammation and ferroptosis platform is vatiquinone. The Company announced topline results from a registration-directed Phase 3 trial of vatiquinone in children and young adults with Friedreich's ataxia ("FA"), called MOVE-FA, in May 2023. While the study did not meet its primary endpoint, vatiquinone treatment did demonstrate significant benefit on key disease subscales, including the upright stability subscale, as well as on other disease relevant endpoints. In October 2024, the Company announced that the pre-specified endpoint for two different FA long-term extension studies was met, with statistically significant evidence of durable treatment benefit on disease progression. In December 2024, the Company submitted an NDA to the FDA for vatiquinone for the treatment of children and adults living with FA. In February 2025, the FDA accepted for filing the NDA and granted priority review with a target regulatory action date of August 19, 2025.

In addition, the Company has a pipeline of product candidates and discovery programs that are in early clinical, pre-clinical and research and development stages focused on the development of new treatments for multiple therapeutic areas for rare diseases.

As of December 31, 2024, the Company had an accumulated deficit of approximately $3,646.9 million. The Company has financed its operations to date primarily through the private offerings of convertible senior notes (see Note 7), public and "at the market offerings" of common stock, proceeds from royalty purchase agreements (see Note 7), net proceeds from its borrowings under its credit agreement with Blackstone (see Note 7), private placements of its convertible preferred stock and common stock, collaborations, bank and institutional lender debt, other convertible debt, grant funding and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease area addressed by the Company's product candidates. The Company has also relied on revenue generated from net sales of Translarna for the treatment of nmDMD in territories outside of the United States since 2014, Emflaza for the treatment of DMD in the United States since 2017 and Upstaza for the treatment of AADC deficiency in the EEA since May 2022. The Company has also relied on revenue associated with milestone and royalty payments from Roche pursuant to the License and Collaboration Agreement (the "SMA License Agreement") dated as of November 23, 2011, by and among

the Company, Roche and, for the limited purposes set forth therein, the SMA Foundation, under its SMA program, and from revenue associated with milestone and royalty payments from RPI (as defined below) pursuant to the Amended and Restated Royalty Purchase Agreement (as defined below) with RPI and, for the limited purposes set forth in the agreement, Royalty Pharma plc. The Company expects that cash flows from the sales of its products, together with the Company's cash, cash equivalents and marketable securities, will be sufficient to fund its operations for at least the next twelve months.

2. Summary of significant accounting policies

Basis of presentation

The accompanying consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Use of estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Significant estimates in these consolidated financial statements have been made in connection with the calculation of net product sales, royalty revenue, certain accruals related to the Company's research and development expenses, valuation procedures for liability for sale of future royalties, indefinite lived intangible assets annual impairment assessment, and the provision for or benefit from income taxes. Actual results could differ from those estimates. Changes in estimates are reflected in reported results in the period in which they become known.

Restricted Cash

Restricted cash included in deposits and other assets on the consolidated balance sheet relates to an unconditional, irrevocable and transferable letter of credit that was entered into during the twelve-month period ended December 31, 2019 in connection with obligations under a facility lease for the Company's leased biologics manufacturing facility in Hopewell Township, New Jersey. The amount of the letter of credit was $7.5 million and was to be maintained for a term of not less than five years and had the potential to be reduced to $3.8 million if after five years the Company was not in default of its lease. In June 2024, in connection with an amendment and restatement of the lease, the letter of credit was reduced to $5.0 million, and has the potential to be reduced to $3.0 million if after July 1, 2025, the Company is not in default of its lease. Restricted cash also contains an unconditional, irrevocable and transferable letter of credit that was entered into during June 2022 in connection with obligations for the Company's new facility lease in Warren, New Jersey. The initial amount of the letter of credit was $8.1 million, but was increased to $10.0 million as a result of a lease amendment executed December 31, 2024. If after July 1, 2027, the Company is not in default of the lease agreement and meets certain creditworthiness guidelines, then the letter of credit will be reduced to $5.0 million. If after December 31, 2028, the Company is not in default of the lease agreement and meets certain creditworthiness guidelines, then the letter of credit will be further reduced to $2.5 million. Both letters of credit are classified within deposits and other assets on the consolidated balance sheet due to the long-term nature of the letters of credit. Refer to Note 5 for further details. Restricted cash also includes a bank guarantee of $0.6 million denominated in a foreign currency.

(In thousands except share and per share amount)

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheet that sum to the total of the same amounts shown in the statement of cash flows:

	End of period- December 31, 2024	Beginning of period- December 31, 2023
Cash and cash equivalents	$ 779,709	$ 594,001
Restricted cash included in deposits and other assets	15,607	16,283
Total Cash, cash equivalents and restricted cash per statement of cash flows	$ 795,316	$ 610,284

Consolidation

The consolidated financial statements include the accounts of PTC Therapeutics, Inc. and its wholly owned subsidiaries. All inter-company accounts, transactions, and profits have been eliminated in consolidation.

Segment information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker ("CODM"), or decision-making group, in deciding how to allocate resources and in assessing performance. The Company's CODM consists of the chief executive officer, the chief financial officer, and the chief business officer. The Company views its operations and manages its business in one operating and reporting segment: life science. The life science segment is focused on the discovery, development and commercialization of the Company's clinically differentiated medicines that provide benefits to patients with rare disorders. The Company is managed on a consolidated basis, and accordingly, the CODM assesses performance for the life science segment based on net loss, with a focus on revenues, research and development expense, and selling general, and administrative expense. Net income is reported on the income statement as consolidated net loss. The measure of segment assets is reported on the balance sheet as total consolidated assets. The Company derives its revenues through its worldwide net sales of its commercial products, collaboration agreements, and royalty revenues. Refer to Note 12 for further segment information on revenues.

The Company expects to continue to incur significant expenses as it advances product candidates through all stages of development and clinical trials and, ultimately, seek regulatory approval. As such, the CODM uses cash forecast models in deciding how to invest into the life science segment. Such cash forecast models are reviewed to assess the entity-wide operating results and performance. Net loss is used to monitor planned versus actual results. Monitoring planned versus actual results is used in assessing performance of the segment and in establishing management's compensation, along with the cash forecast models. Refer to Note 15 for segment information on significant segment expenses and geographic breakdown.

Cash equivalents

The Company considers all highly liquid investments with a maturity of 90 days or less at the time of purchase to be cash equivalents. Cash equivalents are carried at cost which approximates fair value due to their short-term nature.

Marketable securities

The Company's marketable securities consists of both debt securities and equity investments. The Company considers its investments in debt securities with original maturities of greater than 90 days to be available for sale securities. Securities under this classification are recorded at fair value and unrealized gains and losses within accumulated other comprehensive income. The estimated fair value of the available for sale securities is determined based on quoted market prices or rates for similar instruments. In addition, the cost of debt securities in this category is adjusted for amortization of premium and accretion of discount to maturity. For available for sale debt securities in an unrealized loss position, the Company assesses whether it intends to sell or if it is more likely than not that the Company will be required to sell the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the security's amortized cost basis is written down to fair value. If the criteria are not met, the Company evaluates whether the decline in fair value has resulted from a credit loss or other factors. In making this assessment, management considers, among other factors, the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and adverse conditions specifically related to the security. If this assessment indicates that a credit loss exists, 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 the cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for credit losses is recorded for the credit loss, limited by the amount that the fair value is less than the amortized costs basis. Any impairment that has not been recorded through an allowance for credit losses is recognized in other comprehensive income. For the years ended December 31, 2024 and 2023, no allowance was recorded for credit losses.

Marketable securities that are equity investments are measured at fair value, as it is readily available, and as such are classified as Level 1 assets. Unrealized holding gains and losses for these equity investments are components of other income (expense), net within the consolidated statement of operations.

Concentration of credit risk

The Company's financial instruments that are exposed to credit risks consist primarily of cash and cash equivalents, available-for-sale marketable securities and accounts receivable. The Company maintains its cash and cash equivalents in bank accounts, which, at times, exceed federally insured limits. The Company has not experienced any credit losses in these accounts and does not believe it is exposed to any significant credit risk on these funds. The Company's investment policy includes guidelines on the quality of the financial institutions and financial instruments the Company is allowed to invest in, which the Company believes minimizes the exposure to concentration of credit risk.

The Company is subject to credit risk from its accounts receivable related to its product sales. The payment terms are predetermined and the Company evaluates the creditworthiness of each customer or distributor on a regular basis. The Company reserves all uninsured amounts billed directly to a patient until the time of cash receipt as collectability is not reasonably assured at the time the product is received. To date, the Company has not incurred any material credit losses.

(In thousands except share and per share amount)

Fixed assets

Fixed assets are stated at cost. Depreciation is computed starting when the asset is placed into service on a straight-line basis over the estimated useful life of the related asset as follows:

Leasehold improvements	Lesser of useful life or lease term
Computer equipment and software	3 years
Machinery and lab equipment	7 years
Furniture and fixtures	7 years

Inventory and cost of product sales

Inventory

Inventories are stated at the lower of cost and net realizable value, utilizing standard costing, which approximates average costs by product. The Company capitalizes inventory costs associated with products following regulatory approval when future commercialization is considered probable and the future economic benefit is expected to be realized. Products which may be used in clinical development programs are included in inventory and charged to research and development expense when the product enters the research and development process and no longer can be used for commercial purposes. Inventory used for marketing efforts are charged to selling, general and administrative expense. Amounts related to clinical development programs and marketing efforts are immaterial.

The following table summarizes the components of the Company's inventory for the periods indicated:

	December 31, 2024	December 31, 2023
Raw materials	$ 2,538	$ 952
Work in progress	12,216	17,991
Finished goods	8,440	11,634
Total inventory	$ 23,194	$ 30,577

The Company periodically reviews its inventories for excess amounts or obsolescence and writes down obsolete or otherwise unmarketable inventory to its estimated net realizable value. The Company recorded write downs of $13.2 million and $12.5 million for the years ended December 31, 2024 and 2023, respectively, primarily related to adjustments to inventory reserves and product approaching expiration. Additionally, though the Company's product is subject to strict quality control and monitoring which it performs throughout the manufacturing processes, certain batches or units of product may not meet quality specifications resulting in a charge to cost of product sales. For the years ended December 31, 2024 and December 31, 2023, these amounts were immaterial.

Cost of product sales

Cost of product sales consists of the cost of inventory sold, manufacturing and supply chain costs, storage costs, amortization of the acquired intangible asset, royalty payments associated with net product sales, and royalty payments to collaborative partners associated with royalty revenues and collaboration revenue related to milestones. Production costs are expensed as cost of product sales when the related products are sold or royalty revenues and collaboration revenue milestones are earned.

Accumulated other comprehensive (loss) income

Accumulated other comprehensive (loss) income consists of unrealized gains or losses on marketable securities and foreign currency translation adjustments.

Revenue recognition

Net product revenue

The Company's net product revenue primarily consists of sales of Translarna in territories outside of the U.S. for the treatment of nmDMD and sales of Emflaza in the U.S. for the treatment of DMD. The Company recognizes revenue when its performance obligations with its customers have been satisfied. The Company's performance obligations are to provide products based on customer orders from distributors, hospitals, specialty pharmacies or retail pharmacies. The performance obligations are satisfied at a point in time when the Company's customer obtains control of the product, which is typically upon delivery. The Company invoices its customers after the products have been delivered and invoice payments are generally due within 30 to 90 days of the invoice date. The Company determines the transaction price based on fixed consideration in its contractual agreements. Contract liabilities arise in certain circumstances when consideration is due for goods the Company has yet to provide. As the Company has identified only one distinct performance obligation, the transaction price is allocated entirely to product sales. In determining the transaction price, a significant financing component does not exist since the timing from when the Company delivers product to when the customers pay for the product is typically less than one year. Customers in certain countries pay in advance of product delivery. In those instances, payment and delivery typically occur in the same month.

The Company records product sales net of any variable consideration, which includes discounts, allowances, rebates related to Medicaid and other government pricing programs, and distribution fees. The Company uses the expected value or most likely amount method when estimating its variable consideration, unless discount or rebate terms are specified within contracts. The identified variable consideration is recorded as a reduction of revenue at the time revenues from product sales are recognized. These estimates for variable consideration are adjusted to reflect known changes in factors and may impact such estimates in the quarter those changes are known. Revenue recognized does not include amounts of variable consideration that are constrained.

In relation to customer contracts, the Company incurs costs to fulfill a contract but does not incur costs to obtain a contract. These costs to fulfill a contract do not meet the criteria for capitalization and are expensed as incurred. The Company considers any shipping and handling costs that are incurred after the customer has obtained control of the product as a cost to fulfill a promise. Shipping and handling costs associated with finished goods delivered to customers are recorded as a selling expense.

Collaboration and royalty revenue

The terms of these agreements typically include payments to the Company of one or more of the following: nonrefundable, upfront license fees; milestone payments; research funding and royalties on future product sales. In addition, the Company generates service revenue through agreements that generally provide for fees for research and development services and may include additional payments upon achievement of specified events.

At the inception of a collaboration arrangement, the Company needs to first evaluate if the arrangement meets the criteria in Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 808 "Collaborative Arrangements" to then determine if ASC Topic 606 is applicable by considering whether the collaborator

meets the definition of a customer. If the criteria are met, the Company assesses the promises in the arrangement to identify distinct performance obligations.

For licenses of intellectual property, the Company assesses, at contract inception, whether the intellectual property is distinct from other performance obligations identified in the arrangement. If the licensing of intellectual property is determined to be distinct, revenue is recognized for nonrefundable, upfront license fees when the license is transferred to the customer and the customer can use and benefit from the license. If the licensing of intellectual property is determined not to be distinct, then the license will be bundled with other promises in the arrangement into one distinct performance obligation. The Company needs to determine if the bundled performance obligation is satisfied over time or at a point in time. If the Company concludes that the nonrefundable, upfront license fees will be recognized over time, the Company will need to assess the appropriate method of measuring proportional performance.

For milestone payments, the Company assesses, at contract inception, whether the development or sales-based milestones are considered probable of being achieved. If it is probable that a significant revenue reversal will occur, the Company will not record revenue until the uncertainty has been resolved. Milestone payments that are contingent upon regulatory approval are not considered probable of being achieved until the applicable regulatory approvals or other external conditions are obtained as such conditions are not within the Company's control. If it is probable that a significant revenue reversal will not occur, the Company will estimate the milestone payments using the most likely amount method. The Company will re-assess the development and sales-based milestones each reporting period to determine the probability of achievement. The Company recognizes royalties from product sales at the later of when the related sales occur or when the performance obligation to which the royalty has been allocated has been satisfied. If it is probable that a significant revenue reversal will not occur, the Company will estimate the royalty payments using the most likely amount method.

The Company recognizes revenue for reimbursements of research and development costs under collaboration agreements as the services are performed. The Company records these reimbursements as revenue and not as a reduction of research and development expenses as the Company has the risks and rewards as the principal in the research and development activities.

Manufacturing Revenue

The Company has manufacturing revenue related to the production of plasmid deoxyribonucleic acid ("DNA") and adeno-associated virus ("AAV") vectors for gene therapy applications for external customers. Performance obligations vary but may include manufacturing plasmid DNA and/or AAV vectors, material testing, stability studies, and other services related to material development. The transaction prices for these arrangements are fixed and include amounts stated in the contracts for each promised service. Typically, the performance obligations within a manufacturing contract are highly interdependent, in which case, the Company will combine them into a single performance obligation. The Company has determined that the assets created have no alternative use to the Company, and the Company has an enforceable right to payment for the performance completed to date, therefore revenue related to these services are recognized over time and is measured using an output method based on performance of manufacturing milestones completed to date.

Manufacturing service contracts may also include performance obligations related to project management services or obtaining materials from third parties. The Company has determined that these are separate performance obligations for which revenue is recognized at the point in time the services are performed. For performance obligations related to obtaining third-party materials, the Company has determined that it is the principal as the Company has control of the materials and has discretion in setting the price. Therefore, the Company recognizes revenue on a gross basis related to obtaining third-party materials.

Certain arrangements require a portion of the contract consideration to be received in advance at the commencement of the contract, and such advance payment is initially recorded as a contract liability. A contract asset may be recognized in the event the Company's satisfaction of performance obligations outpaces customer billings.

In June 2024, the Company sold its gene therapy manufacturing business in Hopewell Township, New Jersey. Accordingly, the Company does not expect to have manufacturing revenue going forward.

Allowance for doubtful accounts

The Company maintains an allowance for estimated losses resulting from the inability of its customers to make required payments. The Company estimates uncollectible amounts based upon current customer receivable balances, the age of customer receivable balances, the customer's financial condition and current economic trends. The Company also assesses whether an allowance for expected credit losses may be required which includes a review of the Company's receivables portfolio, which are pooled on a customer basis or country basis. In making its assessment of whether an allowance for credit losses is required, the Company considers its historical experience with customers, current balances, levels of delinquency, regulatory and legal environments, and other relevant current and future forecasted economic conditions. For the years ended December 31, 2024 and 2023, no allowance was recorded for credit losses. The allowance for doubtful accounts was $2.3 million as of December 31, 2024 and $1.2 million as of December 31, 2023. For the years ended December 31, 2024, 2023 and 2022, bad debt expense was $1.7 million, $0.9 million, and $0.2 million, respectively.

Liability for sale of future royalties

The Company has a royalty purchase agreement with Royalty Pharma Investments 2019 ICAV ("Royalty Pharma") in which the Company sold its right to receive sales-based royalty payments on worldwide net sales of Evrysdi in exchange for upfront cash consideration from Royalty Pharma. In accordance with the guidance in ASC 470-10-25-2, the Company determined that cash consideration obtained pursuant to the royalty purchase agreement should be classified as debt and is recorded as "liability for sale of future royalties-current" and "liability for sale of future royalties-noncurrent" on the Company's consolidated balance sheet based on the timing of the expected payments to be made to Royalty Pharma. The liability is amortized using the effective interest method over the life of the arrangement, in accordance with the respective guidance, utilizing the prospective method to account for subsequent changes in the estimated future payments to be made to Royalty Pharma and the Company updates the effective interest rate on a quarterly basis. Refer to Note 7 for further details.

Leases

The Company determines if an arrangement is a lease at inception. This determination generally depends on whether the arrangement conveys to the Company the right to control the use of an explicitly or implicitly identified fixed asset for a period of time in exchange for consideration. Control of an underlying asset is conveyed to the Company if the Company obtains the rights to direct the use of and to obtain substantially all of the economic benefits from using the underlying asset. The Company has lease agreements which include lease and non-lease components, which the Company accounts for as a single lease component for all leases. Operating and finance leases are classified as right of use ("ROU") assets, short term lease liabilities, and long term lease liabilities. Operating and finance lease ROU assets and lease liabilities are recognized at the commencement date based on the present value of lease payments over the lease term. ROU assets are amortized and lease liabilities accrete to yield straight-line expense over the term of the lease. Lease payments included in the measurement of the lease liability are comprised of fixed payments.

Variable lease payments associated with the Company's leases are recognized when the event, activity, or circumstance in the lease agreement on which those payments are assessed occurs. Variable lease payments are presented in the Company's consolidated statements of operations in the same line item as expense arising from fixed lease payments for operating leases.

Leases with an initial term of 12 months or less are not recorded on the consolidated balance sheet and the Company recognizes lease expense for these leases on a straight-line basis over the lease term. The Company applies this policy to all underlying asset categories.

A lessee is required to discount its unpaid lease payments using the interest rate implicit in the lease or, if that rate cannot be readily determined, its incremental borrowing rate. As most of the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The Company gives consideration to its recent debt issuances as well as publicly available data for instruments with similar characteristics when calculating its incremental borrowing rates.

The lease term for all of the Company's leases includes the non-cancellable period of the lease plus any additional periods covered by either a Company option to extend (or not to terminate) the lease that the Company is reasonably certain to exercise, or an option to extend (or not to terminate) the lease controlled by the lessor. Leasehold improvements are capitalized and depreciated over the lesser of useful life or lease term. See Note 5 Leases for additional information.

Research and development costs

Research and development expenses include the clinical development costs associated with the Company's product development programs and research and development costs associated with the Company's discovery programs. These expenses include internal research and development costs and the costs of research and development conducted on behalf of the Company by third parties, including sponsored university-based research agreements and clinical study vendors. All research and development costs are expensed as incurred. Costs incurred in obtaining technology licenses are charged immediately to research and development expense if the technology licensed has not reached technological feasibility and has no alternative future uses.

Advance payments made for goods and services that will be used in future research and development activities are deferred if the contracted party has not yet performed the related activities. The amount deferred is then expensed when the research and development activities are performed. As of December 31, 2024 and 2023, the short term deferred research and development advance payments were $7.4 million and $2.6 million, respectively, and are classified as prepaid expenses and other current assets on the consolidated balance sheet. As of December 31, 2024 and 2023, the long term deferred research and development advance payments were $1.7 million and $4.7 million, respectively, and are classified as deposits and other assets on the consolidated balance sheet.

Fair value of financial instruments

The Company follows the fair value measurement rules, which provides guidance on the use of fair value in accounting and disclosure for assets and liabilities when such accounting and disclosure is called for by other accounting literature. These rules establish a fair value hierarchy for inputs to be used to measure fair value of financial assets and liabilities.

This hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three levels: Level 1 (highest priority), Level 2, and Level 3 (lowest priority).

- Level 1—Unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the balance sheet date.

- Level 2—Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly. Level 2 inputs include quoted prices for similar assets and liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, inputs other than quoted prices that are observable for the asset or liability (i.e., interest rates, yield curves, etc.), and inputs that are derived principally from or corroborated by observable market data by correlation or other means (market corroborated inputs).

- Level 3—Inputs are unobservable and reflect the Company's assumptions as to what market participants would use in pricing the asset or liability. The Company develops these inputs based on the best information available.

Cash equivalents, marketable securities, and equity investments are reflected in the accompanying financial statements at fair value. The carrying amounts of receivables and accounts payable and accrued expenses approximate fair value due to the short-term nature of those instruments.

Share-based compensation

The Company measures the cost of employee services received in exchange for an award of equity instruments based on the grant date fair value of the award. Restricted stock awards are measured based on the fair market values of the underlying stock on the dates of grant. For service type awards, share-based compensation expense is recognized on a straight-line basis over the period during which the employee is required to provide service in exchange for the entire award.

The fair value of options is calculated using the Black-Scholes option pricing model to determine the fair value of stock options on the date of grant based on key assumptions such as expected volatility and expected term. The Company estimates the expected volatility of options utilizing the Company's historical stock volatility. The Company estimates the expected term of options utilizing the Company's historical exercise data. The risk-free rate of the option is based on U.S. Government Securities Treasury Constant Maturities yields at the date of grant for a term similar to the expected term of the option. In connection with the adoption of FASB Accounting Standards Update ("ASU") 2016-9, the Company made a policy election to continue its methodology for estimating its forfeiture rate.

Stock-based compensation expense for performance stock units ("PSUs") is determined using the grant date fair value, which is the quoted closing market price per share of the Company's common stock on the Nasdaq Global Select Market on the grant date. Stock-based compensation expense for the PSUs will not be recognized until the achievement of the performance goal is deemed probable (the "Probable Date"), a determination that requires significant judgment by management, as the achievement of these goals have inherent risk and uncertainties. At the Probable Date, the Company records a cumulative catch-up expense for the portion of the grant date fair value attributable to the period from the grant date to the Probable Date. The remaining expense is recognized over the remaining service period on a straight-line basis.

Income taxes

On December 15, 2022, the European Union (EU) member states formally adopted the EU's Pillar Two Directive, which generally provides for a minimum effective tax rate of 15%, as established by the Organization for Economic Co-operation and Development (OECD) Pillar Two Framework that was supported by over 130 countries worldwide. The EU effective dates are January 1, 2024, and January 1, 2025, for different aspects of the directive. A significant number of other countries are also implementing similar legislation. As a result, the tax laws in the U.S. and other countries in which PTC and its affiliates do business could change on a prospective or retroactive basis and any such changes could materially adversely affect the Company's business. The Company is continuing to evaluate the potential impact on future periods of the Pillar Two Framework, pending legislative adoption by additional individual countries, including those within the EU.

On December 22, 2017, the U.S. government enacted the 2017 Tax Cuts and Jobs Act ("TCJA"), which significantly revised U.S. tax law by, among other provisions, lowering the U.S. federal statutory income tax rate to 21%, imposing a mandatory one-time transition tax on previously deferred foreign earnings, and eliminating or reducing certain income tax deductions. The Global Intangible Low-tax Income ("GILTI") provisions of the TCJA require the Company to include in its U.S. income tax return foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. The Company has elected to account for GILTI tax in the period in which it is incurred, and therefore has not provided any deferred tax impacts of GILTI in its consolidated financial statements for the period ended December 31, 2024.

Starting in 2022, TCJA amendments to IRC Section 174 no longer permits an immediate deduction for research and development (R&D) expenditures in the tax year that such costs are incurred. Instead, these IRC Section 174 development costs must now be capitalized and amortized over either a five- or 15-year period, depending on the location of the activities performed. The new amortization period begins with the midpoint of any taxable year that IRC Section 174 costs are first incurred, regardless of whether the expenditures were made prior to or after July 1 and runs until the midpoint of year five for activities conducted in the United States or year 15 in the case of development conducted on foreign soil. This tax law change resulted in an increased current taxable income of the Company by $62.5 million for the year ended December 31, 2024.

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 and net operating loss and credit carryforwards. Deferred tax assets and liabilities are measured at rates expected to apply to taxable income in the years in which those temporary differences and carryforwards 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 statement of operations in the period that includes the enactment date. A valuation allowance is recorded when it is not more likely than not that all or a portion of the net deferred tax assets will be realized.

On August 23, 2018, the Company completed its acquisition of Agilis Biotherapeutics, Inc. ("Agilis"), pursuant to an Agreement and Plan of Merger, dated as of July 19, 2018 (the "Agilis Merger Agreement"), by and among the Company, Agility Merger Sub, Inc., a Delaware corporation and the Company's wholly owned, indirect subsidiary, Agilis and, solely in its capacity as the representative, agent and attorney-in-fact of the equityholders of Agilis, Shareholder Representative Services LLC, (the "Agilis Merger"). The Company recorded a deferred tax liability in conjunction with the Agilis Merger of $122.0 million in 2018, related to the tax basis difference in the In-Process Research and Development, or IPR&D, indefinite-lived intangibles acquired. The Company's policy is to record a deferred tax liability related to acquired IPR&D which may eventually be realized either upon amortization of the asset when the research is completed and a product is

successfully launched or the write-off of the asset if it is abandoned or unsuccessful. In July 2022, the Company received EMEA approval for a portion of the IPR&D assets, and thus, began the amortization of the intangible.

In May 2023, as part of a strategic portfolio prioritization, the Company announced the discontinuation of its preclinical and early research programs for its gene therapy platform, which included programs for FA and Angelman syndrome. In conjunction with the announcement, the Company recorded an impairment to its indefinite-lived intangible for IP research and development relating to the FA and Angelman syndrome gene therapy assets.

In November 2024, the Company was granted FDA approval and received (and subsequently sold) an associated Priority Review Voucher for a portion of the IPR&D assets. Additionally, in the fourth quarter of 2024, the Company recorded an impairment to the remainder of the indefinite-lived intangible IPR&D assets. As a result of this activity, the Company no longer has an associated deferred tax liability associated with the Agilis Merger to carry forward.

Foreign currency

The functional currencies of the Company's foreign subsidiaries primarily are the local currencies of the country in which the subsidiary operates. The Company's asset and liability accounts are translated using the current exchange rate as of the balance sheet date. Stockholders' equity accounts are translated using historical rates at the balance sheet date. Revenue and expense accounts are translated using a weighted average exchange rate over the period ended on the balance sheet date. Adjustments resulting from the translation of the financial statements of the Company's foreign subsidiaries into U.S. dollars are accumulated as a separate component of stockholders' equity within other comprehensive income. Gains or losses resulting from transactions denominated in foreign currencies are included in other income or expense, within the consolidated statements of income.

Net (loss) income per share

Basic net (loss) income per share is calculated by dividing the net (loss) income attributable to common stockholders by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net income per share is calculated by dividing the net income attributable to common stockholders by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method and the if-converted method. During periods in which the Company incurs net losses, both basic and diluted loss per share is calculated by dividing the net loss by the weighted average shares outstanding—potentially dilutive securities are excluded from the calculation because their effect would be anti-dilutive. Dilutive common stock equivalents are comprised of options and unvested restricted stock outstanding under the Company's stock option plans.

Business combinations and asset acquisitions

The Company evaluates 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 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 the Company has acquired inputs and processes that have the ability to create outputs, which would meet the requirements of a business. If determined to be a business combination, the Company accounts for the transaction under the acquisition method of accounting as indicated in ASU 2017-01, "Business Combinations", which requires the acquiring entity in a business combination to recognize the fair value of all assets acquired, liabilities assumed, and any non-controlling interest in the acquiree and establishes the acquisition date as the fair value measurement point. Accordingly, the Company recognizes assets acquired and liabilities assumed in business

combinations, including contingent assets and liabilities, and non-controlling interest in the acquiree based on the fair value estimates as of the date of acquisition. In accordance with ASC 805, the Company recognizes and measures goodwill as of the acquisition date, as the excess of the fair value of the consideration paid over the fair value of the identified net assets acquired.

The consideration for the Company's business acquisitions may include future payments that are contingent upon the occurrence of a particular event or events. The obligations for such contingent consideration payments are recorded at fair value on the acquisition date. The contingent consideration obligations are then evaluated each reporting period. Changes in the fair value of contingent consideration, other than changes due to payments, are recognized as a gain or loss and recorded within the change in the fair value of contingent consideration in the consolidated statements of operations.

If determined to be an asset acquisition, the Company accounts for the transaction under ASC 805-50, which requires the acquiring entity in an asset acquisition to recognize assets acquired and liabilities assumed based on the cost to the acquiring entity on a relative fair value basis, which includes transaction costs in addition to consideration given. No gain or loss is recognized as of the date of acquisition unless the fair value of non-cash assets given as consideration differs from the assets' carrying amounts on the acquiring entity's books. Consideration transferred that is noncash will be measured based on either the cost (which will be measured based on the fair value of the consideration given) or the fair value of the assets acquired and liabilities assumed, whichever is more reliably measurable. Goodwill is not recognized in an asset acquisition and any excess consideration transferred over the fair value of the net assets acquired is allocated to the identifiable assets based on relative fair values.

Contingent consideration payments in asset acquisitions are recognized when the contingency is resolved and the consideration is paid or becomes payable (unless the contingent consideration meets the definition of a derivative, in which case the amount becomes part of the basis in the asset acquired). Upon recognition of the contingent consideration payment, the amount is included in the cost of the acquired asset or group of assets.

Finite-lived intangible assets

The Company records the fair value of purchased intangible assets with finite useful lives as of the transaction date of a business combination or asset acquisition. Purchased intangible assets with finite useful lives are amortized to their estimated residual values over their estimated useful lives.

Impairment of long-lived assets

The Company monitors its long-lived assets and finite-lived intangibles for indicators of impairment. If such indicators are present, the Company assesses the recoverability of affected assets by determining whether the carrying value of such assets is less than the sum of the undiscounted future cash flows of the assets. If such assets are found not to be recoverable, the Company measures the amount of such impairment by comparing the carrying value of the assets to the fair value of the assets, with the fair value generally determined based on the present value of the expected future cash flows associated with the assets. During the year ended December 31, 2024, in connection with the South Plainfield, New Jersey office closure and Warren, New Jersey lease modification, the Company recorded a $4.1 million loss primarily related to fixed assets impairments. As of December 31, 2024, the Company believes that no additional impairment of long-lived assets exists.

Indefinite-lived intangible assets

Indefinite-lived intangible assets consist of IPR&D. IPR&D acquired directly in a transaction other than a business combination is capitalized if the projects will be further developed or have an alternative future use; otherwise they are expensed. The fair values of IPR&D projects and license agreement assets acquired in business combinations are capitalized. Several methods may be used to determine the estimated fair value of the IPR&D and license agreement asset acquired in a business combination. The Company utilizes the "income method" and uses estimated future net cash flows that are derived from projected sales revenues and estimated costs. These projections are based on factors such as relevant market size, patent protection, and expected pricing and industry trends. The estimated future net cash flows are then discounted to the present value using an appropriate discount rate. These assets are treated as indefinite-lived intangible assets until completion or abandonment of the projects, at which time the assets are amortized over the remaining useful life or written off, as appropriate. Intangible assets with indefinite lives, including IPR&D, are tested for impairment if impairment indicators arise and, at a minimum, annually. However, an entity is permitted to first assess qualitative factors to determine if a quantitative impairment test is necessary. Further testing is only required if the entity determines, based on the qualitative assessment, that it is more likely than not that an indefinite-lived intangible asset's fair value is less than its carrying amount. Otherwise, no further impairment testing is required. The indefinite-lived intangible asset impairment test consists of a one-step analysis that compares the fair value of the intangible asset with its carrying amount. If the carrying amount of an intangible asset exceeds its fair value, an impairment loss is recognized in an amount equal to that excess. The Company considers many factors in evaluating whether the value of its intangible assets with indefinite lives may not be recoverable, including, but not limited to, expected growth rates, the cost of equity and debt capital, general economic conditions, the Company's outlook and market performance of the Company's industry and recent and forecasted financial performance.

The Company performed an annual test for its PTC-AADC indefinite-lived intangible asset as of October 1, 2024 and recorded a partial impairment on the PTC-AADC indefinite-lived intangible asset of $159.5 million, which is recorded as intangible asset impairment in the statement of operations. The impairment was related to a decrease in projected cash flows due to refinements in current market assumptions and the timing of patient treatments. To calculate the impairment amount, the Company utilized a discounted cash flow model under the income method, which primarily utilized Level 3 fair value inputs. Some of the more significant assumptions inherent in the development of the model included the estimated annual cash flows, particularly net revenues and operations costs, and the appropriate discount rate to select in order to measure the risk inherent in the future cash flows. Refer to Note 17 for further information regarding the Company's intangible assets.

Goodwill

Goodwill represents the amount of consideration paid in excess of the fair value of net assets acquired as a result of the Company's business acquisitions accounted for using the acquisition method of accounting. Goodwill is not amortized and is subject to impairment testing at a reporting unit level on an annual basis or when a triggering event occurs that may indicate the carrying value of the goodwill is impaired. The Company reassesses its reporting units as part of its annual segment review. As of December 31, 2024, the Company concluded that it continues to operate as one reporting unit. An entity is permitted to first assess qualitative factors to determine if a quantitative impairment test is necessary. Further testing is only required if the entity determines, based on the qualitative assessment, that it is more likely than not that the fair value of the reporting unit is less than its carrying amount. The Company performed an annual test for goodwill as of October 1, 2024. The Company's single reporting unit had a negative carrying value, and thus the Company determined there was no impairment of goodwill.

Tangible asset impairment and losses (gains) on transactions, net

Tangible asset impairment and losses (gains) on transactions, net includes impairments identified on fixed assets, losses and gains on sales of fixed assets, and gains on lease terminations. For the year ended December 31 2024, these amounts consisted of a $4.4 million loss primarily related to the sale of certain assets for gene therapy manufacturing, and a $4.1 million loss primarily related to fixed asset impairments in connection with the South Plainfield, New Jersey office closure and Warren, New Jersey lease modification (Note 4). These amounts were partially offset by a gain of $2.2 million on lease terminations, and a gain of $5.5 million on lease modification (Note 5).

Recent accounting pronouncements

In December 2023, the FASB issued ASU 2023-09, Improvements to Income Tax Disclosures. ASU 2023-09 enhances the transparency about income tax information through improvements to income tax disclosures primarily related to the rate reconciliation and income taxes paid information. The guidance is effective for public business entities for annual periods beginning after December 15, 2024. For entities other than public business entities, the amendments are effective for annual periods beginning after December 15, 2025. Early adoption is permitted. The Company is currently planning to adopt this guidance when effective. The Company is assessing the impact of the adoption on the Company's consolidated financial statements and accompanying footnotes but expects the impact will be enhanced disclosures related to rate reconciliation and income taxes paid.

In November 2024, the FASB issued ASU 2024-03, Income Statement-Reporting Comprehensive Income- Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses. ASU 2024-03 enhances financial reporting by requiring additional information about specific expense categories in the notes to financial statements at interim and annual reporting periods. The guidance is effective for public business entities for annual periods beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027. Early adoption is permitted. The Company is currently planning to adopt this guidance when effective. The Company is assessing the impact of the adoption on the Company's consolidated financial statements and accompanying footnotes but expects the impact will be enhanced disclosures related to income statement expenses.

Impact of recently adopted accounting pronouncement

In November 2023, the FASB issued ASU 2023-07, Segment Reporting (Topic 280) – Improvements to Reportable Segment Disclosures. This ASU requires that a public entity provide additional segment disclosures on an interim and annual basis. The amendments in this ASU should be applied retrospectively to all prior periods presented in the financial statements, unless impracticable. Upon transition, the segment expense categories and amounts disclosed in the prior periods should be based on the significant segment expense categories identified and disclosed in the period of adoption. The ASU is effective for fiscal years beginning after December 15, 2023 and interim periods within fiscal years beginning after December 15, 2024. The Company adopted this guidance for the year ended December 31, 2024 and has updated its disclosures within its footnotes herein to include the required additional segment disclosures.

3. Fair value of financial instruments and investments

The Company follows the fair value measurement rules, which provide guidance on the use of fair value in accounting and disclosure for assets and liabilities when such accounting and disclosure is called for by other accounting literature. Cash equivalents, marketable securities, and equity investments are reflected in the accompanying financial statements at fair value. The carrying amount of receivables and accounts payable and accrued expenses approximate fair value due to the short-term nature of those instruments.

(In thousands except share and per share amount)

The Company uses the market approach to measure fair value for its marketable securities. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets. The Company's marketable securities are classified as Level 2 as they primarily utilize broker quotes in a nonactive market to value these securities.

The Company owns common stock in ClearPoint Neuro, Inc. ("ClearPoint") (formerly MRI Interventions, Inc.), a publicly traded medical device company. The ClearPoint equity investments (collectively, the "ClearPoint Equity Investments") represent financial instruments, and therefore, are recorded at fair value, which is readily determinable. The ClearPoint Equity Investments are components of prepaids and other current assets as of December 31, 2024 and December 31, 2023 on the consolidated balance sheet. The Company classifies its equity investments in ClearPoint as a Level 1 asset within the fair value hierarchy, as the value is based on a quoted market price in an active market, which is not adjusted.

In January 2020, the Company purchased a $10.0 million convertible note from ClearPoint that was convertible into ClearPoint shares at a conversion rate of $6.00 per share at any point throughout the term of the loan, with a maturity date five years from the purchase date. In August 2024, the outstanding principal amount of the convertible note, together with any accrued and unpaid interest thereon, was repaid in full by ClearPoint and therefore the balance at December 31, 2024 was $0. The Company determined that the convertible note represented an available for sale debt security and the Company had elected to record it at fair value under ASC 825. The Company classified its ClearPoint convertible debt security as a Level 2 asset within the fair value hierarchy, as the value was based on inputs other than quoted prices that are observable. The fair value of the ClearPoint convertible debt security was determined at each reporting period by utilizing a Black-Scholes option pricing model, as well as a present value of expected cash flows from the debt security utilizing the risk free rate and the estimated credit spread as of the valuation date as the discount rate. The convertible debt security was included as a component of deposits and other assets on the consolidated balance sheet as of December 31, 2023.

The Company has an investment in mutual funds that is denominated in foreign currency and is classified as marketable securities on the Company's consolidated balance sheets. This equity investment is reported at fair value, as it is readily available, and as such is classified as a Level 1 asset. Unrealized holding gains and losses for this equity investment are included as components of interest expense, net within the consolidated statement of operations.

The table presented below is a summary of changes in the fair value for the Company's marketable securities – equity investments, ClearPoint Equity Investments, and ClearPoint convertible debt security for the years ended December 31, 2024 and 2023:

	Ending Balance at December 31, 2023	Unrealized Gain/(Loss)	Realized Loss	Foreign Currency Unrealized Loss	Investments Purchased	Redemptions/ Sale	Ending Balance at December 31, 2024
Marketable securities - equity investments	$ 22,634	2,572	—	(7,422)	59,377	(48,127)	29,034
ClearPoint Equity Investments	6,074	7,685	—	—	—	—	13,759
ClearPoint convertible debt security	12,553	(1,931)	(622)	—	—	(10,000)	—
Total Fair Value	$ 41,261	$ 8,326	$ (622)	$ (7,422)	$ 59,377	$ (58,127)	$ 42,793

	Ending Balance at December 31, 2022	Unrealized Gain/(Loss)	Realized Gain/(Loss)	Foreign Currency Unrealized Gain	Investments Purchased	Redemptions/ Sale	Ending Balance at December 31, 2023

(In thousands except share and per share amount)

Marketable securities - equity investments	$ 108,261	2,517	4,383	1,384	38,432	(132,343)	$ 22,634
ClearPoint Equity Investments	10,965	(1,515)	(782)	—	—	(2,594)	6,074
ClearPoint convertible debt security	15,231	(2,678)	—	—	—	—	12,553
Total Fair Value	$ 134,457	$ (1,676)	$ 3,601	$ 1,384	$ 38,432	$ (134,937)	$ 41,261

Fair value of marketable securities that are classified as available for sale debt securities is based upon market prices using quoted prices in active markets for identical assets quoted on the last day of the period. In establishing the estimated fair value of the remaining available for sale debt securities, the Company used the fair value as determined by its investment advisors using observable inputs other than quoted prices.

The following represents the fair value using the hierarchy described in Note 2 for the Company's financial assets and liabilities that are required to be measured at fair value on a recurring basis as of December 31, 2024 and 2023:

	December 31, 2024			
	Total	Quoted prices in active markets for identical assets (level 1)	Significant other observable inputs (level 2)	Significant unobservable inputs (level 3)
Marketable securities - available for sale	$ 330,953	$ —	$ 330,953	$ —
Marketable securities - equity investments	$ 29,034	$ 29,034	$ —	$ —
ClearPoint Equity Investments	$ 13,759	$ 13,759	$ —	$ —
Contingent consideration payable- development and regulatory milestones	$ —	$ —	$ —	$ —
Contingent consideration payable- net sales milestones	$ 800	$ —	$ —	$ 800

	December 31, 2023			
	Total	Quoted prices in active markets for identical assets (level 1)	Significant other observable inputs (level 2)	Significant unobservable inputs (level 3)
Marketable securities - available for sale	$ 260,104	$ —	$ 260,104	$ —
Marketable securities - equity investments	$ 22,634	$ 22,634	$ —	$ —
ClearPoint Equity Investments	$ 6,074	$ 6,074	$ —	$ —
ClearPoint convertible debt security	$ 12,553	$ —	$ 12,553	$ —
Contingent consideration payable- development and regulatory milestones	$ 26,600	$ —	$ —	$ 26,600
Contingent consideration payable- net sales milestones and royalties	$ 9,700	$ —	$ —	$ 9,700

No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the years ended December 31, 2024 and 2023.

(In thousands except share and per share amount)

The following is a summary of marketable securities accounted for as available for sale debt securities at December 31, 2024 and 2023:

	December 31, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 44,780	$ —	$ (1)	$ 44,779
Corporate debt securities	89,320	76	(75)	89,321
Government obligations	196,584	269	—	196,853
Total	$ 330,684	$ 345	$ (76)	$ 330,953

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 117,044	$ 128	$ (12)	$ 117,160
Corporate debt securities	1,650	—	(2)	1,648
Government obligations	141,084	212	—	141,296
Total	$ 259,778	$ 340	$ (14)	$ 260,104

For available for sale debt securities in an unrealized loss position, the Company assesses whether it intends to sell or if it is more likely than not that the Company will be required to sell the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the security's amortized cost basis is written down to fair value. For the years ended December 31, 2024 and 2023, no write downs occurred. The Company does not intend to sell the investments and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost basis, which may be maturity. The Company also reviews its available for sale debt securities in an unrealized loss position and evaluates whether the decline in fair value has resulted from credit losses or other factors. This review is subjective, as it requires management to evaluate whether an event or change in circumstances has occurred in that period that may be related to credit issues. For the years ended December 31, 2024 and 2023, no allowance was recorded for credit losses. Unrealized gains and losses are reported as a component of accumulated other comprehensive loss in stockholders' deficit.

For the year ended December 31, 2024, the Company had $3.4 million of realized gains from the sale of available for sale debt securities. For the year ended December 31, 2023, the Company had $0.3 million of realized losses from the sale of available for sale debt securities. Realized gains and losses are reported as a component of interest expense, net in the consolidated statement of operations.

The unrealized losses and fair values of available for sale debt securities that have been in an unrealized loss position for a period of less than and greater than or equal to 12 months as of December 31, 2024 are as follows:

	December 31, 2024					
	Securities in an unrealized loss position less than 12 months		Securities in an unrealized loss position greater than or equal to 12 months		Total	
	Unrealized losses	Fair Value	Unrealized losses	Fair Value	Unrealized losses	Fair Value
Commercial paper	$ (1)	29,810	—	—	(1)	$ 29,810
Corporate debt securities	$ (75)	59,550	—	—	(75)	$ 59,550
Total	$ (76)	$ 89,360	$ —	$ —	$ (76)	$ 89,360

(In thousands except share and per share amount)

The unrealized losses and fair values of available for sale debt securities that have been in an unrealized loss position for a period of less than and greater than or equal to 12 months as of December 31, 2023 are as follows:

	December 31, 2023					
	Securities in an unrealized loss position less than 12 months		Securities in an unrealized loss position greater than or equal to 12 months		Total	
	Unrealized losses	Fair Value	Unrealized losses	Fair Value	Unrealized losses	Fair Value
Commercial paper	$ (12)	44,446	—	—	(12)	$ 44,446
Corporate debt securities	$ —	—	(2)	1,648	(2)	$ 1,648
Total	$ (12)	$ 44,446	$ (2)	$ 1,648	$ (14)	$ 46,094

Available for sale debt securities on the balance sheet at December 31, 2024 and 2023 mature as follows:

	December 31, 2024	
	Less Than 12 Months	More Than 12 Months
Commercial paper	$ 44,779	$ —
Corporate debt securities	89,321	—
Government obligations	196,853	—
Total	$ 330,953	$ —

	December 31, 2023	
	Less Than 12 Months	More Than 12 Months
Commercial paper	$ 117,160	$ —
Corporate debt securities	1,648	—
Government obligations	141,296	—
Total	$ 260,104	$ —

The Company classifies all of its marketable securities as current as they are all either available for sale debt securities or equity investments and are available for current operations.

Convertible senior notes

In September 2019, the Company issued $287.5 million of 1.5% convertible senior notes due September 15, 2026 (the "2026 Convertible Notes). The fair value of the 2026 Convertible Notes, which differs from their carrying values, is influenced by interest rates, the Company's stock price and stock price volatility and is determined by prices for the 2026 Convertible Notes observed in market trading which are Level 2 inputs. The estimated fair value of the 2026 Convertible Notes at December 31, 2024 and December 31, 2023 was $321.3 million and $265.3 million, respectively.

Level 3 valuation

The contingent consideration payable is fair valued each reporting period with the change in fair value recorded as a gain or loss within the change in the fair value of contingent consideration on the consolidated statements of operations. The fair value of the development and regulatory milestones are estimated utilizing a probability adjusted, discounted cash flow approach. The discount rates are estimated utilizing Corporate B rated bonds maturing in the years of expected payments based on the Company's estimated development timelines for the acquired product candidate. The fair value of the net sales milestones is determined utilizing a valuation framework that estimates net sales volatility to simulate a range

(In thousands except share and per share amount)

of possible payment scenarios. The average of the payments in these scenarios is then discounted to calculate present fair value.

In May 2023, as part of the Company's strategic portfolio prioritization, the Company decided to discontinue its preclinical and early research programs in its gene therapy platform, which included programs for FA and Angelman syndrome. As a result, the Company fully impaired the FA and Angelman syndrome intangible assets and determined that the fair value for all of the contingent consideration payable related to FA and Angelman syndrome was $0. The change in fair value for the contingent consideration payable related to FA and Angelman syndrome for the year ended December 31, 2023 was $128.4 million and is included in the change in fair value of the contingent consideration in the statement of operations. The remaining contingent consideration as of December 31, 2023 was $36.3 million, which was solely related to the development and regulatory milestones, and net sales milestones, for AADC product.

In May 2024, the Company's BLA for its gene therapy treatment of AADC deficiency was accepted for filing by the FDA. The application was granted priority review with a target regulatory action date of November 13, 2024. As a result of the acceptance, in accordance with the terms of the Agilis Merger Agreement, the Company paid a $20.0 million milestone payment to the former equityholders of Agilis during the year ended December 31, 2024. On November 13, 2024, the Company's BLA for its gene therapy treatment of AADC deficiency was approved by the FDA. The approval triggered $11.0 million in milestone payments to the former equityholders of Agilis in accordance with the terms of the Agilis Merger Agreement, and was recorded in accounts payable and accrued expenses on the Company's consolidated balance sheet as of December 31, 2024. As of December 31, 2024, there are no remaining development and regulatory milestones for AADC-related product. The remaining contingent consideration balance as of December 31, 2024 is $0.8 million, which is solely related to the net sales milestones for AADC products.

As of December 31, 2024, the weighted average discount rate for the Upstaza net sales milestones was 15.0% and the weighted average probability of success for the net sales milestones was 100%, as the Company has now received regulatory approval in the United States and the EU.

The table presented below is a summary of changes in the fair value of the Company's Level 3 valuation for the contingent consideration payables for the years ended December 31, 2024, and 2023:

	Contingent consideration payable-development and regulatory milestones - Agilis	Contingent consideration payable-net sales milestones and royalties - Agilis
Beginning balance as of December 31, 2022	$ 82,500	$ 81,500
Additions	—	—
Change in fair value	(55,900)	(71,800)
Payments	—	—
Ending balance as of December 31, 2023	$ 26,600	$ 9,700
Additions	—	—
Change in fair value	4,425	(8,900)
Reclassification to accounts payable and accrued expenses	(11,025)	
Payments	(20,000)	—
Ending balance as of December 31, 2024	$ —	$ 800

(In thousands except share and per share amount)

The following significant unobservable inputs were used in the valuation of the contingent consideration payables for the years ended December 31, 2024 and 2023:

	December 31, 2024			
	Fair Value	Valuation Technique	Unobservable Input	Range
Contingent consideration payable- development and regulatory milestones	$0	Probability-adjusted discounted cash flow	Potential development and regulatory milestones Probabilities of success Discount rates Projected years of payments	$0 N/A N/A N/A
Contingent considerable payable- net sales milestones	$800	Option-pricing model with Monte Carlo simulation	Potential net sales milestones Probabilities of success Discount rate Projected years of payments	$0 - $50 million 100% 15% 2026 - 2036

	December 31, 2023			
	Fair Value	Valuation Technique	Unobservable Input	Range
Contingent consideration payable- development and regulatory milestones	$26,600	Probability-adjusted discounted cash flow	Potential development and regulatory milestones Probabilities of success Discount rates Projected years of payments	$0 - $31 million 85% - 92% 5.8% - 6.1% 2024 - 2026
Contingent considerable payable- net sales milestones	$9,700	Option-pricing model with Monte Carlo simulation	Potential net sales milestones Probabilities of success Potential percentage of net sales for royalties Discount rate Projected years of payments	$0 - $50 million 85% - 100% 0% 11% 2026 - 2034

The contingent consideration payables are classified Level 3 liabilities as their valuation requires substantial judgment and estimation of factors that are not currently observable in the market. If different assumptions were used for the various inputs to the valuation approaches, including but not limited to, assumptions involving probability adjusted sales estimates for the gene therapy platform and estimated discount rates, the estimated fair value could be significantly higher or lower than the fair value determined.

4. Fixed assets

Fixed assets, net were as follows at December 31, 2024 and 2023:

	December 31,	
	2024	2023
Leasehold improvements	$ 31,531	$ 30,166
Computer equipment and software	24,043	17,503
Machinery and lab equipment	33,304	62,837
Furniture and fixtures	2,416	3,849
Assets in process	3,034	24,008
	94,328	138,363
Less accumulated depreciation	(33,358)	(51,274)
Total	$ 60,970	$ 87,089

Depreciation expense was approximately $14.9 million, $13.9 million, and $12.3 million for the years ended December 31, 2024, 2023, and 2022, respectively.

During the year end December 31, 2024, the Company recorded a $4.4 million loss primarily related to the sale of certain assets for gene therapy manufacturing. Additionally, in connection with the South Plainfield, New Jersey office closure, as well as the Warren, New Jersey lease modification, the Company recorded a $4.1 million loss primarily related to fixed assets impairments. Both the fixed asset loss on sale and fixed asset impairments are recorded on the Company's consolidated statement of operations within tangible asset impairment and losses (gains) on transactions, net.

5. Leases

Effective April 2024, the Company began utilizing the Warren Premises, as described below, as its principal office space. The Company also leases laboratory space in Bridgewater, New Jersey and other locations throughout the United States and office space in various countries for international employees primarily through workspace providers. The Company's lease for office space in South Plainfield, New Jersey expired in August 2024.

The Company has a lease agreement (the "Warren Lease") with Warren CC Acquisitions, LLC (the "Warren Landlord"). The lease initially related to two entire buildings comprised of approximately 360,000 square feet of shell condition, modifiable space (the "Warren Premises") at a facility located in Warren, New Jersey. The rental term of the Warren Lease commenced on June 1, 2022, with an initial term of seventeen years (the "Warren Initial Term"), followed by three consecutive five-year renewal periods at the Company's option. The aggregate base rent for the Warren Initial Term was approximately $163.0 million; provided, however, that if the Company is not subject to an Event of Default (as defined in the Warren Lease), the Company was entitled to a base rent abatement over the first three years of the Warren Initial Term of approximately $18.6 million, reducing the Company's total base rent obligation to $144.4 million.

On December 31, 2024, the Company and the Warren Landlord entered into a First Amendment to Lease Agreement (the "Warren Lease Amendment"), which amends certain aspects of the Warren Lease dated as of May 24, 2022 between the Company and the Warren Landlord. Pursuant to the Warren Lease Amendment, as of the Surrender Effective Date (as defined in the Warren Lease Amendment) the Company is now only leasing one building comprised of approximately 180,000 square feet. The Company will continue paying rent as scheduled, along with certain maintenance and utilities costs, through the end of December 2027, after which the Company will pay a reduced aggregate base rent of $57.7 million, reflecting a reduction of $57.7 million to initial total base rent obligation.

Under the Warren Lease Amendment, the Company's allowance provided by the Landlord to be used towards certain improvements to the Warren Premises is reduced from $36.1 million to $23.9 million, which is to be paid in accordance with the Warren Lease. In connection with the Warren Lease Amendment the letter of credit associated with the Warren Lease was increased from $8.1 million to $10.0 million.

As the Warren Lease Amendment partially terminated the existing Warren Lease, it was accounted for as a lease modification in accordance with ASC 842-10-25-13. The ROU liability was remeasured using an incremental borrowing rate at the date of modification of 7.8%, and the ROU asset was remeasured based on the proportionate change in the lease liability, which resulted in gain on modification of $5.5 million. The gain is included within tangible asset impairment and losses (gains) on transactions, net on the Company's consolidated statements of operations.

The Company also leases office and laboratory space at a facility located in Hopewell Township, New Jersey pursuant to a Lease Agreement (the "Hopewell Lease") with Hopewell Campus Owner LLC. In connection with the disposition of certain assets related to gene therapy manufacturing, on June 17, 2024, the Company and Hopewell Campus Owner LLC entered into an amendment and restatement of the Hopewell Lease (the "Hopewell Lease Amendment"). At its inception, the Hopewell Lease was determined to have four separate lease components. The Hopewell Lease Amendment terminated three of the four lease components, reducing the leased space from 220,500 square feet to 93,461 square feet and

(In thousands except share and per share amount)

significantly reducing the corresponding rent subject to the lease. The Company did not pay any termination fees in connection with the Hopewell Lease Amendment. As a result of the three terminated lease components, the related ROU asset was written off, the lease liability was derecognized, and the Company recognized a gain of $2.2 million during the year ended December 31, 2024. The gain is included within tangible asset impairment and losses (gains) on transactions, net on the Company's consolidated statements of operations. The Hopewell Lease Amendment did not fully or partially terminate the remaining lease component, which was therefore remeasured using an incremental borrowing rate at the date of modification of 7.5%, which resulted in an increase of the ROU asset and operating lease liability of $1.6 million, respectively. In connection with the Hopewell Lease Amendment, $2.5 million of the letter of credit was returned to the Company.

The Company also has a finance lease related to its commercial manufacturing agreement with MassBiologics of the University of Massachusetts Medical School ("MassBio"). As of December 31, 2024, the balance of the finance lease liabilities-current and finance lease liabilities-non-current are $3.0 million and $15.6 million, respectively, and are directly related to the Company's MassBio agreement. As of December 31, 2023, the balance of the finance lease liabilities-current and finance lease liabilities non-current were $3.0 million and $17.2 million, respectively. Additionally, during the years ended December 31, 2024 and December 31, 2023, the Company recorded finance lease costs of $1.4 million and $1.5 million, respectively, related to interest on the lease liability.

The Company also leases certain vehicles, lab equipment, and office equipment under operating leases. The Company's operating leases have remaining lease terms ranging from 0.1 years to 14.4 years and certain leases include renewal options to extend the lease for up to 15 years. Rent expense was $24.9 million, $29.0 million, and $25.2 million for the years ended December 31, 2024, 2023 and 2022.

The components of lease expense were as follows:

	Year Ended December 31, 2024	Year Ended December 31, 2023	Year Ended December 31, 2022
Operating Lease Cost			
Fixed lease cost	$ 19,264	$ 21,952	$ 19,804
Variable lease cost	4,661	5,846	4,557
Short-term lease cost	1,022	1,186	808
Total operating lease cost	$ 24,947	$ 28,984	$ 25,169

Total operating lease cost is a component of operating expenses on the consolidated statements of operations.

Supplemental lease term and discount rate information related to leases was as follows:

	December 31, 2024	December 31, 2023
Weighted-average remaining lease terms - operating leases (years)	11.62	11.55
Weighted-average discount rate - operating leases	7.64 %	8.69 %
Weighted-average remaining lease terms - finance lease (years)	8.01	9.01
Weighted-average discount rate - finance lease	7.80 %	7.80 %

(In thousands except share and per share amount)

Supplemental cash flow information related to leases was as follows:

	Year Ended December 31,		
	2024	2023	2022
Cash paid for amounts included in the measurement of lease liabilities:			
Operating cash flows from operating leases	$ 16,924	$ 15,338	$ 14,736
Financing cash flows from finance lease	1,490	1,379	1,276
Operating cash flows from finance lease	1,510	1,621	1,724
Right-of-use assets obtained in exchange for lease obligations:			
Operating leases	$ 6,462	$ —	$ 35,817
Changes due to lease modification and termination:			
Net decrease in right-of-use assets	$ 33,105	$ —	$ —
Net decrease in operating lease liabilities	44,184	—	—

Future minimum lease payments under non-cancelable leases as of December 31, 2024 were as follows:

	Operating Leases	Finance Lease
2025	$ 15,986	$ 3,000
2026	16,425	3,000
2027	13,902	3,000
2028	7,620	3,000
2029 and thereafter	73,732	12,000
Total lease payments	127,665	24,000
Less: Imputed Interest expense	42,355	5,426
Total	$ 85,310	$ 18,574

6. Accounts payable and accrued expenses

Accounts payable and accrued expenses at December 31, 2024 and 2023 consist of the following:

	December 31,	
	2024	2023
Employee compensation, benefits, and related accruals	$ 61,575	$ 62,643
Income tax payable	4,701	—
Consulting and contracted research	19,909	27,500
Sales allowance	58,644	77,176
Sales rebates	101,613	131,334
Royalties	8,953	74,111
Accounts payable	17,274	6,045
Milestone payable	11,025	2,500
Other	20,598	10,674
Total	$ 304,292	$ 391,983

As of December 31, 2024 and December 31, 2023, there were $0.1 million and $9.0 million, respectively, of accrued restructuring costs included above within employee compensation, benefits, and related accruals from a reduction in

workforce in the year ended December 31, 2023 in connection with the Company's strategic pipeline prioritization and discontinuation of its preclinical and early research programs in its gene therapy platform.

7. Debt

Liability for sale of future royalties

On July 17, 2020, the Company, RPI Intermediate Finance Trust ("RPI"), and, for the limited purposes set forth in the agreement, Royalty Pharma PLC, entered into a royalty purchase agreement (the "Original Royalty Purchase Agreement"). Pursuant to the Original Royalty Purchase Agreement, the Company sold to RPI 42.933% (the "Original Assigned Royalty Rights") of the Company's right to receive sales-based royalty payments (the "Royalty") on worldwide net sales of Evrysdi and any other product developed pursuant to the License and Collaboration Agreement (the "License Agreement"), dated as of November 23, 2011, by and among the Company, Roche and, for the limited purposes set forth therein, the SMA Foundation under the SMA program. In consideration for the sale of the Original Assigned Royalty Rights, RPI paid the Company $650.0 million in cash consideration. The Company has retained a 57.067% interest in the Royalty and all economic rights to receive the remaining potential regulatory and sales milestone payments under the License Agreement, which remaining milestone payments equal $150.0 million in the aggregate as of December 31, 2024. The Original Royalty Purchase Agreement was set to terminate 60 days following the earlier of the date on which Roche is no longer obligated to make any payments of the Royalty pursuant to the License Agreement and the date on which RPI has received $1.3 billion in respect of the Original Assigned Royalty Rights.

Pursuant to the guidance in ASC 470-10-25-2, the Company determined that the $650.0 million cash consideration obtained pursuant to the Original Royalty Purchase Agreement should be classified as debt and recorded it as "liability for sale of future royalties-current" and "liability for sale of future royalties-noncurrent" on the Company's consolidated balance sheet based on the timing of the expected payments to be made to RPI at the time of the transaction. The liability was subsequently amortized using the effective interest method over the life of the arrangement, in accordance with the respective guidance, utilizing the prospective method to account for subsequent changes in the estimated future payments to be made to RPI.

On October 18, 2023, the Company, Royalty Pharma Investments 2019 ICAV ("Royalty Pharma"), and, for the limited purposes set forth in the agreement, Royalty Pharma plc, entered into an Amended and Restated Royalty Purchase Agreement (the "A&R Royalty Purchase Agreement"), which amends and restates in its entirety the Original Royalty Purchase Agreement. Pursuant to the A&R Royalty Purchase Agreement, the Company has sold or agreed to sell to Royalty Pharma certain portions of the Company's remaining Royalty on worldwide net sales of Evrysdi and any other product (the "Products") developed pursuant to the SMA License Agreement (all such retained Royalty rights of the Company, the "Retained Royalty Rights," and all such Royalty rights that are sold to Royalty Pharma pursuant to the A&R Royalty Purchase Agreement, the "A&R Assigned Royalty Rights"). At closing, Royalty Pharma paid the Company $1.0 billion in cash consideration for 38.0447% of the Company's Retained Royalty Rights (which is in addition to the 42.9330% assigned to Royalty Pharma in connection with the Original Royalty Purchase Agreement, for a total of 80.9777% of the total Royalty) until such time as Royalty Pharma has received payments in respect of the Original Assigned Royalty Rights equal to $1.3 billion in the aggregate, and thereafter 66.6667% of the total Royalty. In addition, the Company may sell to Royalty Pharma the remainder of the Company's Retained Royalty Rights in exchange for an aggregate of $500.0 million in additional cash consideration after the closing of the A&R Royalty Purchase Agreement, less royalties received in respect of the Retained Royalty Rights put to Royalty Pharma, which will be payable by Royalty Pharma pursuant to five put options held by the Company that are exercisable at the Company's option between January 1, 2024 and December 31, 2025. If the Company exercises two or fewer of the put options, Royalty Pharma may exercise a call option during the period from and after January 1, 2026 until and including March 31, 2026 for up to 50% of the

remainder of the Company's Retained Royalty Rights less amounts exercised by the Company via its put options at a purchase price that is proportional to the purchase price of the Company's unexercised put options. Royalty Pharma's exercise of the call option would result in Royalty Pharma owning 90.4888% of the total Royalty until such time as Royalty Pharma has received payments in respect of the Original Assigned Royalty Rights equal to $1.3 billion in the aggregate, and thereafter 83.3333% of the total Royalty. The A&R Royalty Purchase Agreement will terminate 60 days following the date on which Roche is no longer obligated to make any payments of the Royalty pursuant to the License Agreement.

The change in rights and obligations from the A&R Royalty Purchase Agreement resulted in a change in the terms of the liability for sale of future royalties, which was evaluated by the Company in accordance with ASC 470-50, Debt — Modifications and Extinguishments. The Company determined that the present value of the cash flows under the A&R Royalty Purchase Agreement were substantially different from the present value of the cash flows under the Original Royalty Purchase Agreement. This resulted in the derecognition of the old liability for sale of future royalties and the new liability for sale of future royalties being recorded at fair value, which was determined to be $1,809.9 million as of the date of the A&R Royalty Purchase Agreement. This resulted in an extinguishment loss of $44.9 million, which was recorded within loss on extinguishment of debt, within the Company's statement of operations in the year ended December 31, 2023.

The fair value for the new liability for sale of future royalties on the date of the A&R Royalty Purchase Agreement was based on the Company's estimates of future royalties expected to be paid to Royalty Pharma over the life of the arrangement, which was determined using forecasts from market data sources, which are considered Level 3 inputs. The liability is being amortized using the effective interest method over the life of the arrangement, in accordance with ASC 470 and ASC 835. The initial annual effective interest rate was determined to be 10.8%. The Company utilized the prospective method to account for subsequent changes in the estimated future payments to be made to Royalty Pharma and updates the effective interest rate on a quarterly basis. Issuance costs related to the transaction were determined to be immaterial.

In June 2024, the Company, Royalty Pharma and Royalty Pharma plc, entered into an amendment to the A&R Royalty Purchase Agreement. Under the A&R Royalty Purchase Agreement, the Company exercised a put option in June 2024, resulting in the Company receiving $241.8 million in cash consideration. In connection with the put option exercise, the change in rights and obligations resulted in a change in the terms of the liability for sale of future royalties, which was evaluated by the Company in accordance with ASC 470-50, Debt —Modifications and Extinguishments. The Company determined that the present value of the cash flows after the put option exercise was not substantially different and was therefore determined to be a modification. The $241.8 million in cash consideration obtained was added to the liability for sale of future royalties and the annual effective interest rate under the A&R Royalty Purchase Agreement was determined to be 9.9%. The liability is being amortized using the effective interest method over the life of the arrangement, in accordance with the respective guidance, utilizing the prospective method to account for subsequent changes in the estimated future payments to be made to Royalty Pharma and the Company updates the effective interest rate on a quarterly basis.

To date, the Company has sold to Royalty Pharma a total of 90.49% of the Royalty, which will be reduced to 83.33% (the "Assigned Royalty Rights") after Royalty Pharma receives $1.3 billion in aggregate payments (the "Assigned Royalty Cap") from the Royalty assigned at the closing of the Original Purchase Agreement. In exchange for the Assigned Royalty Rights, Royalty Pharma has paid to the Company upfront cash consideration totaling $1.9 billion, less Royalty payments received by the Company with respect to the Assigned Royalty Rights. The Company currently retains 9.51% of the Royalty, which increases to 16.67% after the Assigned Royalty Cap has been met. The Company has the option under the A&R Royalty Purchase Agreement to sell its retained portions of the Royalty to Royalty Pharma in up to three tranches for the following payments: (1) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the

(In thousands except share and per share amount)

Assigned Royalty Cap has been met, (2) $100.0 million in exchange for 3.81% of the Royalty, which increases to 6.67% after the Assigned Royalty Cap has been met, and (3) $50.0 million in exchange for 1.90% of the Royalty, which increases to 3.33% after the Assigned Royalty Cap has been met, in each case less Royalty payments received by the Company with respect to the Assigned Royalty Rights. The A&R Royalty Purchase Agreement will terminate 60 days following the date on which Roche is no longer obligated to make any payments of the Royalty pursuant to the License Agreement.

The following table shows the activity within the "liability for sale of future royalties- current" and "liability for sale of future royalties- noncurrent" accounts for the year ended December 31, 2024:

	Year Ended December 31,	
Liability for sale of future royalties- (current and noncurrent)	**2024**	
Beginning balance as of December 31, 2023	$	1,814,097
Less: Non-cash royalty revenue payable to Royalty Pharma		(181,507)
Plus: Non-cash interest expense recognized		207,394
Plus: Cash received from Royalty Pharma		241,792
Ending balance	$	2,081,776
Effective interest rate as of December 31, 2024		9.8%

Non-cash interest expense is recorded in the statement of operations within "Interest expense, net".

Senior Secured Term Loan

On October 27, 2022 (the "Closing Date"), the Company entered into a credit agreement (the "Blackstone Credit Agreement") for fundings of up to $950.0 million consisting of a committed loan facility of $450.0 million and further contemplating the potential for up to $500.0 million of additional financing, to the extent that the Company requested such additional financing and subject to the Lenders' agreement to provide such additional financing and to mutual agreement on terms, among the Company, certain subsidiaries of the Company (together with the Company, the "Loan Parties") and funds and other affiliated entities advised or managed by Blackstone Life Sciences and Blackstone Credit (collectively, "Blackstone", and such lenders, together with their permitted assignees, the "Lenders" and each a "Lender") and Wilmington Trust, National Association, as the administrative agent for the Lenders.

The Blackstone Credit Agreement provided for a senior secured term loan facility funded on the Closing Date in the aggregate principal amount of $300.0 million (the "Initial Loans") and a committed delayed draw term loan facility of up to $150.0 million (the "Delayed Draw Loans" and, together with the Initial Loans, the "Loans") to be funded at the Company's request within 18 months of the Closing Date subject to specified conditions. In addition, the Blackstone Credit Agreement contemplated the potential for further financings by Blackstone, by providing for incremental discretionary uncommitted further financings of up to $500.0 million. The Company capitalized approximately $11.6 million of debt issuance costs which are presented on the balance sheet as a direct deduction from the debt liability and are being amortized over the term of the senior secured term loan facility using the effective interest rate method.

The Loans were to mature on the date that is seven years from the Closing Date. Borrowings under the Blackstone Credit Agreement bore interest at a variable rate equal to, at the Company's option, either an adjusted Term SOFR rate plus seven and a quarter percent (7.25%) or the Base Rate plus six and a quarter percent (6.25%), subject to a floor of one percent (1%) and two percent (2%) with respect to Term SOFR rate and Base Rate (each as defined in the Blackstone

(In thousands except share and per share amount)

Credit Agreement), respectively. Payment of the Loans were subject to certain premiums specified in the Blackstone Credit Agreement, in each case, from the date of the applicable Loan funded.

On October 19, 2023, the Company terminated the Blackstone Credit Agreement. In connection with the termination of the Credit Agreement, the Company repaid outstanding principal of $300.0 million, accrued interest of $2.1 million, an additional $82.0 million in prepayment premiums, exit fees, and creditor expenses, and $0.2 million in legal fees. The Company recorded a loss on the extinguishment of debt of $92.7 million which was included on the statement of operations for the period ended December 31, 2023. The loss on extinguishment of debt consisted of $82.0 million in prepayment premiums, exit fees, and creditor expenses and debt issuance costs of $10.7 million. All liens and security interests securing the loans made pursuant to the Blackstone Credit Agreement were released upon termination.

The Blackstone Credit Agreement consisted of the following:

	December 31, 2024	December 31, 2023
Principal	$ —	$ 300,000
Less: Debt issuance costs	—	—
Repayment of senior secured term loan	—	(300,000)
Net carrying amount	$ —	$ —

The following table sets forth total interest expense recognized related to the Blackstone Credit Agreement:

	Year Ended December 31, 2024	Year Ended December 31, 2023
Contractual interest expense	$ —	$ 30,198
Amortization of debt issuance costs	—	702
Total	$ —	$ 30,900
Effective interest rate	— %	13.1 %

2026 Convertible Notes

In September 2019, the Company issued, at par value, $287.5 million aggregate principal amount of 1.50% convertible senior notes due 2026, which included an option to purchase up to an additional $37.5 million in aggregate principal amount of the 2026 Convertible Notes, which was exercised in full by the initial purchasers. The 2026 Convertible Notes bear cash interest at a rate of 1.50% per year, payable semi-annually on March 15 and September 15 of each year, beginning on March 15, 2020. The 2026 Convertible Notes will mature on September 15, 2026, unless earlier repurchased or converted. The net proceeds to the Company from the offering were $279.3 million after deducting the initial purchasers' discounts and commissions and the offering expenses payable by the Company.

The 2026 Convertible Notes are governed by an indenture (the "2026 Convertible Notes Indenture") with U.S Bank National Association as trustee (the "2026 Convertible Notes Trustee").

Holders of the 2026 Convertible Notes may convert their 2026 Convertible Notes at their option at any time prior to the close of business on the business day immediately preceding March 15, 2026 only under the following circumstances:

- during any calendar quarter commencing on or after December 31, 2019 (and only during such calendar quarter), if the last reported sale price of the Company's common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;

- during the five business day period after any five consecutive trading day period (the "measurement period") in which the trading price (as defined in the 2026 Convertible Notes Indenture) per $1,000 principal amount of 2026 Convertible Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of the Company's common stock and the conversion rate on each such trading day;

- during any period after the Company has issued notice of redemption until the close of business on the scheduled trading day immediately preceding the relevant redemption date; or

- upon the occurrence of specified corporate events.

On or after March 15, 2026, until the close of business on the business day immediately preceding the maturity date, holders may convert their 2026 Convertible Notes at any time, regardless of the foregoing circumstances. Upon conversion, the Company will pay or deliver, as the case may be, cash, shares of the Company's common stock or any combination thereof at the Company's election.

The conversion rate for the 2026 Convertible Notes was initially, and remains, 19.0404 shares of the Company's common stock per $1,000 principal amount of the 2026 Convertible Notes, which is equivalent to an initial conversion price of approximately $52.52 per share of the Company's common stock. The conversion rate may be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest.

The Company was not permitted to redeem the 2026 Convertible Notes prior to September 20, 2023. The Company may redeem for cash all or any portion of the 2026 Convertible Notes, at its option, if the last reported sale price of its common stock has been at least 130% of the conversion price then in effect on the last trading day of, and for at least 19 other trading days (whether or not consecutive) during, any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which the Company provides notice of redemption, at a redemption price equal to 100% of the principal amount of the 2026 Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. No sinking fund is provided for the 2026 Convertible Notes, which means that the Company is not required to redeem or retire the 2026 Convertible Notes periodically.

If the Company undergoes a "fundamental change" (as defined in the 2026 Convertible Notes Indenture), subject to certain conditions, holders of the 2026 Convertible Notes may require the Company to repurchase for cash all or part of their 2026 Convertible Notes at a repurchase price equal to 100% of the principal amount of the 2026 Convertible Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

The 2026 Convertible Notes represent senior unsecured obligations and will rank senior in right of payment to the Company's future indebtedness that is expressly subordinated in right of payment to the notes, equal in right of payment to the Company's existing and future unsecured indebtedness that is not so subordinated, effectively junior in right of

(In thousands except share and per share amount)

payment to any of the Company's secured indebtedness to the extent of the value of the assets securing such indebtedness, and structurally subordinated to all existing and future indebtedness and other liabilities (including trade payables) incurred by the Company's subsidiaries. The 2026 Convertible Notes Indenture contains customary events of default with respect to the 2026 Convertible Notes, including that upon certain events of default (including the Company's failure to make any payment of principal or interest on the 2026 Convertible Notes when due and payable) occurring and continuing, the 2026 Convertible Notes Trustee by notice to the Company, or the holders of at least 25% in principal amount of the outstanding 2026 Convertible Notes by notice to the Company and the Convertible Notes Trustee, may, and the 2026 Convertible Notes Trustee at the request of such holders (subject to the provisions of the 2026 Convertible Notes Indenture) will, declare 100% of the principal of and accrued and unpaid interest, if any, on all the 2026 Convertible Notes to be due and payable. In case of certain events of bankruptcy, insolvency or reorganization, involving the Company or a significant subsidiary, 100% of the principal of and accrued and unpaid interest on the 2026 Convertible Notes will automatically become due and payable. Upon such a declaration of acceleration, such principal and accrued and unpaid interest, if any, will be due and payable immediately.

The 2026 Convertible Notes consist of the following:

	Year ended December 31,	
	2024	2023
Principal	$ 287,500	$ 287,500
Less: Debt issuance costs	(2,088)	(3,287)
Net carrying amount	$ 285,412	$ 284,213

As of December 31, 2024, the remaining contractual life of the 2026 Convertible Notes is approximately 1.7 years.

The following table sets forth total interest expense recognized related to the 2026 Convertible Notes:

	December 31,	
	2024	2023
Contractual interest expense	$ 4,319	$ 4,305
Amortization of debt issuance costs	1,198	1,171
Total	$ 5,517	$ 5,476
Effective interest rate	1.9 %	1.9 %

8. Capital structure

Common stock

In August 2019, the Company entered into an At the Market Offering Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald and RBC Capital Markets, LLC (together, the "Sales Agents"), pursuant to which, the Company may offer and sell shares of its common stock, having an aggregate offering price of up to $125.0 million from time to time through the Sales Agents by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. No shares were sold pursuant to the Sales Agreement during the years ended December 31, 2024, 2023, and 2022. The remaining shares of the Company's common

stock available to be issued and sold, under the Sales Agreement, have an aggregate offering price of up to $93.0 million as of December 31, 2024.

In connection with the execution of the Blackstone Credit Agreement, the Company and certain entities affiliated with the Lenders (the "Purchasers") also entered into a stock purchase agreement (the "Stock Purchase Agreement") on the Closing Date for the sale and issuance of 1,095,290 shares of common stock (the "Shares") to the Purchasers at a price of $45.65 per share, for an aggregate purchase price of approximately $50.0 million. The per share price represents the closing price of the Company's common stock on the Nasdaq Global Select Market on October 26, 2022.

Under the Stock Purchase Agreement, the Company agreed to register the resale of the Shares on a registration statement to be filed with the Securities and Exchange Commission within 60 days of the Closing Date. The Company agreed to keep such registration statement effective for a period of six months following the Closing Date. In addition, subject to certain conditions, the Purchasers were entitled to participate in registered underwritten public offerings by the Company during such period.

Pursuant to the terms of the Stock Purchase Agreement, the Purchasers and certain of their controlled affiliates agreed not to, without the prior written approval of the Company and subject to specified conditions, directly or indirectly acquire shares of the Company's outstanding common stock in excess of specified thresholds, seek or propose any acquisition of all or substantially all of the assets of the Company, seek or propose a merger or other business combination involving the Company, solicit proxies or consents with respect to any securities of the Company, seek to influence the management, board of directors or policies of the Company, or undertake other specified actions related to the potential acquisition of additional equity interests in the Company, or to encourage others to do any of the above (the "Standstill Restrictions"). The Standstill Restrictions terminated upon the termination of the Blackstone Credit Agreement.

The Purchasers also agreed not to sell or transfer the Shares without the prior written approval of the Company for a period of 90 days following the Closing Date, subject to certain exceptions.

In February 2023, the Company completed enrollment of its Phase 3 placebo-controlled clinical trial for sepiapterin for PKU. In connection with this event and pursuant to the Censa Merger Agreement, the Company paid a $30.0 million development milestone to the former Censa securityholders during the year ended December 31, 2023. The Company elected to pay this milestone in the form of shares of its common stock, less certain cash payments in accordance with the Censa Merger Agreement. Pursuant to such election, the Company issued 657,462 shares of its common stock and paid $0.4 million to the former Censa securityholders.

As of December 31, 2024, the Company's number of authorized shares of common stock was 250,000,000.

9. Net loss per share

Basic and diluted net loss per share is computed by dividing net loss available to common stockholders by the weighted-average number of common shares outstanding. Potentially dilutive securities were excluded from the diluted calculation because their effect would be anti-dilutive.

(In thousands except share and per share amount)

The following table sets forth the computation of basic and diluted net loss per share for common stockholders:

	Year ended December 31,		
	2024	2023	2022
Numerator			
Net loss	$ (363,295)	$ (626,604)	$ (559,017)
Denominator			
Denominator for basic and diluted net loss per share	76,845,055	74,838,392	71,728,634
Net loss per share:			
Basic and diluted	$ (4.73)*	$ (8.37)*	$ (7.79)*

* For the years ended December 31, 2024, 2023, and 2022, the Company experienced a net loss and therefore did not report any dilutive share impact.

The following table shows historical dilutive common share equivalents outstanding, which are not included in the above historical calculation, as the effect of their inclusion is anti-dilutive during each period.

	As of December 31,		
	2024	2023	2022
Stock Options	403,884	900,026	1,107,490
Unvested restricted stock units	773,462	779,188	402,230
Total	1,177,346	1,679,214	1,509,720

10. Stock award plan

In May 2013, the Company's Board of Directors and stockholders approved the 2013 Long Term Incentive Plan, which became effective upon the closing of the Company's IPO. The 2013 Long Term Incentive Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards and other stock-based awards. On June 8, 2022 (the "Restatement Effective Date"), the Company's stockholders approved the Amended and Restated 2013 Long-Term Incentive Plan (the "Amended 2013 LTIP"). The Amended 2013 LTIP provides for the grant of incentive stock options, nonstatutory stock options, restricted stock units and other stock-based awards. The number of shares of common stock reserved for issuance under the Amended 2013 LTIP is the sum of (A) the number of shares of the Company's common stock (up to 16,724,212 shares) that is equal to the sum of (1) the number of shares issued under the 2013 Long-Term Incentive Plan prior to the Restatement Effective Date, (2) the number of shares that remain available for issuance under the 2013 Long-Term Incentive Plan immediately prior to the Restatement Effective Date and (3) the number of shares subject to awards granted under the 2013 Long-Term Incentive Plan prior to the Restatement Effective Date that are outstanding as of the Restatement Effective Date, plus (B) from and after the Restatement Effective Date, an additional 8,475,000 shares of Common Stock. As of December 31, 2024, awards for 6,893,006 shares of common stock were available for issuance under the Amended 2013 LTIP.

There are no additional shares of common stock available for issuance under the Company's 1998 Employee, Director and Consultant Stock Option Plan, 2009 Equity and Long Term Incentive Plan or 2013 Stock Incentive Plan.

In January 2020, the Company's Board of Directors approved the 2020 Inducement Stock Incentive Plan. The 2020 Inducement Stock Incentive Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards and other stock-based awards, initially up to an aggregate of 1,000,000 shares of common stock. Any grants made under the 2020 Inducement Stock Incentive Plan must be made pursuant to the Nasdaq Listing Rule 5635(c)(4)

inducement grant exception as a material component of the Company's new hires' employment compensation. In December 2020, the Company's Board of Directors approved an additional 1,000,000 shares of common stock that may be issued under the 2020 Inducement Stock Incentive Plan. In April 2022, the Company's Board of Directors approved a reduction in the total number of shares of common stock that may be issued under the 2020 Inducement Stock Incentive Plan to 1,300,000 shares. In December 2022, the Company's Board of Directors approved an additional 1,700,000 shares of common stock that may be issued under the 2020 Inducement Stock Inventive Plan. As of December 31, 2024, awards for 1,923,916 shares of common stock are available for issuance under the 2020 Inducement Stock Incentive Plan.

The Board of Directors has the authority to select the individuals to whom options are granted and determine the terms of each option, including (i) the number of shares of common stock subject to the option; (ii) the date on which the option becomes exercisable; (iii) the option exercise price, which, in the case of incentive stock options, must be at least 100% (110% in the case of incentive stock options granted to a stockholder owning in excess of 10% of the Company's stock) of the fair market value of the common stock as of the date of grant; and (iv) the duration of the option (which, in the case of incentive stock options, may not exceed ten years). Options typically vest over a four-year period.

Inducement stock option awards

Pursuant to the Nasdaq inducement grant exception, during the year ended December 31, 2024, the Company issued options to purchase an aggregate of 61,720 shares of common stock to certain new hire employees at a weighted-average exercise price of $36.62 per share under the 2020 Inducement Stock Incentive Plan. Additionally, during the year ended December 31, 2024, the Company issued 84,985 restricted stock units under the 2020 Inducement Stock Incentive Plan. An aggregate of 532,930 options and 12,977 restricted stock units previously granted as inducement awards were forfeited during the year ended December 31, 2024 in connection with employee separations from the Company.

Stock option activity—A summary of stock option activity is as follows:

	Number of options	Weighted-average exercise price	Weighted-average remaining contractual term	Aggregate intrinsic value(in thousands)
Outstanding at December 31, 2021	10,772,582	$ 43.66		
Granted	1,685,435	$ 38.55		
Exercised	(496,863)	$ 29.45		
Forfeited	(458,737)	$ 48.75		
Outstanding at December 31, 2022	11,502,417	$ 43.33		
Granted	1,117,284	$ 40.19		
Exercised	(822,482)	$ 29.25		
Forfeited	(2,196,820)	$ 45.85		
Outstanding at December 31, 2023	9,600,399	$ 43.59		
Granted	970,875	$ 26.73		
Exercised	(824,813)	$ 34.63		
Forfeited/Cancelled	(1,263,972)	$ 45.20		
Outstanding at December 31, 2024	8,482,489	$ 42.29	5.54 years	$ 63,739
Expected to vest at December 31, 2024	1,500,910	$ 34.48	8.37 years	$ 18,009
Exercisable at December 31, 2024	6,844,675	$ 44.22	4.85 years	$ 43,849

(In thousands except share and per share amount)

The fair values of grants made in the years ended December 31, 2024, 2023 and 2022 were contemporaneously estimated on the date of grant using the following assumptions:

	2024	2023	2022
Risk-free interest rate	3.51% - 4.66%	3.54% - 4.69%	1.55% - 4.57%
Expected volatility	53% - 55%	53% - 56%	54% - 74%
Expected term	5.5 years	5.5 years	5.5 years

The Company assumed no expected dividends for all grants. The weighted average grant date fair value of options granted during the years ended December 31, 2024, 2023 and 2022 was $14.04, $21.27, and $23.54 per share, respectively.

Restricted Stock Units—Restricted stock units are granted subject to certain restrictions, including in some cases service conditions (restricted stock). The grant-date fair value of restricted stock units, which has been determined based upon the market value of the Company's shares on the grant date, is expensed over the vesting period.

The following table summarizes information on the Company's restricted stock units:

	Restricted Stock Units	
	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2023	2,866,270	$ 41.82
Granted	1,897,100	26.29
Vested	(963,543)	43.67
Forfeited	(272,252)	36.29
Unvested at December 31, 2024	3,527,575	$ 33.39

Performance-based Restricted Stock Units—In December 2023, the Company granted 150,000 performance-based restricted stock units ("PSUs") to its Chief Executive Officer, Dr. Matthew Klein, which will vest only if challenging performance goals relating to development and regulatory milestones are achieved over an approximately two year performance period. In December 2024, the Company granted 25,000 performance-based restricted stock units to Dr. Matthew Klein, which will vest only if challenging performance goals relating to development, regulatory, or commercial goals are achieved over an approximately five year performance period and granted an additional 31,250 PSUs, which will vest only if challenging performance goals relating to stock price goals are achieved over an approximately five year performance period. As of December 31, 2024, the achievements of the performance goals have not yet been deemed probable and therefore no expense has been recognized to date.

Employee Stock Purchase Plan—In June 2016, the Company established an Employee Stock Purchase Plan (as amended, "ESPP" or the "Plan") for certain eligible employees. The Plan is administered by the Company's Board of Directors or a committee appointed by the Board. In June 2021, the Plan was amended to increase the total number of shares available for purchase under the Plan from one million shares to two million shares of the Company's common stock. Employees may participate over a six-month period through payroll withholdings and may purchase, at the end of the six-month period, the Company's common stock at a purchase price of at least 85% of the closing price of a share of the Company's common stock on the first business day of the offering period or the closing price of a share of the Company's common stock on the last business day of the offering period, whichever is lower. No participant will be

(In thousands except share and per share amount)

granted a right to purchase the Company's common stock under the Plan if such participant would own more than 5% of the total combined voting power of the Company or any subsidiary of the Company after such purchase. For the period ending December 31, 2024, the Company recorded $2.2 million in compensation expense related to the ESPP.

The Company recorded share-based compensation expense in the statement of operations related to incentive stock options, nonstatutory stock options, restricted stock units and the ESPP as follows:

	Year ended December 31,		
	2024	2023	2022
Research and development	$ 36,629	$ 52,941	$ 55,869
Selling, general and administrative	37,986	48,695	54,464
Total	$ 74,615	$ 101,636	$ 110,333

As of December 31, 2024, there was approximately $99.0 million of total unrecognized compensation cost related to unvested share-based compensation arrangements granted under the Company's Plans. This cost is expected to be recognized as compensation expense over the weighted average remaining service period of approximately 2.3 years.

11. Other comprehensive (loss) income and accumulated other comprehensive items

Other comprehensive (loss) income includes changes in equity that are excluded from net loss, such as unrealized gains and losses on marketable securities.

The following table summarizes other comprehensive (loss) income and the changes in accumulated other comprehensive items, by component, for the years ended December 31, 2024, 2023, and 2022, respectively.

	Unrealized (Losses) Gains On Marketable Securities, net of tax	Foreign Currency Translation	Total Accumulated Other Comprehensive Items
Balance at December 31, 2021	$ (602)	$ (23,680)	$ (24,282)
Other comprehensive income before reclassifications	4,072	28,970	33,042
Amounts reclassified from other comprehensive items	(3,964)	—	(3,964)
Other comprehensive income	108	28,970	29,078
Balance at December 31, 2022	$ (494)	$ 5,290	$ 4,796
Other comprehensive income (loss) before reclassifications	1,135	(6,901)	(5,766)
Amounts reclassified from other comprehensive items	(315)	—	(315)
Other comprehensive income (loss)	820	(6,901)	(6,081)
Balance at December 31, 2023	$ 326	$ (1,611)	$ (1,285)
Other comprehensive loss before reclassifications	(3,492)	(24,544)	(28,036)
Amounts reclassified from other comprehensive items	3,435	—	3,435
Other comprehensive loss	(57)	(24,544)	(24,601)
Balance at December 31, 2024	$ 269	$ (26,155)	$ (25,886)

Reclassified amounts from other comprehensive items were determined using the actual realized gains and losses from the sales of marketable securities.

12. Revenue recognition

Net product sales

During the years ended December 31, 2024, 2023 and 2022, net product sales in the United States were $207.2 million, $255.1 million, and $218.3 million, respectively, consisting solely of sales of Emflaza, and net product sales outside of the United States were $393.8 million, $406.1 million, and $316.9 million respectively, consisting of sales of Translarna, Tegsedi, Waylivra, and Upstaza. Translarna net product revenues made up $339.9 million, $355.8 million, and $288.6 million of the net product sales outside the United States for the years ended December 31, 2024, 2023 and 2022, respectively. During the year ended December 31, 2024, three countries, the United States, Russia, and Brazil, accounted for at least 10% of the Company's net product sales, representing $207.2 million, $105.4 million, and $72.1 million of the net product sales, respectively. During the years ended December 31, 2023, and 2022, two countries, the United States and Russia, accounted for at least 10% of the Company's net product sales, representing $255.1 million and $86.0 million, and $218.3 million and $59.7 million of the net product sales, respectively. For the years ended December 31, 2024, 2023 and 2022, two of the Company's distributors each accounted for over 10% of the Company's net product sales.

As of December 31, 2024 and 2023, the Company does not have a contract liabilities balance related to net product sales, and has not made significant changes to the judgments made in applying ASC Topic 606.

Collaboration revenue and Royalty revenue

In November 2011, the Company and the Spinal Muscular Atrophy Foundation ("SMA Foundation") entered into a licensing and collaboration agreement with F. Hoffman-La Roche Ltd and Hoffman- La Roche Inc. (collectively, "Roche"). Under the terms of the SMA License Agreement, Roche acquired an exclusive worldwide license to the Company's SMA program.

Under the agreement, the Company is eligible to receive additional payments from Roche if specified events are achieved with respect to each licensed product, including up to $135.0 million in research and development event milestones, up to $325.0 million in sales milestones upon achievement of certain sales events, and up to double digit royalties on worldwide annual net sales of a commercial product.

For the year ended December 31, 2024, collaboration revenue related to the SMA License Agreement with Roche was immaterial. For the years ended December 31, 2023 and 2022, the Company recognized collaboration revenue related to the SMA License Agreement with Roche of $100.0 million, and $50.1 million, respectively. The below summarizes the milestone achievements associated with the Company's SMA program during the years ended December 31, 2024, 2023 and 2022.

The SMA program currently has one approved product, Evrysdi, which was approved in August 2020 by the FDA for the treatment of SMA in adults and children two months and older. In September 2022, the Company recognized a sales milestone of $50.0 million for the achievement of $750.0 million in worldwide annual net sales from Evrysdi. For the year ended December 31, 2023, the Company recognized a sales milestone of $100.0 million for the achievement of $1.5 billion in worldwide annual net sales from Evrysdi, which was recorded on the balance sheet within prepaid expenses and other current assets as of December 31, 2023. The remaining potential sales milestones as of December 31, 2024 is $150.0 million upon achievement of certain sales events. As of December 31, 2024, the Company does not have any remaining research and development milestones that can be received.

(In thousands except share and per share amount)

In addition to research and development and sales milestones, the Company is eligible to receive up to double-digit royalties on worldwide annual net sales of a commercial product under the SMA License Agreement. For the years ended December 31, 2024, 2023 and 2022 the Company has recognized $203.9 million, $168.9 million, and $113.5 million of royalty revenue related to Evrysdi, respectively.

Manufacturing Revenue

For the years ended December 31, 2024 and 2023, the Company recognized $1.7 million and $7.7 million of manufacturing revenue, respectively, related to the production of DNA and AAV vectors for gene therapy applications for external customers. No manufacturing revenue was recognized for the year ended December 31, 2022. The Company has not made significant changes to the judgments made in applying ASC Topic 606 for the years ended 2024, 2023, and 2022.

As of December 31, 2024, the Company does not have a contract liabilities balance related to the production of plasmid DNA and AAV vectors for gene therapy applications for external customers. As of December 31, 2023, the Company had a contract liabilities balance of $0.8 million related to the production of plasmid DNA and AAV vectors for external customers, which is recorded within deferred revenue on the consolidated balance sheet. For the year ended December 31, 2024, the Company recognized $0.8 million related to the amounts included in the contract liability balance at the beginning of the period.

As of December 31, 2024, the Company has no contract assets related to plasmid DNA and AAV production for external customers. As of December 31, 2023, the Company had contract assets of $0.2 million related to plasmid DNA and AAV production for external customers, which was recorded within prepaid expenses and other current assets on the consolidated balance sheet.

In June 2024, the Company sold its gene therapy manufacturing business in Hopewell Township, New Jersey. Accordingly, the Company does not expect to have manufacturing revenue going forward.

Remaining performance obligations

There are no remaining performance obligations as of December 31, 2024. The Company's remaining performance obligations of $0.8 million as of December 31, 2023 were fully recognized during the year ended December 31, 2024.

13. Income taxes

The loss from operations before tax (expense) benefit consisted of the following for the years ended December 31, 2024, 2023, and 2022:

	2024	2023	2022
Domestic	$ (598,807)	$ (784,744)	$ (591,126)
Foreign	235,688	88,634	3,639
Total	$ (363,119)	$ (696,110)	$ (587,487)

(In thousands except share and per share amount)

The Income Tax Provision consisted of the following for the years ended December 31, 2024, 2023 and 2022:

	2024	2023	2022
Current:			
U.S. Federal	$ (26,798)	$ —	$ —
U.S. State and Local	(19,419)	27,226	(4,224)
Foreign	(8,896)	(4,003)	(1,582)
Deferred:			
U.S. Federal	49,511	36,408	23,689
U.S. State and Local	6,397	10,521	10,587
Foreign	(971)	(646)	—
Total tax (expense) benefit	$ (176)	$ 69,506	$ 28,470

A reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows:

	December 31,		
	2024	2023	2022
Federal income tax provision at statutory rate	21.00 %	21.00 %	21.00 %
State income tax provision, net of federal benefit	(1.57)	0.32	3.07
Permanent differences	11.79	(1.43)	(1.83)
Research and development	5.07	4.59	5.89
Change in valuation allowances	(27.99)	(16.86)	(23.36)
Change in deferred tax assets	—	—	(0.10)
Foreign tax rate differential	9.14	0.05	(0.17)
Tax rate change	(11.69)	(1.26)	0.34
Release (accrual) of uncertain tax positions	(5.90)	3.71	—
Other	0.13	(0.12)	—
Effective income tax rate	(0.02)%	10.00 %	4.84 %

Accounting for income taxes under U.S. GAAP requires that individual tax-paying entities of the company offset all deferred tax liabilities and assets within each particular tax jurisdiction and present them as a noncurrent deferred tax liability or asset. Amounts in different tax jurisdictions cannot be offset against each other. The noncurrent deferred income tax asset is recorded within deposits and other assets on the balance sheet. The amount of deferred income taxes are as follows:

	December 31,	
	2024	2023
Assets:		
Noncurrent deferred income taxes	$ —	$ —
Liabilities:		
Noncurrent deferred income taxes	—	(55,905)
Deferred income taxes - net	$ —	$ (55,905)

(In thousands except share and per share amount)

The significant components of the Company's deferred tax assets and liabilities at December 31, 2024 and 2023 are as follows:

	2024	2023
Deferred tax assets:		
Accrued expense	$ 8,744	$ 25,400
Amortization	102,308	137,808
Federal tax credits	146,515	205,485
State tax credits	9,822	9,817
Federal net operating losses	—	60,270
State net operating losses	13,319	18,680
Foreign net operating losses	3,265	4,052
Capitalized research and development costs	157,234	149,683
Share based compensation and other	24,219	30,757
Liability for sale of future royalties	394,132	190,659
Noncash interest expense	10,413	9,410
Other comprehensive loss	(647)	(728)
Total gross deferred tax assets	869,324	841,293
Less valuation allowance	(857,584)	(833,810)
Total deferred tax assets, net of valuation allowance	$ 11,740	$ 7,483
Deferred tax liabilities:		
Depreciation	$ (11,740)	$ (7,483)
Indefinite lived intangible	—	(55,905)
Total gross deferred tax liabilities	(11,740)	(63,388)
Net deferred tax assets (liabilities)	$ —	$ (55,905)

For the year ended December 31, 2024, the Company generated taxable income in the U.S. of $810.3 million. The Company has recorded a federal income tax provision expense of $26.8 million and a state income tax expense of $19.4 million which are driven by the recognition of previously deferred revenue from the A&R Royalty Purchase Agreement.

At December 31, 2024 and 2023, the Company recorded a valuation allowance against its net deferred tax assets of $857.6 million and $833.8 million, respectively. The change in the valuation allowance during the years ended December 31, 2024 and 2023 was $23.8 million and $161.6 million, respectively. A valuation allowance has been recorded since, in the judgment of management, these assets are not more likely than not to be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during periods in which those temporary differences and carryforwards become deductible or are utilized. As of December 31, 2024, the Company had $204.9 million, and $9.8 million of state and foreign net operating loss carryforwards, respectively. Further, the Company expects to utilize all federal net operating loss carryforwards in the 2024 tax year.

The Company recorded a deferred tax liability in conjunction with the Agilis Merger of $122.0 million in 2018, related to the tax basis difference in the IPRD indefinite-lived intangibles acquired. The Company's policy is to record a deferred tax liability related to acquired IPR&D which may eventually be realized either upon amortization of the asset when the research is completed, and a product is successfully launched or the write-off of the asset if it is abandoned or unsuccessful. In July 2022, the Company received EMEA approval for a portion of the IPR&D assets, and thus, began the amortization of the intangible. In May 2023, the Company announced the discontinuation of its preclinical and early research programs in gene therapy as part of a strategic portfolio prioritization. In conjunction with the announcement, the Company recorded an impairment to its indefinite-lived intangible for IP research and development relating to the FA and Angelman syndrome

gene therapy assets. In November 2024, the Company was granted U.S. FDA approval and received (and subsequently sold) an associated Priority Review Voucher for a portion of the IPR&D assets. Additionally, in the fourth quarter of 2024, the Company recorded an impairment to the remainder of the indefinite-lived intangible IPR&D assets. As a result of this activity, the Company no longer has an associated deferred tax liability associated with the Agilis Merger to carry forward.

As of December 31, 2024, the combined Research and Development and Orphan Drug Credit carryforward for federal purposes is $146.5 million.

The income tax (expense) benefit for the years ended December 31, 2024 and 2023 differed from the amounts computed by applying the U.S. federal income tax rate of 21% to loss before tax expense as a result of the IPR&D assets becoming partially amortizable in 2022, foreign taxes, the impact of temporary difference, including the updated section 174, the impact of permanent differences, including "global intangible low-taxed income" ("GILTI"), tax credits generated, true up of net operating loss carryforwards, and increase in the Company's valuation allowance.

Under the 2017 Tax Cuts and Jobs Act, the ability to currently deduct qualifying research and experimental costs under section 174, as well as software development costs, are eliminated for tax years beginning after December 31, 2021. Under the new rule, these costs must be capitalized and amortized over a five-year or fifteen-year period, depending on whether the research is conducted in the U.S. or abroad, respectively. The rule became effective for the Company during the 2022 tax year, and resulted in an increased current taxable income of the Company by $62.5 million for the tax year ended December 31, 2024.

The Company applies the elements of FASB ASC 740-10 regarding accounting for uncertainty in income taxes. This clarifies the accounting for uncertainty in income taxes recognized in financial statements and required impact of a tax position to be recognized in the financial statements if that position is more likely than not of being sustained by the taxing authority. As of December 31, 2024, the Company recorded unrecognized tax benefits in the amount of $108.0 million including interest and penalties through 2024. The Company's policy is to recognize interest and penalties related to tax matters within the income tax provision. Tax years beginning in 2014 are generally subject to examination by taxing authorities, although net operating losses from all years are subject to examinations and adjustments for at least three years following the year in which the attributes are used. The Company is currently under a corporate business tax audit in New Jersey for tax years 2020 through 2022. Although the outcome of tax audits is always uncertain, the company does not expect any adjustment to result for these years as of December 31, 2024.

For all years through December 31, 2016, the Company generated research credits but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

As a result of U.S. tax reform legislation, distributions of profits from non-U.S. subsidiaries are not expected to cause a significant incremental U.S. tax impact in the future. However, distributions may be subject to non-U.S. withholding taxes if profits are distributed from certain jurisdictions. As of December 31, 2024, for purposes of ASC 740-10-25-3, the Company had $425.3 million of undistributed earnings from non-U.S. subsidiaries that it intends to reinvest permanently in its non-U.S. operations. As these ASC 740-10-25-3 earnings are considered permanently reinvested, no tax provision has been accrued. It is not feasible to estimate the amount of tax that might be payable on the eventual remittance of such earnings.

(In thousands except share and per share amount)

Unrecognized Tax Benefits

A reconciliation of the gross amount of unrecognized tax benefits, excluding accrued interest and penalties, is as follows:

	Unrecognized Tax Benefits
Balance at December 31, 2023	1,360
Increases in uncertain tax benefits	106,628
Balance at December 31, 2024	$ 107,988

Uncertain tax positions, for which management's assessment is that there is a more than 50% probability of sustaining the position upon challenge by a taxing authority based upon its technical merits, are subject to certain recognition and measurement criteria. The nature of the uncertain tax positions is often very complex and subject to change, and the amounts at issue can be substantial. The Company develops its cumulative probability assessment of the measurement of uncertain tax positions using internal experience, judgment, and assistance from professional advisors. The Company re-evaluates these uncertain tax positions on a quarterly basis based on a number of factors including, but not limited to, changes in facts or circumstances, changes in tax law, and effectively settled issues under audit and new audit activity. Any change in these factors could result in the recognition of a tax benefit or an additional charge to the tax provision.

The Company records penalties and tax-related interest expense on unrecognized tax benefits as a component of the provision for income taxes in the accompanying consolidated statement of operations. The Company has recorded interest related to uncertain tax positions for the year ended December 31, 2024, in the accompanying consolidated balance sheet. Future changes in the Company’s unrecognized tax benefits will affect the Company’s annual effective tax rate.

14. Commitments and contingencies

Under various agreements, the Company will be required to pay royalties and milestone payments upon the successful development and commercialization of products. The Company has entered into a collaboration agreement with the SMA Foundation. The Company was obligated to pay the SMA Foundation single-digit royalties on worldwide net product sales of any collaboration product that was successfully developed and subsequently commercialized or, with respect to collaboration products the Company outlicensed, including Evrysdi, a specified percentage of certain payments the Company received from its licensee. The Company was not obligated to make such payments unless and until annual sales of a collaboration product exceeded a designated threshold. Since inception, the SMA Foundation has earned $52.5 million in royalty payments, all of which was paid as of December 31, 2024. The Company has reached its obligations to make such payments to the SMA Foundation of an aggregate of $52.5 million, and therefore, there are no further payment obligations due.

Pursuant to the asset purchase agreement ("Asset Purchase Agreement") between the Company and Marathon Pharmaceuticals, LLC (now known as Complete Pharma Holdings, LLC) (“Marathon”), Marathon was entitled to receive contingent payments from the Company based on annual net sales of Emflaza up to a specified aggregate maximum amount over the expected commercial life of the asset. This amount was achieved during the year ended December 31, 2024, therefore no future payments will be due. In addition, Marathon received a $50.0 million sales-based milestone during the year ended December 31, 2022.

Pursuant to the Agilis Merger Agreement with Agilis, Agilis equityholders were previously entitled to receive contingent consideration payments from the Company based on (i) the achievement of certain development milestones up to an aggregate maximum amount of $60.0 million, (ii) the achievement of certain regulatory approval milestones together with a milestone payment following the receipt of a priority review voucher up to an aggregate maximum amount of $535.0 million, (iii) the achievement of certain net sales milestones up to an aggregate maximum amount of $150.0 million, and (iv) a percentage of annual net sales for FA and Angelman syndrome during specified terms, ranging from 2%-6%. The Company was required to pay $40.0 million of the development milestone payments upon the passing of the second anniversary of the closing of the Agilis Merger, regardless of whether the applicable milestones have been achieved.

On April 29, 2020, the Company, certain of the former equity holders of Agilis ("the Participating Rightholders"), and, for the limited purposes set forth in the agreement, Shareholder Representative Services LLC, entered into a Rights Exchange Agreement (the "Rights Exchange Agreement"). Pursuant to the terms of the Rights Exchange Agreement, the Participating Rightholders canceled and forfeited their rights under the Agilis Merger Agreement to receive (i) $174.0 million, in the aggregate, of potential milestone payments based on the achievement of certain regulatory milestones and (ii) $37.6 million, in the aggregate, of $40.0 million in development milestone payments that would have been due upon the passing of the second anniversary of the closing of the Agilis Merger, regardless of whether the milestones are achieved.

The Rights Exchange Agreement has no effect on the Agilis Merger Agreement other than to provide for the cancellation and forfeiture of the Participating Rightholders' rights to receive $211.6 million, in the aggregate, of the milestone payments described above. As a result, all other rights and obligations under the Agilis Merger Agreement remain in effect pursuant to their terms, including the Company's obligation to pay up to an aggregate maximum amount of $20.0 million upon the achievement of certain development milestones (representing the remaining portion of potential development milestone payments for which rights were not canceled and forfeited pursuant to the Rights Exchange Agreement while excluding the remaining $2.4 million milestone payment that was due and paid upon the passing of the second anniversary of the closing of the Agilis Merger), up to an aggregate maximum amount of $361.0 million upon the achievement of certain regulatory milestones (representing the remaining portion of potential regulatory milestone payments for which rights were not canceled and forfeited pursuant to the Rights Exchange Agreement), up to a maximum aggregate amount of $150.0 million upon the achievement of certain net sales milestones and a percentage of annual net sales for FA and Angelman syndrome during specified terms, ranging from 2% to 6%, pursuant to the terms of the Agilis Merger Agreement.

In July 2022, the EC approved Upstaza for the treatment of AADC deficiency for patients 18 months and older within the EEA. As a result of such approval, the Company paid the former equityholders of Agilis $50.0 million in accordance with the terms of the Agilis Merger Agreement in the year ended December 31, 2022. In May 2023, as part of the Company's strategic portfolio prioritization, the Company decided to discontinue its preclinical and early research programs in its gene therapy platform, which included programs for FA and Angelman syndrome. As a result, the Company does not expect the milestones related to FA and Angelman syndrome to be achieved. In addition, the Company does not expect to pay the 2% to 6% royalties on annual net sales related to FA and Angelman syndrome.

In March 2024, the Company submitted a BLA to the FDA for its gene therapy treatment for AADC deficiency in the United States. In May 2024, the FDA accepted the filing for the BLA and granted priority review with a target regulatory action date of November 13, 2024. As a result of the acceptance, the Company paid a $20.0 million milestone payment to former equity holders of Agilis during the year ended December 31, 2024. On November 13, 2024, the Company's BLA for its gene therapy treatment of AADC deficiency was approved by the FDA. In connection with the approval, the Company was granted a rare disease PRV. The FDA approval and PRV triggered $11.0 million in regulatory milestones, which were recorded in accounts payable and accrued expenses on the balance sheet as of December 31, 2024. As of

December 31, 2024, there are no remaining regulatory milestones. As of December 31, 2024, the remaining potential sales milestones related to Upstaza/Kebilidi is $50.0 million.

On October 25, 2019, the Company completed the acquisition of substantially all of the assets of BioElectron Technology Corporation ("BioElectron"), a Delaware corporation, including certain compounds that the Company has begun to develop as part of its Bio-e platform, pursuant to an asset purchase agreement by and between the Company and BioElectron, dated October 1, 2019 (the "BioElectron Asset Purchase Agreement"). BioElectron was a private company with a pipeline focused on inflammatory and central nervous system (CNS) disorders. The lead program, vatiquinone, is in late stage development for CNS disorders with substantial unmet need and significant commercial opportunity that are complementary to PTC's existing pipeline.

Subject to the terms and conditions of the BioElectron Asset Purchase Agreement, BioElectron may become entitled to receive contingent milestone payments of up to $200.0 million (in cash or in shares of the Company's common stock, as determined by the Company) from the Company based on the achievement of certain regulatory and net sales milestones. Subject to the terms and conditions of the BioElectron Asset Purchase Agreement, BioElectron may also become entitled to receive contingent payments based on a percentage of net sales of certain products.

Subject to the terms and conditions of the Agreement and Plan of Merger, dated as of May 5, 2020 (the "Censa Merger Agreement") by and among the Company, Hydro Merger Sub, Inc., the Company's wholly owned, indirect subsidiary, and, solely in its capacity as the representative, agent and attorney-in-fact of the securityholders of Censa, Shareholder Representative Services LLC (such merger pursuant thereto, the "Censa Merger"), former Censa securityholders may become entitled to receive contingent payments from the Company based on (i) the achievement of certain development and regulatory milestones up to an aggregate maximum amount of $217.5 million for sepiapterin's two most advanced programs and receipt of a priority review voucher from the FDA as set forth in the Censa Merger Agreement, (ii) $109.0 million in development and regulatory milestones for each additional indication of sepiapterin, (iii) the achievement of certain net sales milestones up to an aggregate maximum amount of $160.0 million, (iv) a percentage of annual net sales during specified terms, ranging from single to low double digits of the applicable net sales threshold amount, and (v) any sublicense fees paid to the Company in consideration of any sublicense of Censa's intellectual property to commercialize sepiapterin, on a country-by-country basis, which contingent payment shall equal to a mid-double digit percentage of any such sublicense fees.

In February 2023, the Company completed enrollment of its Phase 3 placebo-controlled clinical trial for sepiapterin for PKU. In connection with this event and pursuant to the Censa Merger Agreement, the Company paid a $30.0 million development milestone to the former Censa securityholders during the year ended December 31, 2023. The Company elected to pay this milestone in the form of shares of its common stock, less certain cash payments in accordance with the Censa Merger Agreement. Pursuant to such election, the Company issued 657,462 shares of its common stock and paid $0.4 million to the former Censa securityholders.

In May 2024, the Company announced the validation and acceptance for review of an MMA for sepiapterin by the EMA for the treatment of PKU. Pursuant to the Censa Merger Agreement, the acceptance triggered a $15.0 million regulatory milestone to the former Censa securityholders. In July 2024, the Company announced the submission of an NDA to the FDA for sepiapterin for the treatment of pediatric and adult patients with PKU, including the full spectrum of ages and disease subtypes. Pursuant to the Censa Merger Agreement, the decision to submit the NDA triggered a $25.0 million regulatory milestone to the former Censa securityholders. In September 2024, the Company announced the FDA acceptance for filing of the NDA. Pursuant to the Censa Merger Agreement, the acceptance triggered a $25.0 million regulatory milestone to the former Censa securityholders. Together, the $65.0 million of regulatory milestones were paid

(In thousands except share and per share amount)

and recorded within research and development expense on the Company's consolidated statements of operations for the year ended December 31, 2024.

The Company also has the Tegsedi-Waylivra Agreement for the commercialization of Tegsedi and Waylivra, and products containing those compounds in countries in Latin America and the Caribbean. Akcea is entitled to receive royalty payments subject to certain terms set forth in the Tegsedi-Waylivra Agreement.

The Company has employment agreements with certain employees which require the funding of a specific level of payments, if certain events, such as a change in control or termination without cause, occur. Additionally, the Company has royalty payments associated with Translarna, Emflaza, and Upstaza net product revenue, payable quarterly or annually in accordance with the terms of the related agreements.

From time to time in the ordinary course of its business, the Company is subject to claims, legal proceedings and disputes. The Company is not currently aware of any material legal proceedings against it.

15. Segment and geographic information

The Company views its operations and manages its business in one operating segment: life science. The table below summarizes the significant expense categories for the life science segment regularly reviewed by the CODM for the years ended December 31, 2024, 2023, and 2022:

	Years Ended December 31,		
	2024	2023	2022
Total revenues	$ 806,780	$ 937,822	$ 698,801
Less:			
Cost of Product Sales	26,901	27,404	15,355
Program Spend	211,230	258,705	292,044
Employee Costs	251,184	334,305	298,716
Manufacturing Costs	64,120	86,641	108,032
Administrative Costs	72,420	70,531	68,001
Occupancy Costs	34,913	42,085	38,260
Milestones	65,000	30,000	—
Other segment items (a)	444,307	714,755	437,410
Segment Net Loss	$ (363,295)	$ (626,604)	$ (559,017)
Reconciliation of profit or loss			
Adjustments and reconciling items	—	—	—
Consolidated Net Loss	$ (363,295)	$ (626,604)	$ (559,017)

(a) Other segment items includes cost of goods sold ("COGS") amortization of intangible assets, COGS royalty, travel and expense, distribution costs, bad debt expense, finance costs, depreciation and amortization, contract labor costs, stock compensation expense, intangible impairment expense, change in the fair value of contingent consideration, interest expense, net, other income/expense, gain on the sale of the PRV, loss on extinguishment of debt, and income tax expense (benefit).

(In thousands except share and per share amount)

The following table presents financial information based on the geographic location of the facilities of the Company as of and for the years ended:

	Year Ended December 31, 2024		
	United States	Non-US	Total
Total assets	$ 1,343,234	$ 361,790	$ 1,705,024
Fixed assets, net	$ 59,748	$ 1,222	$ 60,970
Revenue	$ 413,044	$ 393,736	$ 806,780

	Year Ended December 31, 2023		
	United States	Non-US	Total
Total assets	$ 1,582,962	$ 312,736	$ 1,895,698
Fixed assets, net	$ 86,421	$ 668	$ 87,089
Revenue	$ 531,661	$ 406,161	$ 937,822

16. 401(k) plan

The Company maintains a 401(k) plan for its employees. Employee contributions are voluntary. The Company may match employee contributions in amounts to be determined at the Company's sole discretion. The Company provided an 100% matching contribution for up to the first 6% of each contributing employee's base salary contributions for the years ended December 31, 2024, 2023 and 2022, respectively. The Company made matching contributions to the 401(k) plan and recorded expense of approximately $7.3 million, $10.9 million, and $8.4 million for the years ended December 31, 2024, 2023 and 2022, respectively.

17. Intangible assets and goodwill

Definite-lived intangibles

Definite lived intangible assets consisted of the following at December 31, 2024 and 2023:

Definite-lived intangibles assets, gross	Ending Balance at December 31, 2023	Additions	Reclass from Indefinite Lived to Definite Lived	Foreign currency translation	Ending Balance at December 31, 2024
Emflaza	$ 527,417	$ —	$ —	$ —	$ 527,417
Waylivra	10,218	2,874	—	(695)	12,397
Tegsedi	13,322	5,936	—	(1,009)	18,249
Kebilidi	—	—	10,731	—	10,731
Upstaza	89,550	—	17,387	—	106,937
Total definite-lived intangibles, gross	$ 640,507	$ 8,810	$ 28,118	$ (1,704)	$ 675,731

(In thousands except share and per share amount)

Definite-lived intangibles assets, accumulated amortization	Ending Balance at December 31, 2023	Amortization	Foreign currency translation	Ending Balance at December 31, 2024
Emflaza	$ (478,618)	$ (48,799)	$ —	$ (527,417)
Waylivra	(3,965)	(1,602)	294	(5,273)
Tegsedi	(3,311)	(2,581)	283	(5,609)
Kebilidi	—	(112)	—	(112)
Upstaza	(10,882)	(7,644)	—	(18,526)
Total definite-lived intangibles, accumulated amortization	$ (496,776)	$ (60,738)	$ 577	$ (556,937)
Total definite-lived intangibles, net				$ 118,794

Marathon was entitled to receive contingent payments from the Company based on annual net sales of Emflaza beginning in 2018, up to a specified aggregate maximum amount over the expected commercial life of the asset, which expired February 2024. In accordance with the guidance for an asset acquisition, the Company recorded the milestone payments when they became payable to Marathon and increased the cost basis for the Emflaza rights intangible asset. As of December 31, 2024, the Emflaza rights intangible asset was fully amortized, therefore, milestones are recorded on the consolidated statement of operations within cost of product sales, excluding amortization of acquired intangible assets from February 2024 onward.

Akcea is also entitled to receive royalty payments subject to certain terms set forth in the Tegsedi-Waylivra Agreement related to sales of Waylivra and Tegsedi. In accordance with the guidance for an asset acquisition, the Company records royalty payments when they become payable to Akcea and increase the cost basis for the Waylivra and Tegsedi intangible assets, respectively. For the year ended December 31, 2024, royalty payments of $5.9 million and $2.9 million were recorded for Tegsedi and Waylivra, respectively. As of December 31, 2024, the royalties payable for Tegsedi and Waylivra were immaterial.

The Company received multiple approvals during the fourth quarter of 2024 related to PTC-AADC. In October 2024, the Company received regulatory approval for Upstaza in Brazil. In November 2024, the Company's BLA for its gene therapy treatment of AADC deficiency was approved by the FDA, and is marketed under the brand name Kebilidi. With these approvals, $10.7 million and $17.4 million for Kebilidi and Upstaza, respectively, was reclassified from the PTC-AADC indefinite lived intangible asset to definite lived intangible assets. The Company will amortize these allocated balances of $10.7 million and $17.4 million over its expected useful life of 12 years on a straight-line basis.

For the years ended December 31, 2024, 2023 and 2022, the Company recognized amortization expense of $60.7 million, $222.6 million, and $116.6 million respectively, related to the Emflaza rights, Waylivra, Tegsedi, and Upstaza/Kebilidi intangible assets.

(In thousands except share and per share amount)

The estimated future amortization of the Emflaza rights, Waylivra, Tegsedi, and Upstaza/Kebilidi intangible assets is expected to be as follows:

	As of December 31, 2024
2025	$ 14,374
2026	14,364
2027	14,364
2028	14,364
2029 and thereafter	61,328
Total	$ 118,794

The weighted average remaining amortization period of the definite-lived intangibles as of December 31, 2024 is 9.3 years.

Indefinite-lived intangibles

Indefinite lived intangible assets consisted of the following at December 31, 2024 and 2023:

Indefinite-lived intangibles assets	Ending Balance at December 31, 2023	Additions	Reclass from Indefinite Lived to Definite Lived	Priority Review Voucher Book Value Derecognized Upon Sale	Impairment	Ending Balance at December 31, 2024
PTC AADC (Upstaza and Kebilidi)	$ 235,766	$ —	$ (28,118)	$ (48,100)	$ (159,548)	$ —
Total indefinite-lived intangibles	$ 235,766	$ —	$ (28,118)	$ (48,100)	$ (159,548)	$ —
Total intangible assets, net						$ 118,794

In connection with the acquisition of the Company's gene therapy platform from Agilis, the Company acquired rights to Upstaza, for the treatment of AADC deficiency. AADC deficiency is a rare CNS disorder arising from reductions in the enzyme AADC that result from mutations in the dopa decarboxylase gene. In accordance with the acquisition method of accounting, the Company allocated the acquisition cost for the Agilis Merger to the underlying assets acquired and liabilities assumed, based upon the estimated fair values of those assets and liabilities at the date of acquisition. The Company classified the fair value of the acquired IPR&D as indefinite lived intangible assets until the successful completion or abandonment of the associated research and development efforts.

The Company performed an annual test for its PTC-AADC indefinite-lived intangible asset as of October 1, 2024 and recorded a partial impairment on the PTC-AADC indefinite lived intangible asset of $159.5 million, which is recorded as intangible asset impairment in the statement of operations. The impairment was related to a decrease in projected cash flows due to refinements in current market assumptions and the timing of patient treatments. To calculate the impairment amount, the Company utilized a discounted cash flow model under the income method, which primarily utilized Level 3 fair value inputs. The discount rate utilized in the discounted cash flow model was 15%, and the probability of success was 100% as the Company received regulatory approval in Brazil and the United States.

In connection with the Company's FDA approval of Kebilidi, the Company received a PRV. The Company sold the PRV for aggregate net proceeds of $150.0 million, excluding $2.0 million in broker fees which were recorded in accounts payable and accrued expenses on the consolidated balance sheet as of December 31, 2024. The Company had previously recorded an indefinite lived intangible asset for the PRV of $48.1 million in connection with its acquisition of Agilis in 2018, which was included as part of the book balance of the Company's PTC-AADC indefinite lived intangible asset. Accordingly, the Company derecognized the book value of the PRV and recorded a gain of $99.9 million upon the sale, which is recorded as gain on sale of priority review voucher on the consolidated statement of operations.

The Company reclassified the remaining $28.1 million from the PTC-AADC indefinite lived intangible asset to definite lived intangible assets as denoted above. As such, there is no remaining indefinite lived intangible asset balance as of December 31, 2024.

Goodwill

As a result of the Agilis Merger on August 23, 2018, the Company recorded $82.3 million of goodwill. There have been no changes to the balance of goodwill since the date of the Agilis Merger. Accordingly, the goodwill balance as of December 31, 2024 and 2023 was $82.3 million. The Company performed an annual impairment test for goodwill as of October 1, 2024. The Company's single reporting unit had a negative carrying value and thus the Company determined there was no impairment of goodwill.

18. Subsequent events

In January 2025, the transaction contemplated by the Novartis Agreement closed, upon which the Company received an upfront payment of $1.0 billion. The Company may also be entitled to receive up to $1.9 billion in development, regulatory and sales milestones and tiered double-digit royalties on ex-U.S. sales. The Company will also share U.S. profits and losses, with 40% share to the Company and 60% share to Novartis. Pursuant to the Novartis Agreement, the Company will continue to conduct the ongoing Phase 2A Clinical Trial and the ongoing OLE Clinical Trial pursuant to its existing development plan, with the goal of transitioning the ongoing OLE Clinical Trial to Novartis within 12 months after the effective date of the Novartis Agreement. Novartis will be responsible for all other development of licensed compounds and licensed products and the manufacture and commercialization of licensed compounds and licensed products worldwide.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer (principal executive officer) and Chief Financial Officer (principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024. The term "disclosure controls and procedures", as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2024, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for our company. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's 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 GAAP and includes those policies and procedures that: (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 our company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our company's assets that could have a material effect on the financial statements.

Internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements prepared for external purposes in accordance with generally accepted accounting principles. 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.

Our management, with the participation of our Chief Executive Officer (principal executive officer) and Chief Financial Officer (principal financial officer), assessed the effectiveness of our internal control over financial reporting as of December 31, 2024. In making this assessment, our management used the criteria set forth in the *Internal Control—Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2024 based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2024, has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which appears herein.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting occurred during the quarter ended December 31, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of PTC Therapeutics, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited PTC Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2024, 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, PTC Therapeutics, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, 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 accompanying consolidated balance sheets of the Company as of December 31, 2024 and 2023, the related consolidated statements of operations, comprehensive loss, stockholders' equity/(deficit) and cash flows for each of the three years in the period ended December 31, 2024, and the related notes and our report dated February 27, 2025 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 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

Iselin, New Jersey
February 27, 2025

Item 9B. Other Information.

Director and Officer Trading Arrangements

A portion of the compensation of our directors and officers (as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) is in the form of equity awards and, from time to time, directors and officers engage in open-market transactions with respect to the securities acquired pursuant to such equity awards or other Company securities, including to satisfy tax withholding obligations when equity awards vest or are exercised, and for diversification or other personal reasons.

Transactions in Company securities by directors and officers are required to be made in accordance with our insider trading policy, which requires that the transactions be in accordance with applicable U.S. federal securities laws that prohibit trading while in possession of material nonpublic information. Rule 10b5-1 under the Exchange Act provides an affirmative defense that enables directors and officers to prearrange transactions in Company securities in a manner that avoids concerns about initiating transactions while in possession of material nonpublic information.

The following table describes, for the quarterly period covered by this report, each trading arrangement for the sale or purchase of Company securities adopted or terminated by our directors and officers that is either (1) a contract, instruction or written plan for the purchase or sale of the Company's securities intended to satisfy the affirmative defense conditions of Rule 10b5-1(c), or a "Rule 10b5-1 trading arrangement", or (2) a "non-Rule 10b5-1 trading arrangement" (as defined in Item 408(c) of Regulation S-K):

Name (Title)	Action Taken (Date of Action)	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Arrangement	Aggregate Number of Securities
Mark Boulding (Chief Legal Officer)	Adoption (December 5, 2024)	Rule 10b5-1 trading arrangement	Sale	Until March 3, 2026 or such earlier date upon which all transactions are completed.	Up to 207,636 shares
Eric Pauwels (Chief Business Officer)	Adoption (December 13, 2024)	Rule 10b5-1 trading arrangement	Sale	Until May 30, 2025, or such earlier date upon which all transactions are completed.	Up to 110,799 shares
Neil Almstead (Chief Technical Operations Officer)	Adoption (December 10, 2024)	Rule 10b5-1 trading arrangement	Sale	Until March 31, 2026, or such earlier date upon which all transactions are completed	Up to 396,436 shares

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item as set forth under the captions "Proposal 1—Election of Directors", "Executive Officers", "Delinquent Section 16(a) Reports", "Corporate Governance—Code of Conduct", "Corporate Governance—Director Nominations", "Corporate Governance—Board Committees and Audit Committee", Corporate Governance—Insider Trading Policy" and "Stockholder Proposals and Nominations for Director" in our Proxy Statement for the 2025 Annual Meeting of Shareholders is incorporated in this Annual Report on Form 10-K by reference.

Code of Ethics

We have adopted a written Code of Business Conduct and Ethics, which is a code of ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a current copy of the Code of Business Conduct and Ethics on the Corporate Governance page of the Investors section of our website, *www.ptcbio.com*, and it is available in print to any person who requests it. We intend to post on our website all disclosures that are required by applicable law, the rules of the Securities and Exchange Commission or the Nasdaq Global Select Market concerning any amendment to, or waiver from, any provision of the Code of Business Conduct and Ethics.

Item 11. Executive Compensation

The information required by this item (other than the information required by Item 402(v) of Regulation S-K) as set forth in under the captions "Executive Compensation", "2024 Director Compensation", "Corporate Governance—Risk Oversight" and "Corporate Governance—Compensation Committee Interlocks and Insider Participation" in our Proxy Statement for the 2025 Annual Meeting of Shareholders is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item as set forth under the captions "Equity Compensation Plan Information" and "Principal Stockholders" in our Proxy Statement for the 2025 Annual Meeting of Shareholders is incorporated in this Annual Report on Form 10-K by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item as set forth under the captions "Corporate Governance—Policies and Procedures for Related Person Transactions", "Corporate Governance—Related Person Transactions", and "Corporate Governance—Director Independence" in our Proxy Statement for the 2025 Annual Meeting of Shareholders is incorporated in this Annual Report on Form 10-K by reference.

Item 14. Principal Accountant Fees and Services

The information required by this item as set forth under the caption "Proposal 2—Ratification of Election of Independent Registered Public Accounting Firm" in our Proxy Statement for the 2025 Annual Meeting of Shareholders is incorporated in this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

Financial Statements

The following statements and supplementary data are included in Part II, Item 8. of the Annual Report on Form 10-K.

- Reports of independent registered public accounting firm
- Consolidated Balance Sheets as of December 31, 2024 and 2023
- Consolidated Statements of Operations for the years ended December 31, 2024, 2023 and 2022
- Consolidated Statements of Comprehensive Loss for the years ended December 31, 2024, 2023 and 2022
- Consolidated Statements of Stockholders' Equity (Deficit) for the years ended December 31, 2024, 2023 and 2022
- Consolidated Statements of Cash Flows for the years ended December 31, 2024, 2023 and 2022
- Notes to Consolidated Financial Statements

Exhibits

Those exhibits required to be filed by Item 601 of Regulation S-K are listed in the Exhibit Index immediately preceding the exhibits hereto and such listing is incorporated herein by reference.

Exhibit Index

Exhibit Number	Description of Exhibit
2.1	Asset Purchase Agreement, dated March 15, 2017, between PTC Therapeutics, Inc. and Complete Pharma Holdings, LLC (f/k/a Marathon Pharmaceuticals, LLC) (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K filed by the Registrant on March 16, 2017)
2.2	Amendment to Asset Purchase Agreement, dated April 20, 2017, between PTC Therapeutics, Inc. and Complete Pharma Holdings, LLC (f/k/a Marathon Pharmaceuticals, LLC) (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K filed by the Registrant on April 20, 2017)
2.3†	Agreement and Plan of Merger, dated July 19, 2018, by and among PTC Therapeutics, Inc., Agility Merger Sub, Inc., Agilis Biotherapeutics, Inc. and, solely in its capacity as equityholder representative, Shareholder Representative Services LLC (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K filed by the Registrant on July 19, 2018)
2.4*	Asset Purchase Agreement by and between PTC Therapeutics, Inc. and BioElectron Technology Corporation, dated October 1, 2019 (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K filed by the Registrant on October 30, 2019)
2.5*	Agreement and Plan of Merger, dated May 5, 2020, by and among PTC Therapeutics, Inc., Hydro Merger Sub, Inc., Censa Pharmaceuticals Inc. and, solely in its capacity as securityholder representative, Shareholder Representative Services LLC (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K filed by the Registrant on May 6, 2020)

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant, as amended (incorporated by reference to Exhibit 3.1 to the Quarterly Report on Form 10-Q filed by the Registrant on July 29, 2021)
3.2	Amended and Restated Bylaws of the Registrant, effective December 5, 2022 (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed by the Registrant on December 6, 2022)
4.1	Description of Registered Securities (incorporated by reference to Exhibit 4.1 to the Annual Report on Form 10-K filed by the Registrant on February 22, 2022)
4.2	Specimen Stock Certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
4.3	Indenture (including Form of Notes), dated as of September 20, 2019, by and between PTC Therapeutics, Inc. and U.S. Bank National Association, a national banking association, as trustee (incorporated by reference to Exhibit 4.1 to the Current Report on Form 8-K filed by the Registrant on September 20, 2019)
10.1+	PTC Therapeutics, Inc. Amended and Restated 2013 Long-Term Incentive Plan (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed by the Registrant on June 9, 2022)
10.2+	Form of Nonqualified Stock Option Agreement Inducement Grant Agreement—2014-2022 (incorporated by reference to Exhibit 10.14 to the Annual Report on Form 10-K filed by the Registrant on March 2, 2015)
10.3+	Form of Incentive Stock Option Agreement under 2013 Long Term Incentive Plan—2014-2022 (incorporated by reference to Exhibit 10.15 to the Annual Report on Form 10-K filed by the Registrant on March 2, 2015)
10.4+	Form of Nonstatutory Stock Option Agreement under 2013 Long Term Incentive Plan—2014-2022 (incorporated by reference to Exhibit 10.16 to the Annual Report on Form 10-K filed by the Registrant on March 2, 2015)
10.5+	Form of Nonstatutory Stock Option Agreement under 2013 Long Term Incentive Plan—Non-employee Director (incorporated by reference to Exhibit 10.31 to the Annual Report on Form 10-K filed by the Registrant on February 29, 2016)
10.6+	Form of Restricted Stock Unit Agreement under 2013 Long Term Incentive Plan —2016-2022 (incorporated by reference to Exhibit 10.32 to the Annual Report on Form 10-K filed by the Registrant on February 29, 2016)
10.7+	Form of Restricted Stock Agreement under 2013 Long Term Incentive Plan —2017-2022 (incorporated by reference to Exhibit 10.19 to the Annual Report on Form 10-K filed by the Registrant on March 16, 2017)
10.8+	Form of Nonqualified Restricted Stock Award Agreement Inducement Grant Agreement-2018 (incorporated by reference to Exhibit 99.3 to the Registration Statement on Form S-8 (File No. 333-229126), of the Registrant)
10.9+	Form of Incentive Stock Option Agreement under Amended and Restated 2013 Long Term Incentive Plan (incorporated by reference to Exhibit 10.18 to the Annual Report on Form 10-K filed by the Registrant on February 21, 2023)
10.10+	Form of Nonstatutory Stock Option Agreement under Amended and Restated 2013 Long Term Incentive Plan (incorporated by reference to Exhibit 10.19 to the Annual Report on Form 10-K filed by the Registrant on February 21, 2023)

Exhibit Number	Description of Exhibit
10.11+	Form of Nonstatutory Stock Option Agreement under Amended and Restated 2013 Long Term Incentive Plan—Non-employee Director (incorporated by reference to Exhibit 10.20 to the Annual Report on Form 10-K filed by the Registrant on February 21, 2023)
10.12+	Form of Restricted Stock Unit Agreement under Amended and Restated 2013 Long Term Incentive Plan (incorporated by reference to Exhibit 10.21 to the Annual Report on Form 10-K filed by the Registrant on February 21, 2023)
10.13+	Amended and Restated Employment Agreement between the Registrant and Mark E. Boulding (incorporated by reference to Exhibit 10.22 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.14+	Amended and Restated Employment Agreement between the Registrant and Neil Almstead (incorporated by reference to Exhibit 10.24 to the Registration Statement on Form S-1, as amended (File No. 333-188657), of the Registrant)
10.15†	Amended and Restated Exclusive License and Supply Agreement, dated June 2, 2023, by and between PTC Therapeutics, Inc. and Faes Farma, S.A. (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on August 8, 2024)
10.16†	Commercial Manufacturing Agreement, dated as of September 18, 2015, as amended, by and between Alcami Corporation (f/k/a/ AAI Pharma Services Corp.) and Complete Pharma Holdings, LLC (f/k/a Marathon Pharmaceuticals, LLC), as assigned by Complete Pharma Holdings, LLC to the Registrant on April 20, 2017 (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed by the Registrant on May 3, 2022)
10.17+	Employment Agreement, as amended, between the Registrant and Christine Utter (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed by the Registrant on August 6, 2019)
10.18†	License and Technology Transfer Agreement, dated December 23, 2015, by and among National Taiwan University, Professor Wuh-Lian(Paul) Hwu and Agilis Biotherapeutics, Inc. (formerly Agilis Biotherapeutics, LLC) (incorporated by reference to Exhibit 10.3 on Form 10-Q filed by the Registrant on November 5, 2018)
10.19*	License and Technology Transfer Agreement Amendment No. 2, dated December 1, 2019, by and among National Taiwan University, Professor Wu-Lian (Paul) Hwu and PTC Therapeutics GT, Inc. (incorporated by reference to Exhibit 10.42 on Form 10-K filed by the Registrant on March 2, 2020)
10.20†	Collaboration and License Agreement, dated August 1, 2018, by and between PTC Therapeutics International Limited and Akcea Therapeutics, Inc. (incorporated by reference to Exhibit 10.3 on Form 10-Q filed by the Registrant on November 5, 2018)
10.21	Amended and Restated 2016 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed by the Registrant on June 9, 2021)
10.22+	2020 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 99.3 to the Registration Statement on Form S-8 (File No. 333-235823), of the Registrant)
10.23+	Form of Inducement Option Agreement under the 2020 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 99.4 to the Registration Statement on Form S-8 (File No. 333-235823), of the Registrant)

Exhibit Number	Description of Exhibit
10.24+	Form of Inducement Restricted Stock Agreement under the 2020 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 99.5 to the Registration Statement on Form S-8 (File No. 333-235823), of the Registrant)
10.25+	Amendment No. 1 to 2020 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 99.3 to the Registration Statement on Form S-8 (File No. 333-251878) of the Registrant)
10.26+	Amendment No. 2 to 2020 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 99.1 to Post-Effective Amendment No. 1 to the Registration Statement on Form S-8 (File No. 333-251878) of the Registrant)
10.27+	Amendment No. 3 to 2020 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 99.4 to the Registration Statement on Form S-8 (File No. 333-268851), of the Registrant)
10.28*	License Agreement dated as of February 8, 2016, as amended, by and between Shiratori Pharmaceutical Co. Ltd. and Censa Pharmaceuticals Inc. (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on August 5, 2020)
10.29+	Amended and Restated Employment Agreement between the Registrant and Matthew Klein (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed by the Registrant on April 18, 2023)
10.30+	Employment Agreement, as amended, between the Registrant and Eric Pauwels (incorporated by reference to Exhibit 10.4 to the Quarterly Report on Form 10-Q filed by the Registrant on August 5, 2020)
10.31*	Rights Exchange Agreement, by and among PTC Therapeutics, Inc., the Rightholders set forth therein, and, for the limited purposes set forth therein, Shareholder Representatives Services LLC, dated as of April 29, 2020 (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed by the Registrant on April 30, 2020)
10.32	At the Market Offering Sales Agreement, dated August 7, 2019, among PTC Therapeutics, Inc., Cantor Fitzgerald & Co. and RBC Capital Markets, LLC (incorporated by reference to Exhibit 1.1 to the Current Report on Form 8-K filed by the Registrant on August 7, 2019)
10.33*	Lease Agreement dated May 24, 2022, between Warren CC Acquisitions, LLC and PTC Therapeutics, Inc. (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on August 4, 2022)
10.34*	First Amendment to Lease Agreement, dated December 31, 2024, between Warren CC Acquisitions, LLC and PTC Therapeutics, Inc.**
10.35	Irrevocable Transferable Standby Letter of Credit, dated June 22, 2022, issued by HSBC Bank USA, N.A. in favor of Warren CC Acquisitions LLC c/o Vision Real Estate Partners for the Account of PTC Therapeutics, Inc. (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed by the Registrant on August 4, 2022)
10.36	Amendment, dated February 14, 2025, to Irrevocable Transferable Standby Letter of Credit, dated June 22, 2022, issued by HSBC Bank USA, N.A. in favor of Warren CC Acquisitions LLC c/o Vision Real Estate Partners for the Account of PTC Therapeutics, Inc.**
10.37*	Letter Agreement re: Collaboration and License Agreement, dated July 25, 2022, by and between Akcea Therapeutics, Inc. and PTC Therapeutics International Limited (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on October 27, 2022)

Exhibit Number	Description of Exhibit
10.38*	Letter Agreement re: Collaboration and License Agreement, dated September 14, 2022, by and between Akcea Therapeutics, Inc. and PTC Therapeutics International Limited (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on October 27, 2022)
10.39†	License and Collaboration Agreement, dated as of November 23, 2011, as amended, by and among the Registrant, F. Hoffmann-La Roche Ltd and Hoffmann-La Roche, Inc. and Spinal Muscular Atrophy Foundation (incorporated by reference to Exhibit 10.14 to the Registration Statement on Form S-1, as amended (File No. 333 188657), of the Registrant)
10.40*	Sponsored Research Agreement, as amended dated as of June 1, 2006, by and between the Registrant and Spinal Muscular Atrophy Foundation (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on April 27, 2023)
10.41*	Amendment No. 5 to License Agreement dated April 28, 2023 by and between Shiratori Pharmaceutical Co. Ltd. and PTC Therapeutics MP, Inc. (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on August 3, 2023)
10.42+	Employment Agreement between PTC Therapeutics, Inc. and Pierre Gravier (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed by the Registrant on July 17, 2023)
10.43+	Employment Agreement between PTC Therapeutics, Inc. and Lee Golden (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on April 25, 2024)
10.44*	Amended and Restated Royalty Purchase Agreement, dated as of October 18, 2023, among the Registrant, Royalty Pharma Investments 2019 ICAV, and solely for the purposes of Section 5.15 thereof, Royalty Pharma plc (incorporated by reference to Exhibit 10.48 to the Annual Report on Form 10-K filed by the Registrant on February 29, 2024)
10.45*	Amendment No. 1 to Amended and Restated Royalty Purchase Agreement and First Put Option Exercise Agreement, dated June 17, 2024, by and among PTC Therapeutics, Inc., Royalty Pharma Investments 2019 ICAV, and Royalty Pharma plc (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed by the Registrant on August 8, 2024)
10.46*	Asset Purchase Agreement, dated November 26, 2024, by and between the Buyer and PTC Therapeutics, Inc.**
10.47*	License and Collaboration Agreement, dated as of November 27, 2024, among PTC Therapeutics, Inc., PTC Therapeutics HD, Inc. and Novartis Pharmaceuticals Corporation**
19.1	Insider Trading Policy of the Registrant**
21.1	Subsidiaries of the Registrant**
23.1	Consent of Independent Registered Public Accounting Firm**
24.1	Power of attorney (included on the signature page to this Form 10-K)
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**

Exhibit Number	Description of Exhibit
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002**
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002**
97.1	PTC Therapeutics, Inc. Clawback Policy (incorporated by reference to Exhibit 97.1 to the Annual Report on Form 10-K filed by the Registrant on February 29, 2024)
101.INS	Inline XBRL Instance Document**
101.SCH	Inline XBRL Taxonomy Extension Schema Document**
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document**
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Database**
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document**
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document**
104	Cover Page Interactive Data File (formatted Inline XBRL and contained in Exhibit 101)

† Confidential treatment has been granted for certain portions that are omitted from this exhibit. The omitted information has been filed separately with the U.S. Securities and Exchange Commission (the "SEC") pursuant to the registrant's application for confidential treatment. In addition, schedules have been omitted from this exhibit pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule will be furnished supplementally to the SEC upon request; provided, however, that the registrant may request confidential treatment for any document so furnished.

+ Management contract, compensatory plan or arrangement.

* Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

** Submitted electronically herewith.

Stockholders may obtain (without charge) a copy of this Annual Report on Form 10-K (including the financial statements and financial statement schedules) and a copy of any exhibit thereto (upon payment of a fee limited to our reasonable expenses in furnishing such exhibit) by writing to PTC Therapeutics, Inc., 500 Warren Corporate Center Drive, Warren, New Jersey 07059.

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, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

PTC THERAPEUTICS, INC.

Date: February 27, 2025

By: /s/ MATTHEW B. KLEIN, M.D.
Matthew B. Klein, M.D.
Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

We, the undersigned officers and directors of PTC Therapeutics, Inc., hereby severally constitute and appoint Matthew B. Klein and Mark E. Boulding, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Dated: February 27, 2025

By: /s/ MATTHEW B. KLEIN, M.D.
Matthew B. Klein, M.D.
Chief Executive Officer and Director
(Principal Executive Officer)

Dated: February 27, 2025

By: /s/ PIERRE GRAVIER
Pierre Gravier
Chief Financial Officer
(Principal Financial Officer)

Dated: February 27, 2025

By: /s/ CHRISTINE UTTER
Christine Utter
Chief Accounting Officer
(Principal Accounting Officer)

Dated: February 27, 2025

By: /s/ MICHAEL SCHMERTZLER
Michael Schmertzler
Director

Dated: February 27, 2025

By: /s/ ALLAN JACOBSON
Allan Jacobson
Director

Dated: February 27, 2025

By: /s/ STEPHANIE S. OKEY
Stephanie S. Okey

Director

Dated: February 27, 2025 By: /s/ EMMA REEVE
Emma Reeve
Director

Dated: February 27, 2025 By: /s/ MARY SMITH
Mary Smith
Director

Dated: February 27, 2025 By: /s/ DAVID P. SOUTHWELL
David P. Southwell
Director

Dated: February 27, 2025 By: /s/ GLENN D. STEELE
Glenn D. Steele
Director

Dated: February 27, 2025 By: /s/ ALETHIA YOUNG
Alethia Young
Director

Dated: February 27, 2025 By: /s/ JEROME B. ZELDIS
Jerome B. Zeldis
Director

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Board of Directors

Michael Schmertzler
Chairman

Matthew B. Klein, M.D., M.S., FACS
Chief Executive Officer, PTC Therapeutics

Allan Jacobson, Ph.D.
University of Massachusetts Chan Medical School

Stephanie S. Okey, M.S.
Former SVP, Head of North America, Rare Disease – Genzyme

Emma Reeve
Independent Board Director

Mary L. Smith
The VENG Group

David P. Southwell
Former CEO, TScan Therapeutics

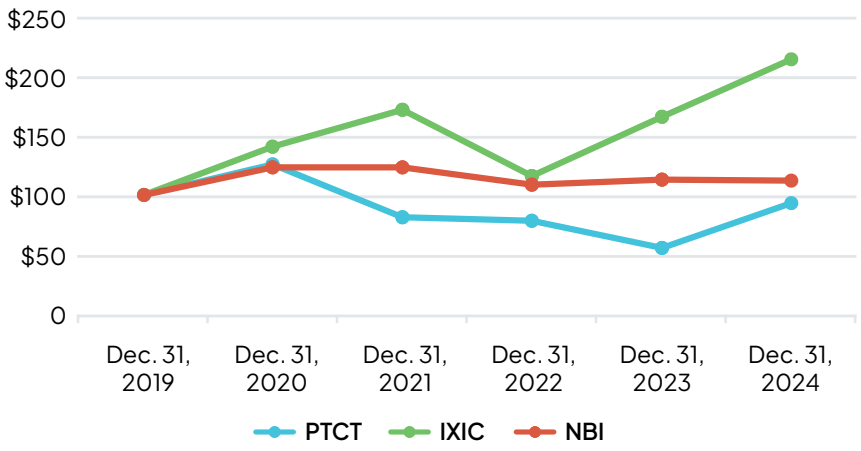
Glenn D. Steele, Jr., M.D., Ph.D.
Chairman, GSteele Health Solutions

Alethia Young
Chief Financial Officer, Bicycle Therapeutics

Jerome B. Zeldis, M.D., Ph.D.
Independent Board Director

Stock Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return on the Common Stock of PTC Therapeutics' Stock from investing on Jan 1, 2020 through Dec 31, 2024 in two indices: The NASDAQ Biotechnology Index (NBI) and the NASDAQ Composite Index (IXIC). Data for the NASDAQ Biotechnology Index (NBI) and the NASDAQ Composite Index (IXIC) assume reinvestment of dividends. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



** The information contained in this Stock Performance Graph shall not be deemed "soliciting material" or to be "filed" with the SEC, for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any filing of under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing.*

	Dec. 31, 2019	Dec. 31, 2020	Dec. 31, 2021	Dec. 31, 2022	Dec. 31, 2023	Dec. 31, 2024
PTCT	$100	$127	$83	$79	$57	$94
IXIC	$100	$144	$174	$117	$167	$215
NBI	$100	$126	$125	$111	$115	$114

Executive Committee

Matthew B. Klein, M.D., M.S., FACS
Chief Executive Officer

Neil Almstead, Ph.D.
Chief Technical Operations Officer

John Baird, Ph.D.
Chief of Staff to the CEO

Mark E. Boulding
Executive Vice President and Chief Legal Officer

Lee Golden, M.D.
Chief Medical Officer

Pierre Gravier
Chief Financial Officer

Mary Frances Harmon
Senior Vice President, Corporate and Patient Relations

Linda Montella-Carter
Senior Vice President and Chief Information Officer

Eric Pauwels
Chief Business Officer

Hege Sollie-Zetlmayer
Chief Human Resources Officer

Christine Utter
Senior Vice President, Chief Accounting Officer and Head of People Services

Stockholder Information

Market Information
PTC's common stock trades on the Nasdaq Global Select Market under the ticker symbol PTCT.

Global Corporate Headquarters
PTC Therapeutics, Inc.
500 Warren Corporate Center Drive
Warren, NJ 07059

International Headquarters
PTC Therapeutics International Limited
Unit 1, 52–55 Sir John Rogerson's Quay
Dublin 2, D02 NA07 Ireland

Annual Meeting
The Annual Meeting of the Stockholders will be held on Tuesday, June 17, 2025 at 9 a.m. ET. The meeting will be held in a virtual format via live webcast. There will not be a physical meeting location and Stockholders will not be able to attend the Annual Meeting in person.

Transfer Agent
Equiniti Trust Company, LLC
55 Challenger Road 2nd floor
Ridgefield Park, NJ 07660
Attn: Shareholder Services Department

Independent Registered Public Accounting Firm
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