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, 2021

or

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

For the transition period from _____ to _____

Commission file number: 001-40880

XERIS BIOPHARMA HOLDINGS, INC.

(Exact name of the registrant as specified in its charter)

Delaware	**87-1082097**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
180 N. LaSalle Street, Suite 1600 Chicago, Illinois	**60601**
(Address of principal executive offices)	(Zip Code)

(844) 445-5704

(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, $0.0001 par value per share	**XERS**	**The 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 by Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the 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. ☐

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

As of June 30, 2021, the aggregate market value of the Registrant's common stock held by non-affiliates of the Registrant was approximately $266.0 million based on the closing sales price as reported on the Nasdaq Exchange.

As of February 28, 2022, 135,523,511 shares, par value $0.0001 per share, of common stock were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates certain information by reference from the Registrant's Definitive Proxy Statement to be filed with the Commission in connection with the Registrant's 2022 Annual Meeting of Shareholders. Such Definitive Proxy Statement will be filed not later than 120 days after the conclusion of the Registrant’s fiscal year ended December 31, 2021.

Summary of the Material Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties that you should be aware of in evaluating our business. These risks include, but are not limited to, the following:

- Our business may be adversely affected by the ongoing coronavirus pandemic.
- As a company, we have a limited operating history and limited experience commercializing pharmaceutical products and have incurred significant losses since inception. We expect to incur losses over the next few years and may not be able to achieve or sustain revenues or profitability in the future.
- Although we generate revenue from Gvoke, Keveyis and Recorlev, we have not yet generated revenue from any of our current or future product candidates, and may never be profitable.
- We may require additional capital to sustain our business, and this capital may cause dilution to our stockholders and might not be available on terms favorable to us, or at all, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.
- Our business depends entirely on the commercial success of our products and product candidates. Even if approved, our product candidates may not be accepted in the marketplace and our business may be materially harmed.
- If we are unable to establish or do not maintain sufficient marketing, sales and distribution capabilities or enter into agreements with third parties to market, sell and distribute our products on terms acceptable to us, we may not be able to generate product revenues and our business, results of operations, and financial condition will be materially adversely affected.
- Our reliance on third-party suppliers, including single-source suppliers, and a limited number of options for alternate sources for Gvoke, Keveyis, and Recorlev or our product candidates could harm our ability to develop our product candidates or to commercialize Gvoke, Keveyis, Recorlev or any product candidates that are approved.
- Reimbursement decisions by third-party payors and consolidation within the healthcare industry and among competitors more generally may have an adverse effect on pricing and market acceptance. If there is not sufficient reimbursement for our products, it is less likely that they will be widely used and pricing pressure may impact our ability to sell our products at prices necessary to support our current business strategies.
- Clinical failure may occur at any stage of clinical development, and the results of our clinical trials may not support our proposed indications for our product candidates. If our clinical trials fail to demonstrate efficacy and safety to the satisfaction of the FDA or other regulatory authorities, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate.
- Gvoke, Keveyis, Recorlev and our product candidates may have undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require them to include safety warnings, require them to be taken off the market or otherwise limit their sales.
- Our failure to successfully identify, develop and market additional product candidates, or acquire additional product candidates or enter into collaborations or other commercial agreements could impair our ability to grow.
- We operate in a competitive business environment and, if we are unable to compete successfully against our existing or potential competitors, our sales and operating results may be negatively affected and we may not successfully commercialize our products or product candidates, even if approved.
- Our success depends on our ability to protect our intellectual property and proprietary technology, as well as the ability of our collaborators to protect their intellectual property and proprietary technology.
- We may not be able to successfully integrate and combine the businesses of Xeris and Strongbridge following the completion of the Transactions and we may not realize the anticipated benefits from the Transactions.
- Our stock price has been and will likely continue to be volatile, and you may not be able to resell shares of our common stock at or above the price you paid.

The summary risk factors described above should be read together with the text of the full risk factors below in the section entitled “Risk Factors” and the other information set forth in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes, as well as in other documents that we file with the U.S. Securities and Exchange Commission. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

XERIS BIOPHARMA HOLDINGS, INC.

Index to Annual Report on Form 10-K
Year Ended December 31, 2021

Solely for convenience, the trademarks and trade names in this Annual Report on Form 10-K (this “Annual Report”) are referred to without the ® and ™ symbols, but absence of such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. The trademarks, trade names and service marks appearing in this Annual Report are the property of their respective owners.

Cautionary Statements for Forward-Looking Information

This Annual Report on Form 10-K contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the rate and degree of market acceptance and clinical utility of Gvoke, Keveyis and Recorlev;
- the pricing and reimbursement of Gvoke, Keveyis and Recorlev or any of our product candidates, if approved;
- the effect of uncertainties related to the current coronavirus pandemic, or any other health epidemic, on U.S. and global markets, our business, financial condition, operations, third-party suppliers or the global economy as a whole;
- our estimates regarding the market opportunities for Gvoke, Keveyis and Recorlev and our product candidates;
- the commercialization, marketing and manufacturing of Gvoke, Keveyis and Recorlev and our product candidates, if approved;
- our ability to manufacture, or the ability of third parties to deliver, sufficient quantities of components and drug product for commercialization of Gvoke, Keveyis and Recorlev or any of our product candidates, if approved;
- our expectations related to the anticipated launch of Ogluo in certain European countries;
- the rate and degree of market acceptance and clinical utility of any of our product candidates for which we receive marketing approval in the future;
- the initiation, timing, progress and results of our research and development programs and future preclinical and clinical studies;
- our ability to advance any other product candidates into, and successfully complete, clinical studies and obtain regulatory approval for them;
- our ability to identify additional product candidates;
- the implementation of our strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to use the proceeds of our public offerings and borrowings in ways that increase the value of your investment;
- our expectations related to the use of proceeds from our public offerings and borrowings and estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to maintain and establish collaborations;
- our financial performance;
- our ability to effectively manage our anticipated growth;
- developments relating to our competitors and our industry, including the impact of government regulation; and
- other risks and uncertainties, including those listed under the section entitled "Risk Factors" (refer to Part 1, Item 1A, of this Annual Report on Form 10-K).

In some cases, forward-looking statements can be identified by terminology such as "will," "would," "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" and terms of similar meaning. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section entitled "Risk Factors". If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance.

While we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for Gvoke, Keveyis and Recorlev and our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

PART I

ITEM 1. BUSINESS

Overview

We are a biopharmaceutical company committed to developing and commercializing innovative solutions to enhance the lives of people with life-threatening diseases. Our primary focus is on therapies for patient populations in endocrinology, neurology, and gastroenterology. We currently have three commercially available products, Gvoke, a ready-to-use liquid glucagon for the treatment of severe hypoglycemia, Keveyis, the first and only U.S. Food and Drug Administration ("FDA") approved therapy for primary periodic paralysis ("PPP") and Recorlev, approved by the FDA in December 2021 for the treatment of endogenous hypercortisolemia in adult patients with Cushing's Syndrome. We also have a pipeline of development programs to extend our current marketed products into new indications and uses or bring new products forward using our proprietary formulation technology platforms, XeriSol™ and XeriJect™.

Commercial Products

Our number one priority is maximizing the commercial potential of our three commercial products: Gvoke, Keveyis and Recorlev.

- *Gvoke (Gvoke HypoPen, Gvoke PFS, Gvoke Kit)* is the first ready-to-use liquid stable glucagon for severe hypoglycemia. The product is indicated for use in pediatric and adult patients with diabetes age 2 years and above and can be administered in 2 simple steps. The estimated total addressable market for this therapy is approximately $4.0 billion in the United States.

  Throughout this document, unless otherwise noted, references to Gvoke include Gvoke PFS, Gvoke HypoPen, Gvoke Kit and Ogluo.

- *Keveyis* is the first and only therapy approved in the United States to treat hyperkalemic, hypokalemic, and related variants of PPP. PPP is a rare genetic, neuromuscular disorder that can cause extreme muscle weakness and/or paralysis; some forms are also commonly associated with myotonia or muscle stiffness. The estimated total addressable market for this therapy is greater than $0.5 billion in the United States.

- *Recorlev* is a cortisol synthesis inhibitor proved for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative. Endogenous Cushing's syndrome is a rare but serious and potentially fatal endocrine disease caused by chronic elevated cortisol exposure. The estimated total addressable market for this therapy is approximately $2.0 billion in the United States. Recorlev was approved by FDA on December 30, 2021 and launched in the United States in January 2022.

Our pipeline

The following table summarizes key information about our internal products and product candidates.

Product Candidate	Indication	Development Stage
		Preclinical / Phase 1 / Phase 2 / Phase 3 / NDA Submitted / Marketed
Gvoke® (US)	Severe Hypoglycemia	Marketed
Keveyis®	Primary Periodic Paralysis†	Marketed
Recorlev®	Endogenous Cushing's syndrome†	Marketed
Ogluo® (EU)	Severe Hypoglycemia	Available in UK*
Self-Administered Glucagon for prevention	Exercise-Induced Hypoglycemia	Phase 2
Levothyroxine	Endocrinology: Hypothyroidism	Phase 1
XP-9164	Gastroenterology	Phase 1

† Orphan Drug Designation

* Through Tetris Pharma

Our Strategy

Our goal is to build a leading and profitable biopharmaceutical company that innovates products that transform the lives of people with life-threatening diseases. To achieve our goal, we are pursuing the following strategies:

- ***Maximize the commercial potential of our three commercial products.*** We have built out a robust endocrinology and rare disease-focused commercial infrastructure – including fully operational patient and provider support teams – primed to bring the benefits of our products to a wider range of patients with unmet needs. Our sales, marketing, market access and patient service capabilities in the United States are positioned to drive the growth of our products. We believe that our ability to execute on this strategy is enhanced by the significant commercial experience of key members of our management team.
- ***Create momentum through commercial execution leading to profitability.*** We have three innovative commercial assets: Gvoke, Keveyis and Recorlev. Gvoke and Keveyis are growing in large untapped addressable markets. We are executing a rapid launch of Recorlev, leveraging our experienced, endocrinology-focused commercial infrastructure, in a large and unsatisfied Cushing Syndrome marketplace. Through the momentum created by the execution of our three commercial products, we believe we will have a path to profitability.
- ***Continue to leverage our technology and expertise to develop a portfolio of product candidates.*** We have an extensive pipeline of development programs to extend the current marketed products into important new indications and uses, and bring new products forward using our formulation technology platforms, supporting long-term product development and commercial success. XeriSol and XeriJect have broad application and have the potential to be utilized across a range of potential product candidates in endocrinology, neurology and other therapeutic areas.
- ***Collaborate with pharmaceutical and biotechnology companies to apply our technology platforms to enhance the formulations of their proprietary products and candidates***. We are pursuing formulation and development partnerships to apply our XeriSol and XeriJect technology platforms to broaden our revenue stream and enhance the formulation, delivery and clinical profile of other companies' proprietary drugs and biologics. We currently are working with several major pharmaceutical companies on feasibility programs to evaluate the formulation of their proprietary therapeutics with XeriSol or XeriJect. Our strategic goal is to enter into broader development and ultimately commercial licensing agreements with these partners upon successful completion of the feasibility programs.

We believe these four pillars of our strategy can bring new products to market and transform the lives of patients with life-threatening diseases and ultimately drive value for Xeris' shareholders. Pursuing these strategies provides Xeris with a range of value driving opportunities that are incremental to the value already realized by the Xeris enterprise.

Business Combination

On May 24, 2021, Xeris Pharmaceuticals, Inc. ("Xeris Pharma") entered into a definitive agreement with Strongbridge Biopharma plc ("Strongbridge") to acquire Strongbridge (the "Transaction"). Following consummation of the Transaction on October 5, 2021, Xeris Biopharma Holdings, Inc. ("Xeris Biopharma") became the parent company of both Xeris Pharma and Strongbridge. The common stock of both Xeris Pharma and Strongbridge were de-registered after completion of the Transaction. On October 6, 2021, Xeris Biopharma's common stock, par value $0.0001 per share, commenced trading on the Nasdaq Global Select Market ("Nasdaq") under the ticker symbol "XERS." Xeris Pharma was determined to be the accounting acquirer in the Transaction. For further discussion on the Transaction, refer to "Item 1A. Risk Factors," and "Note 3 - Business combination" in the Notes to Consolidated Financial Statements.

Our Technology Platforms

Overview

Our proprietary non-aqueous formulation technology platforms are designed to address the challenges presented by current aqueous formulations of certain drugs. Injectable pharmaceuticals have conventionally used aqueous delivery systems to administer drugs and biologics, but, in the presence of water, many drugs have poor solubility and low stability. To optimize their stability and enable longer-term storage, many of these products are freeze dried into a powder and, when needed, must be reconstituted with a liquid diluent, which is often a challenging multi-step procedure with the potential for error. Furthermore, the drug product begins to break down once combined with water, which requires the drug to be used immediately or otherwise refrigerated. In addition, these products can require complicated formulations and large injection volumes to make them soluble. For many products, these volumes are too large for SC or IM delivery and instead necessitate IV infusion over several hours. These drugs can be difficult or painful to administer and have limited portability, resulting in an overall poor experience for patients and caregivers.

Our proprietary XeriSol and XeriJect platforms offer the opportunity to eliminate the need for reconstitution and refrigeration, enable long-term room-temperature stability, significantly reduce injection volume and allow for a more convenient SC or IM administration as opposed to IV infusion, all of which we believe are distinct advantages over existing aqueous formulations of marketed products and development-stage product candidates. We believe that our technology platforms can lead to products that will improve outcomes and enable easier administration while reducing costs for payors and the healthcare system.

Our XeriJect formulation platform is best suited for drugs and biologics consisting of large molecules, such as proteins, monoclonal antibodies and vaccines. XeriSol is best suited for peptides and small molecules that currently encounter formulation challenges. With XeriJect, we routinely formulate suspensions with a protein concentration in excess of 400 mg/mL, far exceeding current aqueous formulation systems with maximum achievable protein concentrations of 50-250 mg/mL. These biocompatible non-aqueous, injectable solutions or suspensions formulated using our technology platforms can then be packaged for administration in a commercially available auto-injector, pre-filled syringe, vial, multi-dose pen or infusion pump.

Our Products

Gvoke

Gvoke offers ready-to-use, room-temperature stable glucagon that is designed to be administered subcutaneously in a simple two-step process via a pre-filled syringe (Gvoke PFS), auto-injector (Gvoke HypoPen) or soon-to-be available single dose vial and syringe kit (Gvoke Kit). In our human factors studies, 99% of users were able to successfully administer the full dose with either Gvoke PFS or Gvoke HypoPen. Conversely, in published human factors studies of traditional emergency liquid glucagon kits, only 6% to 31% of users were able to successfully administer the full dose. We believe we can establish Gvoke as a preferred emergency glucagon product and drive greater adoption and penetration of emergency glucagon therapy for patients and caregivers. Gvoke was approved in September 2019 by the FDA for the treatment of severe hypoglycemia, a potentially life-threatening condition, in pediatric and adult patients with diabetes ages two years and older. We began the field launch of Gvoke PFS and Gvoke HypoPen in January 2020 and July 2020, respectively. Both presentations are available in two doses: a 0.5 mg/0.1 mL dose for pediatric patients and a 1 mg/0.2 mL dose for adolescent and adult patients.

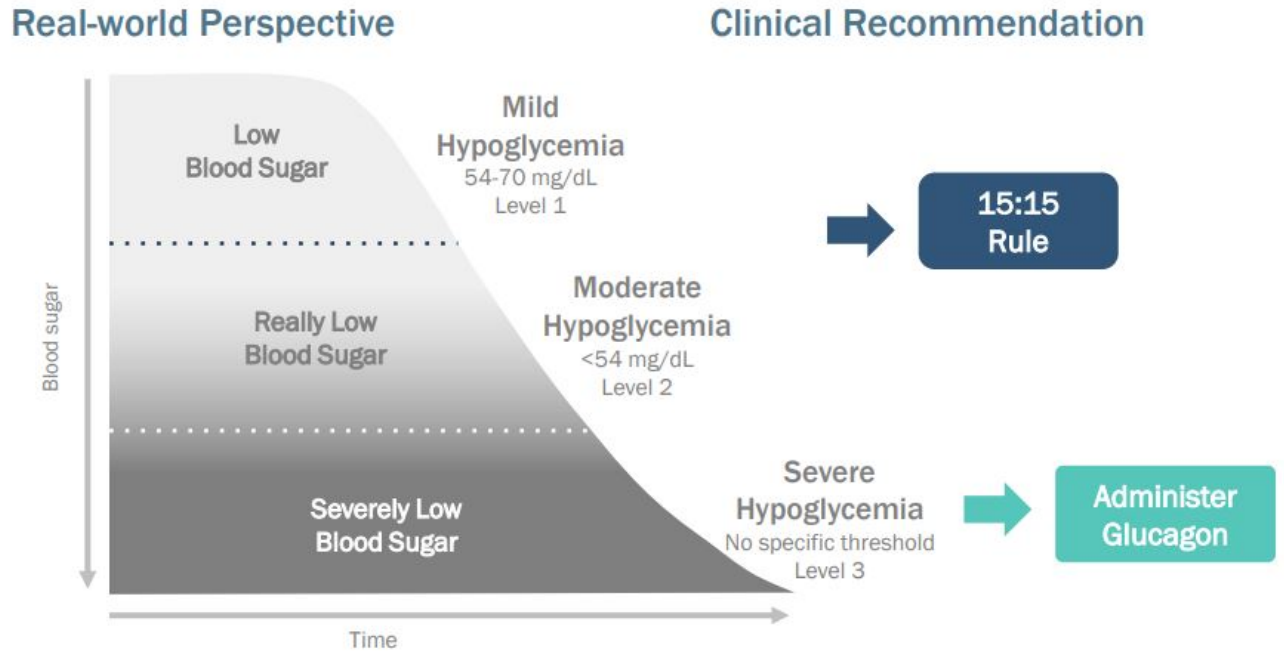
On August 23, 2021, we announced that a supplemental new drug application (sNDA) of Gvoke Kit was approved by the FDA. Gvoke Kit will be sold as a 1 mg/0.2 mL single dose vial and syringe kit. Gvoke Kit contains one (1) single-dose sterile syringe with markings for 0.1 mL (0.5 mg pediatric dose) and 0.2 mL (1 mg adult dose), and one single-dose vial containing 0.2 mL of solution. The Gvoke Kit will be available in March 2022.

On July 19, 2021, we announced that we had entered into an exclusive agreement with Tetris Pharma Limited (“Tetris”) for the commercialization of Ogluo in the European Economic Area, United Kingdom, and Switzerland (the “Territory”). Under the terms of the applicable agreements, Xeris will be responsible for product supply and Tetris will be responsible for commercialization of Ogluo in the Territory. Subject to the terms and conditions set forth in the agreements, Xeris will receive consideration tied to the first commercial sale and other time-, launch- and sales-related milestones and collect a royalty on sales. We commercially launched Ogluo in United Kingdom through our commercialization partner, Tetris, in December 2021. We plan to pursue development and commercialization collaborations for most, if not all, of the non-U.S. markets we seek to enter.

Overview of Hypoglycemia

Diabetes is a widespread condition that affects an estimated 537 million people worldwide with an estimated 22 million drug-treated people in the United States. Among people with diabetes in the United States, essentially all of the approximately 1.6 million people with T1D and 5.4 million people with T2D require insulin therapy to lower their blood glucose levels to achieve normal blood sugar levels and avoid hyperglycemia. Insulin treatment in people with diabetes can also lead to hypoglycemia, a deficiency of glucose in the bloodstream, which is more common in people with diabetes who are treated with insulin or substances that promote production of insulin. Hypoglycemia is the primary adverse reaction associated with insulin.

Hypoglycemia is categorized by level of severity, expressed as mild (Level 1), moderate (Level 2) or severe (Level 3) hypoglycemic events. Definitions, symptoms and treatment recommendations for hypoglycemia per the Americans with Disabilities Act ("ADA") and the American Association of Clinical Endocrinologists ("AACE") are summarized in the figure below:



Hypoglycemic events of any severity are a daily concern for people with diabetes. Severe hypoglycemic events are extremely frightening for patients and caregivers and can result in cardiovascular disease, seizure, coma, and, if left untreated, death. Fear of hypoglycemia and the morbidity and mortality risks associated with it are a constant reality for people with diabetes. According to scientific literature, fear of hypoglycemia is a critical impediment to psychological well-being and quality of life and represents the greatest barrier to optimal glycemic control. Studies have shown that only 14% of those aged 18–25 years and 29% of those aged 26–50 years achieved optimal glycemic control by taking insulin.

While patients can take preventive measures, hypoglycemic events still occur. On average, people with T1D experience an episode of mild or moderate hypoglycemia twice per week and 30% to 40% of people with T1D experience one to three episodes of severe hypoglycemia per year. On average, half of people with T2D treated with insulin experience an episode of mild or moderate hypoglycemia and 20% experience at least one severe episode a year. According to recent statistics, hypoglycemia demanded 242,000 visits to the emergency department in 2018, and resulted in approximately $1.8 billion dollars in direct costs associated with emergency care, inpatient care, and ambulatory care in 2009. Additionally, severe hypoglycemia has been attributed to 27,000 deaths per year.

The ADA Standards of Medical Care in Diabetes recommends that glucagon be prescribed for all individuals at increased risk of Level 2 or Level 3 hypoglycemia so that it is available should it be needed. Glucagon works to raise the glucose levels in a person’s blood by inducing the liver to convert glycogen, a type of stored sugar in the body, into glucose.

Limitations of Existing Emergency Liquid Glucagon Kits

Because of the urgent nature of severe hypoglycemia, the majority of severe hypoglycemic events are treated on an emergency basis, outside of a healthcare facility. Prior to the FDA's approval of Gvoke in September 2019 and Eli Lilly's Baqsimi, a nasally administered glucagon powder, in July 2019, there were only two emergency glucagon products available to treat severe hypoglycemia: Eli Lilly’s Glucagon Emergency Kit ("GEK") and Novo Nordisk’s GlucaGen® HypoKit®. Each of these products is sold as a vial of lyophilized glucagon powder with an exposed needle/syringe that contains a liquid diluent. The glucagon powder must be combined with the liquid diluent at the time of use and drawn into a syringe in accordance with a complex multi-step reconstitution and dose calibration procedure. Long-term storage of the combined solution is impractical because once the lyophilized glucagon is combined with water, the solution becomes unstable and can fibrillate, rendering it inactive and potentially toxic. The multi-step reconstitution and dose calibration procedure required for traditional glucagon kits can be intimidating, particularly in an emergency situation, for likely glucagon kit users, a group that includes caregivers, co-workers, friends, teachers or other bystanders.

In 2018, we conducted a quantitative study with 700 caregivers and people with diabetes evaluating the market perceptions of traditional glucagon kits, which we refer to as our Caregiver and Patient Perceptions Study. In that study, only one third of respondents had a highly favorable opinion of the traditional kits and only half were confident that a glucagon kit user would be able to correctly administer the traditional emergency glucagon products. Furthermore, in three published comparative human factors

studies with traditional kits, only 6% to 31% of users were able to successfully administer the full dose of glucagon. In other words, in these studies, test subjects failed to deliver the full dose of glucagon 69% to 94% of the time. Accordingly, a diabetes patient experiencing a severe hypoglycemic episode who relies on a bystander to administer glucagon may not receive the full dose of glucagon needed to restore their blood glucose levels. Failure to promptly treat severe hypoglycemia leaves the person at critical risk of irreversible brain damage and heart problems, especially in people who already have coronary artery disease. If emergency medical treatment is not successful, the severe hypoglycemic event can be fatal.

Of the units of glucagon rescue products dispensed in the United States at the end of 2021, legacy kits and Baqsimi represented approximately 42% and 38%, respectively, Gvoke represented approximately 20% and Zegalogue represented less than 1%.

Gvoke Key Features and Benefits

Leveraging our patented XeriSol technology, we believe Gvoke offers an important advancement in the treatment of severe hypoglycemia. Gvoke is the first ready-to-use, room-temperature stable liquid glucagon product approved that can be administered via a pre-filled syringe (Gvoke PFS), auto-injector (Gvoke HypoPen) or single dose vial and syringe kit (Gvoke Kit). Gvoke is currently available in two doses: a 0.5 mg/0.1 mL dose for pediatric patients and a 1 mg/0.2 mL dose for adolescent and adult patients. These innovative formats are designed to provide the reliability of a ready-to-use liquid glucagon while allowing patients or caregivers to administer it quickly and simply.

The key features of Gvoke PFS and Gvoke HypoPen are:

- *Ready-to-use:* With its two-step administration process, the user of Gvoke HypoPen, pulls off the cap and pushes down on the skin for five seconds until the viewing window turns red, or with Gvoke PFS, pulls off the cap, inserts the needle at a 90-degree angle and pushes the plunger down as far as it will go. There is no reconstitution required at the time of emergency.
- *Reliable administration*: In our human factors studies, 99% of users were able to successfully administer the full dose.
- *No dose calibration required:* Gvoke is offered in two pre-measured doses: 0.5 mg/0.1 mL dose for pediatric patients and 1 mg/0.2 mL dose for adolescent and adult patients.
- *24 to 30 months room-temperature stability:* No refrigeration is required at any time.

In addition, key features specific to the Gvoke HypoPen are:

- *No visible needle:* The needle in the Gvoke HypoPen is not visible to the user.
- *Auto-retraction:* The needle auto-retracts after administration for safety.
- *Auto-locks:* The device auto-locks after use for safety.

In our Caregiver and Patient Perceptions Study conducted in 2018, more than 75% of subjects responded that they would prefer Gvoke HypoPen over the then-existing traditionally available glucagon kits. Also in 2018, we conducted a quantitative study of over 400 healthcare professionals, which we refer to as our Healthcare Professional Perceptions Study. In that study, results indicated that glucagon would be prescribed to more people across all clinically appropriate patient segments if Gvoke HypoPen was available. Based on this market research, we believe that the glucagon market will become more penetrated and that Gvoke HypoPen will become the preferred emergency glucagon delivery solution to the existing traditionally available glucagon kits.

Gvoke Market Potential

Based on current market data as well as our Caregiver and Patient and Healthcare Professional Perceptions Studies, we believe that Gvoke has the opportunity to increase penetration of the glucagon market in severe hypoglycemia by increasing the number of people with diabetes who have a filled glucagon prescription and by increasing the number of glucagon rescue devices they have on hand.

There are approximately 22 million drug-treated people with diabetes in the United States, and the annual growth rate in incidence of diagnosed and treated people with diabetes is approximately 4% per year. An additional 96 million people in the United States are pre-diabetic and may progress to T2D. The ADA recommends that glucagon be prescribed for all individuals at increased risk of Level 2 or Level 3 hypoglycemia so that it is available should it be needed. Based on our Healthcare Professional Perceptions Study, we believe all people on insulin are considered clinically appropriate for glucagon. In the United States, there is an estimated 1.6 million people with T1D who are treated with insulin because their bodies do not naturally produce insulin and approximately 5.4 million additional people with T2D who are treated with insulin because their bodies do not use insulin properly. In the aggregate, we estimate that the potential target population for emergency glucagon therapy totals approximately 7.0 million people in the United States. We believe every person who is on insulin therapy should have ready-to-use glucagon available for a potential severe hypoglycemic episode. With such an expansion in glucagon prescriptions, and also by increasing penetration into the market for emergency glucagon kits, the United States potential market opportunity may be up to $4.0 billion.

Despite the risk of experiencing a severe hypoglycemic event, we believe that emergency glucagon therapy is under-appreciated, under-evaluated and under-taught, resulting in a market that is underpenetrated. In the United States, approximately 693,000 total

prescriptions for emergency glucagon were written in 2021, or an 7% increase from 2020. In 2021, a total of approximately 1 million units of emergency glucagon products were dispensed in the United States, representing total sales of approximately $281 million.

We commercially launched Ogluo in the United Kingdom through our commercialization partner, Tetris, in December 2021. Considering the European Economic Area, United Kingdom, and Switzerland, we estimate that there are an additional 5 million people with diabetes on insulin. However, annually there are only approximately 1.2M units of glucagon sold in the retail setting, which we believe indicates that the market for emergency glucagon products is significantly underpenetrated in the Territory.

Commercial Strategy

Our commercial strategy is to increase the number of prescribed and dispensed emergency glucagon products, specifically Gvoke, for people on insulin therapy. Our sales force is focused on driving awareness and adoption of Gvoke by healthcare professionals.

We began the field launch of Gvoke PFS in January 2020, Gvoke HypoPen in July 2020 and Gvoke Kit in 2022. Our strategy for Gvoke includes the following:

- **Drive awareness, adoption and utilization of Gvoke**. We plan to drive awareness and adoption of Gvoke to expand glucagon adoption.
  - **Healthcare Professionals:** We are targeting certified diabetes care and education specialists and high insulin and glucagon prescribing healthcare professionals. We are reaching these professionals using our field and inside sales teams.
  - **Patients and Caregivers:** We are activating patients through patient advocacy organizations and leveraging channels such as direct-to-consumer advertising, patient influencer content, digital presence, traditional off-line channels, social media and press coverage to drive awareness and communicate our value proposition to patients and caregivers.
- **Penetrate the market**. We believe that the Gvoke market is currently significantly underpenetrated due to the lack of, and limitations in, previous treatment options. We have designed Gvoke to offer healthcare professionals, patients and caregivers a ready-to-use alternative that facilitates administration of the full dose of glucagon every time it is used. We believe this product offering, paired with our commercial focus, has the potential to grow the market in two ways:
  - **Healthcare Professionals:** In addition to certified diabetes care and education specialists and high insulin and glucagon prescribing healthcare professionals, we are targeting healthcare professionals who are high mealtime insulin prescribers but who are not high prescribers of glucagon. We are reaching these professionals using our field and inside sales teams.
  - **Patients and Caregivers:** We believe there are opportunities to activate patient and caregiver demand for Gvoke. Gvoke is designed as a ready-to-use solution for a segment of patients and caregivers who currently lack the confidence in administering traditional emergency glucagon kits and would rather rely on emergency responders for treatment.
- **Promote access.** Of our target patient population, approximately 60% are commercially insured, approximately 20% are covered by Medicare and approximately 20% are covered by Medicaid and other government programs. We plan to continue our focus on promoting access to Gvoke. We believe that all patients should have access to potentially lifesaving products such as Gvoke. We have engaged with payors to more fully understand their drivers and barriers and convey the health and pharmacoeconomic value of Gvoke.
- **Impact of the ongoing COVID-19 pandemic.** We believe that customer demand has been adversely impacted by the COVID-19 pandemic. Initially, we suspended in-person interactions by our sales and marketing personnel in healthcare settings. We are engaging with these customers remotely, via webinar programs and virtual meetings, as we seek to continue to support healthcare professionals and patient care. Some of our sales and marketing personnel began to reengage with a limited number of in-person interactions. However, with the resurgence of COVID-19 variants in early 2022, our ability to connect with our customers in person became much more limited and we quickly moved back to more remote interactions. In addition, several conferences and other programs at which we intended to market Gvoke have been postponed or transitioned to virtual meetings. Remote interactions may be less effective than in-person interactions. We have also revised our patient copay assistance program to offer a copay card with a buy-down to $0 for commercially eligible patients in response to the COVID-19 pandemic.

We have established a distribution channel in the United States for the commercialization of Gvoke, which is currently being sold primarily to wholesale pharmaceutical distributors, who, in turn, sell Gvoke to pharmacies and other customers. We use a third-party logistics provider for key services related to logistics, warehousing and inventory management, distribution, contract administration, order management and chargeback processing and accounts receivable management.

Keveyis

Keveyis (dichlorphenamide) is the first and only therapy approved in the United States to treat hyperkalemic, hypokalemic and related variants of PPP, a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis.

Overview of PPP

PPP is a rare, genetic, neuromuscular disorder related to a defect in muscle ion channels with multiple variants and subtypes. The disease is characterized by episodes of muscle weakness and paralysis. It often interferes with daily activities and, as patients get older, it can lead to permanent muscle weakness. PPP may be localized (“focal”) or more widespread (“generalized”), and it often

goes underdiagnosed and/or undertreated. Types of periodic paralysis are differentiated by criteria including underlying genetic mutations and changes in blood potassium during an episode. The two most common forms of PPP are hypokalemic, when episodes can be induced by low blood levels of potassium, and hyperkalemic, when episodes are associated with elevated levels of blood potassium. We believe, based on our market research, that there are approximately 4,000 to 5,000 patients in the United States diagnosed with PPP.

Keveyis Features and Benefits

Keveyis is an oral carbonic anhydrase inhibitor that was approved by the FDA in the United States in August 2015 to treat hyperkalemic, hypokalemic and related variants of PPP. The exact mechanism(s) through which oral carbonic anhydrase inhibitors, and Keveyis in particular, decrease the frequency and severity of periodic paralysis attacks is unknown. However, it is believed that their effects are mediated both locally (i.e., in muscle) and systemically. It is not known whether their effects are disease-modifying. Keveyis has received orphan drug exclusivity status in the United States through August 7, 2022.

Keveyis has been studied in two separate double-blind, placebo-controlled multi-center studies and proven to be an effective treatment for PPP. Keveyis was shown to decrease the number of PPP episodes. In addition, episodes that did occur were shorter in duration and not as severe. The most common adverse reactions with incidence ≥10% and rates greater than placebo in patients treated with Keveyis were paresthesia, cognitive disorder, dysgeusia, and confusional state. Less than 10% (3/36) of all patients treated with Keveyis in one study withdrew due to an adverse reaction in the double-blind phase; 17% of hyperkalemic patients (2/12) and ~4% (1/24) of hypokalemic patients discontinued treatment.

Keveyis Market Potential

We believe, based on our market research, that there are approximately 4,000 to 5,000 patients in the United States diagnosed with PPP and we believe that we can address the market by targeting physicians who are managing patients with PPP, including neuromuscular specialists, general neurologists and primary care physicians.

Keveyis Commercial Strategy

Our commercial strategy for Keveyis is to promote its unique benefits, as well as a concerted effort to raise awareness about the underlying PPP disease among the physician/patient/caregiver community with the goal of increasing the rate of diagnosis when the symptoms may otherwise be overlooked. In addition to a specialty sales force, we established a field-based group of patient access managers and medical affairs liaisons. We use a single, specialty pharmacy to provide reimbursement, clinical and distribution support for Keveyis and to develop cost-sharing and patient assistance programs to support qualified, commercially insured patients, federal- and state-insured patients, and uninsured or under-insured patients. We also donate money to independent charitable foundations dedicated to this cause. Our ultimate goal is to ensure that no PPP patient is denied access to Keveyis for financial reasons. We work with the patient community to advocate for patients improving diagnosis, genetic testing and treatment.

Recorlev

Recorlev (levoketoconazole), the pure 2S,4R enantiomer of the enantiomeric pair comprising ketoconazole. Recorlev is a next-generation steroidogenesis inhibitor. The active pharmaceutical ingredient in Recorlev, levoketoconazole, exerts its primary therapeutic effect by blocking the synthesis of cortisol in the adrenal glands, leading to the reduction and, ideally, the normalization of blood cortisol. Levoketoconazole has been granted orphan drug designation by the FDA and the EMA for the treatment of endogenous Cushing's syndrome.

Levoketoconazole inhibits the cortisol synthesis pathway at several points. Based on the results from our SONICS and LOGICS clinical trials, we believe that Recorlev can have a beneficial impact on hypercortisolism, the hallmark of endogenous Cushing's syndrome, as well as benefits related to several comorbidities of endogenous Cushing's syndrome, including those associated with cardiovascular disease risk, such as diabetes, weight gain and elevation in LDL-cholesterol.

On December 30, 2021 we announced the FDA approval of Recorlev for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative. Recorlev is not approved for the treatment of fungal infections. The approval of Recorlev was based upon safety and efficacy data from two positive Phase 3 studies that evaluated a combined study population of 166 patients, which was representative of the adult drug-treated U.S. population with Cushing's syndrome. The SONICS study met its primary and key secondary endpoints, significantly reducing and normalizing mean urinary free cortisol concentrations without a dose increase. LOGICS, a double-blind, placebo-controlled randomized-withdrawal study that met its primary and key secondary endpoints, confirmed the efficacy and safety of Recorlev in normalizing and maintaining therapeutic response compared with placebo.

Overview of Endogenous Cushing's Syndrome

There are two variants of Cushing's syndrome: exogenous, which is caused by factors outside the body (*e.g.*, corticosteroid or cortisol-like medications) and endogenous, which is caused by factors within the body. The signs and symptoms may be the same in both forms. The much more common form is exogenous Cushing's syndrome, which is often found in people taking cortisol-like medications for long periods of time or for shorter periods of time using more potent forms. Cortisol-like medications are often used to treat inflammatory disorders such as asthma and rheumatoid arthritis. Unlike endogenous Cushing's syndrome, exogenous Cushing's syndrome may be alleviated by withdrawing the inciting medication.

Endogenous Cushing's syndrome is a rare endocrine disorder characterized by sustained elevated blood cortisol. Cortisol is a hormone produced in the adrenal gland and is naturally secreted as an end-product of the activity of the hypothalamic-pituitary-adrenal axis. Corticotropin-releasing-hormone ("CRH") is secreted from the hypothalamus and stimulates the secretion and release of adrenocorticotropin ("ACTH") from the pituitary gland, which in turn stimulates cortisol (and other hormone) secretion from the adrenal gland. Cortisol itself exerts negative feedback control on both CRH in the hypothalamus and ACTH in the pituitary gland, thereby reducing CRH and ACTH secretion, keeping cortisol levels in a normal range.

The most common form of endogenous Cushing's syndrome is called Cushing's disease, which is typically caused by a benign pituitary tumor that secretes ACTH autonomously. Cushing's disease represents approximately 70% to 80% of patients with endogenous Cushing's syndrome. Other causes of endogenous ACTH-dependent Cushing's syndrome include extrapituitary tumors producing ACTH, known as ectopic ACTH, or less often CRH (ectopic CRH). The source of ectopic ACTH/CRH secretion is most often small-cell carcinoma of the lung or bronchial carcinoid tumors, but neuroendocrine tumors found in many different organs can also be sources. In a smaller number of cases, approximately 20%, endogenous Cushing's syndrome is ACTH-independent, meaning that it does not arise through tumor secretion of ACTH but rather results from excess autonomous secretion of cortisol itself in the adrenal gland by adrenocortical tumors, either benign or malignant, or by non-malignant enlargement of the adrenal glands called hyperplasia.

In patients with endogenous Cushing's syndrome, the normal feedback mechanisms of the hypothalamic-pituitary-adrenal axis are disrupted. This causes chronic exposure to high circulating cortisol levels that give rise to the clinical state of Cushing's syndrome. The most common signs and symptoms of the syndrome include: weight gain, sometimes with unusual fat accumulation in the upper body with a rounded face ("moon face") and extra fat on the upper back and above the collarbones, along with abdominal fat; high blood sugar or diabetes mellitus; high blood pressure or hypertension; thin bones or osteoporosis; muscle loss or sarcopenia; thin, fragile skin that bruises easily; purple-red stretch marks called striae, usually over the abdomen and under the arms; depression and difficulty thinking clearly; too much facial hair, or hirsutism, usually noticed only in women; irregular or absent menstrual periods and infertility; reduced sex drive or libido; and in children, poor height growth.

An estimated 25,000 patients in the United States are diagnosed with endogenous Cushing's syndrome. When first diagnosed, patients are most commonly adults aged 20 to 50 and five times more often women than men. However, endogenous Cushing's syndrome is believed to be underdiagnosed due to lack of disease recognition, resulting in a delay in diagnosis of six years on average. Endogenous Cushing's syndrome patients are believed to have a mortality risk two to three times that of the age-and-gender-matched general population, with cardiovascular disease, including venous thrombosis and infections being the primary causes of death.

Current Treatment Landscape and Limitations of Current Treatment Options

Treatment of endogenous Cushing's syndrome varies depending on the cause of the disease. For patients with Cushing's disease, initial treatment is almost always the attempted surgical removal of the pituitary tumor. In anticipation of surgery and when surgery is not effective or not an option, drug or radiation therapy, or both, is used to suppress excessive cortisol production and the accompanying clinical symptoms.

A typical approach to drug therapy is to inhibit cortisol synthesis through the oral administration of an inhibitor of enzymes that regulate adrenal cortisol synthesis. Although approved in the European Union for this indication, ketoconazole is not approved for this indication by the FDA and is therefore prescribed "off-label". The percentage of endogenous Cushing's syndrome patients treated with ketoconazole monotherapy who achieve normalized levels of cortisol, assessed by measuring UFC has been reported from retrospective, uncontrolled studies, with varying definitions of normalization, to be between 33% and 100%.

Metyrapone is another cortisol synthesis inhibitor that blocks cortisol in a different way than ketoconazole or Recorlev. It is not approved for treatment of Cushing's syndrome in the US but is used off-label. Metyrapone is approved for use in the United Kingdom and certain other countries as a therapeutic drug for CS. Elsewhere, including in the US, it is approved as a diagnostic agent in Cushing's disease. A drug that works through a similar pathway as metyrapone, called Isturisa (osilodrostat), was granted a marketing authorization in the European Union on January 15, 2020 and in the United States on March 6, 2020. Etomidate is an intravenously administered sedative that potently inhibits 11β-hydroxylase, like metyrapone and osilodrostat, and is highly effective to reduce cortisol, but its use is typically limited to the inpatient setting.

An alternative medical approach to treating Cushing's syndrome targets pituitary tumors that produce ACTH (*i.e.*, in Cushing's disease). Among Cushing's disease patients, the dopamine agonist cabergoline, which is not approved for use to treat Cushing's disease in the United States, has been shown to achieve normalization of UFC levels, gold-standard evidence of disease control, in about 30% of patients. The SSA (somatosatin analog) pasireotide, which is marketed as Signifor and Signifor LAR for the treatment of Cushing's disease in the United States, has shown normalization of UFC levels with stable dosing of the immediate-release formulation in 15% of patients at a dosage of 600 µg twice-daily and in 26% of patients at a dosage of 900 µg twice-daily over a six-month period. Certain SSAs, including Signifor, are known to have undesirable side effects on glucose metabolism. Forty percent of patients with Cushing's disease treated with Signifor in its Phase 3 clinical trial reported the occurrence of hyperglycemia-related adverse events, and in the cohort receiving Signifor 900 µg twice-daily, glycated hemoglobin ("HbA1c") increased from 5.8% at baseline to 7.3% at Month 6.

Another alternative drug therapy, Korlym, or mifepristone, works by inhibiting the action of cortisol at the cortisol-receptor level but does not lower blood cortisol levels, which actually tend to increase during therapy. As a result of this mechanism of action, it is not possible to monitor response (*i.e.*, effectiveness and safety) to Korlym by measuring UFC or cortisol levels (from blood or saliva), which are the standard ways clinicians monitor disease progression and response to treatment. As a result, Korlym is usually titrated

and monitored through use of clinical signs and symptoms improvements (e.g., blood sugar reductions). Korlym has been approved in the United States to control hyperglycemia secondary to hypercortisolism in patients with endogenous Cushing's syndrome who also have diabetes mellitus. About one-third of patients with endogenous Cushing syndrome have diabetes. Korlym is contraindicated in pregnant women and in women with a history of unexplained vaginal bleeding, as its side effects include termination of pregnancy, endometrial thickening and vaginal bleeding. It is also frequently associated with hypokalemia.

Mitotane is an adrenolytic agent (*i.e.*, it destroys the adrenal gland at higher doses) that inhibits steroidogenesis non-selectively at low doses, mainly at 20,22-desmolase (cholesterol side-chain cleavage). It seems to be used primarily in adrenocortical cancer, where it had an FDA indication. There are no prospective clinical trials describing the use of mitotane in non-malignant endogenous CS, and it is not approved for that use.

We believe that the efficacy and usage limitations and safety concerns associated with other currently available drug therapies for endogenous Cushing's syndrome are an important reason why a significant unmet medical need exists among endogenous Cushing's syndrome patients with persistent or recurrent disease post-surgery. In a survey we commissioned in 2019 of 253 U.S. physicians treating patients with Cushing's syndrome. When asked what percentage of their endogenous Cushing's patients currently receiving pharmacological therapy, they would consider have symptoms controlled vs. uncontrolled by their medication(s) for CS, the surveyed physicians indicated that approximately 39% of patients were uncontrolled vs. 61% were controlled. We believe that our potential addressable market for Recorlev includes diagnosed endogenous Cushing's syndrome patients that at any time are eligible for drug therapy, including patients for whom surgery or radiation is not feasible, is contraindicated or has been unsuccessful.

Recorlev Clinical Trials Program

The Phase 3 program for Recorlev included SONICS and LOGICS, two multinational studies designed to evaluate the safety and efficacy of Recorlev when used to treat endogenous Cushing's syndrome. The SONICS study met its primary and secondary endpoints, significantly reducing and normalizing mean urinary free cortisol concentrations without a dose increase. The LOGICS study, which met its primary endpoint and key secondary endpoint, was a double-blind, placebo-controlled randomized-withdrawal study of Recorlev that was designed to supplement the efficacy and safety information provided by SONICS. The ongoing open-label OPTICS study will gather further useful information related to the long-term use of Recorlev.

The key secondary efficacy endpoint the LOGICS study was the proportion of patients with mUFC normalization, defined as a patient with mUFC at or below the upper limit of normal reference range (ULN) at the end of randomized withdrawal phase without meeting a requirement for early rescue during the randomized withdrawal phase. Out of the 79 patients who entered the dose titration and maintenance phase, 37 (47%) patients who met the requirement to be on a stable therapeutic dose for at least 4 weeks and established normal mUFC at the end of the dose titration and maintenance phase, and 2 patients who did not meet the requirement due to abnormal mUFC, continued to the randomized-withdrawal phase. Out of 5 patients from the SONICS study who were enrolled directly in the randomized withdrawal phase, 2 patients had normal mUFC. Among the 39 patients who had normal mUFC at the randomized withdrawal phase baseline, 21 were randomized to the Recorlev group and 18 to the placebo group. The number and percent of patients who had normal mUFC at the end of the randomized withdrawal phase was 11/21 (52.4%) in Recorlev group and 1/18 (5.6%) in placebo group, and the treatment difference (CI) was 46.8% (16.5%, 70.2%). Out of 11 patients with normal mUFC at the end of the randomized-withdrawal phase, 7 patients in the Recorlev group had normal mUFC throughout the randomized-withdrawal phase.

The primary efficacy endpoint of the SONICS study was the proportion of patients with normalization of mUFC at the end of the 6-month maintenance phase. Normalization of mUFC was defined as mUFC at or below the ULN based on central laboratory result without requiring a dose increase during the maintenance phase. At the end of the maintenance phase, 29 of 94 patients (30.9%, 95% exact confidence interval 21.7%, 41.2%) met the primary endpoint.

The most common adverse reactions (incidence > 20%) for LOGICS and SONICS were nausea/vomiting, hypokalemia, hemorrhage/contusion, systemic hypertension, headache, hepatic injury, abnormal uterine bleeding, erythema, fatigue, abdominal pain/dyspepsia, arthritis, upper respiratory infection, myalgia, arrhythmia, back pain, insomnia/sleep disturbances, and peripheral edema.

Elevations in AST or ALT post baseline were reported in patients treated with Recorlev who had AST or ALT ≤ ULN at baseline in LOGICS and SONICS. There were 11 out of 166 patients who had an AST or ALT above the ULN to ˂3 x ULN at baseline. Of these patients, 3 had increases above 3 x ULN, and none had increases above 5 x ULN. Liver test abnormalities improved with cessation of medication.

In the LOGICS and SONICS studies combined, there were 4 (2.4%) patients who experienced QTcF>500 msec, and 23 (14.7%) patients who experienced change-from-baseline QTcF >60 msec, respectively. Adverse reactions reported around the same time that may have been associated with QT prolongation included fatigue, hypertension, nausea/vomiting, and ventricular extrasystoles.

The FDA-approved labeling for Recorlev includes a boxed warning for hepatotoxicity and QT prolongation Recorlev has been associated with serious hepatotoxicity and dose-related QT interval prolongation.

OPTICS Phase 3 Clinical Trial

In 2018, we initiated a long-term, open-label extension trial with Recorlev ("OPTICS") to capture longer-term safety, tolerability and efficacy data from patients who complete either SONICS or LOGICS and who chose to continue therapy with Recorlev. OPTICS will continue to accrue data on each enrolled patient for a minimum of three years or until Recorlev has become available in their own country, whichever comes first.

Market Potential

On December 30, 2021, the FDA approved Recorlev for the treatment of endogenous hypercortisolemia in adult patients with Cushing's Syndrome for whom surgery is not an option or has not been curative and Recorlev became commercially available in January 2022. We believe approximately 8,000 Cushing's patients are managed pharmacologically in the U.S. with a tremendous amount of unmet need since nearly 40% of patients are poorly controlled on their current medication. We believe that this values the Cushing's market in the U.S. at approximately $2 billion annually. Cushing's Syndrome is a complex disease, and we believe that patients could significantly benefit from additional support services and educational resources in conjunction with therapy. For this reason, we have partnered with a specialty pharmacy to provide a customized support and product distribution program, Xeris CareConnection™, for members of the Recorlev ecosystem, including appropriate patients, caregivers, physicians, and payors. Xeris CareConnection provides support services throughout the entire treatment journey to patients and healthcare professionals with direct access to pharmacists, reimbursement specialists and access managers. The comprehensive patient support program includes welcome information, therapy onboarding, at-home delivery of medication, a discreet courier service for urinary free cortisol (UFC) test collection, automatic monthly refill shipments, financial assistance programs, one-on-one support, and ongoing educational resources.

Our Product Candidates

Ready-to-Use Glucagon (XP-9164) for Gastroenterology

We are currently in Phase 1 development with product candidate XP-9164, an early-stage compound for gastroenterology.

XP-9164 is intended to address unmet needs in the growing procedural gastroenterology market. Glucagon transiently decreases peristalsis of smooth muscle in the gastrointestinal tract. Glucagon administration during gastrointestinal imaging permits more precise visualization for studies and procedures. It is also used in abdominal vascular procedures such as treating esophageal varices and other GI bleeds. Glucagon is also utilized in biopsies, abscess drainage, GI stenting, gastrostomy tube placement and colonoscopies. In 2019 there were ~17M colonoscopies performed in the U.S. A ready-to-use glucagon may potentially address a number of areas of needed improvement: improved operational efficiency, no reconstitution (and thus fewer reconstitution errors), room temperature stable liquid, faster preparation and possibly less waste.

Ready-to-Use Glucagon for Exercise-Induced Hypoglycemia(EIH) in Diabetes

Exercise-induced (or exercise-associated) hypoglycemia and the complexity of management aimed at its prevention represent major barriers to the adoption of regular physical activity for many individuals with diabetes treated with insulin. Although carbohydrate ingestion, including oral glucose tablets, can help ameliorate hypoglycemia, patients' carbohydrate requirements can be as high as 1 gram per minute of exercise, which can be counterproductive to weight management. Aerobic exercise, in particular, often results in a significant drop in blood glucose concentrations. Qualitative feedback has shown that the challenges in current exercise management strategies and the need to consume carbohydrates are frustrating and may lead to minimized or complete omission of exercise for many patients. People with diabetes who are on intensive insulin regimens are at risk of EIH. We believe there is a subset of these individuals that exercises at least three times per week per current guidelines who could potentially use a mini-dose of ready-to-use glucagon each time they exercise.

Xeris Offering—Mini-doses of Ready-to-Use Glucagon for Treatment of EIH

We are developing a mini-dose of our ready-to-use, liquid-stable glucagon and have observed appropriate dose-dependent PK and PD responses when administered subcutaneously at doses of 75, 150 and 300 µg in adults with T1D. A proof-of-concept study further demonstrated that a mini-dose of 150 µg of glucagon prevented non-severe hypoglycemia to a substantially similar degree as oral glucose tablets that are commonly used during exercise to prevent or correct non-severe hypoglycemia in adults with T1D. As such, the use of mini-dose glucagon enabled patients to avoid the unnecessary caloric intake inherent in glucose tablets or other types of carbohydrates.

There currently are no FDA-approved glucagon products that enable individuals to modestly increase glucagon levels at the start of exercise. Glucagon rescue kits exist as a lyophilized powder that must be reconstituted in diluent immediately prior to injection as they are unstable in aqueous solutions for extended periods of time. Despite the challenging reconstitution process, there has been significant documented off-label use, in which patients with T1D mini-dose glucagon using the traditional glucagon kits.

Clinical Experience

We have successfully completed a number of preclinical studies in multiple species to support the safety of mini-dose glucagon, as well as Phase 2 safety and efficacy clinical trials in subjects with T1D.

Phase 2 Clinical Trials

XSMP-203: The Use of Mini-Dose Glucagon to Prevent Exercise-Induced Hypoglycemia in Type 1 Diabetes

Based on previous dose-finding trials (XSMP-201 and XSMP-202), we collaborated on a third Phase 2 clinical trial of mini-dose glucagon for EIH in the first quarter of 2016. The primary analysis of this trial was comparison of the glycemic response of 150 µg mini-dose glucagon against current standards of care, including basal insulin reduction and glucose tablet consumption, to mitigate EIH.

The study concluded that mini-dose glucagon (150 µg) was more effective at preventing EIH than insulin reduction which was associated with a similar rate and magnitude of hypoglycemia as no intervention. Moreover, while mini-dose glucagon was as effective as glucose tablets for preventing EIH, mini-dose glucagon resulted in less post-intervention hyperglycemia than ingestion of carbohydrates and avoided the consumption of unnecessary calories. The results of this study were published in 2018 in the journal *Diabetes Care*.

XSMP-204: A Phase 2 Randomized, Placebo-Controlled, Double-Blind, Parallel Study to Evaluate Glucagon RTU (Glucagon Injection) Compared to Standard of Care for the Prevention of Exercise-Induced Hypoglycemia During Regular Aerobic Exercise in Adults with Type 1 Diabetes

This trial was a randomized, placebo-controlled, double-blind, two-treatment, two-period, crossover comparison in a clinical research center (CRC) setting, followed by a randomized, placebo-controlled, double-blind two-arm comparison with a third open-label arm in an outpatient setting to evaluate the preliminary efficacy and safety of RTU glucagon to prevent EIH in adults with T1D who perform regular, moderate-to-high intensity aerobic exercise. In January 2020, we reported that a mini-dose of RTU glucagon was adequate to maintain normal blood glucose levels during prolonged, moderate-to-high intensity aerobic exercise in the CRC setting.

In the outpatient stage, the trial was examining if the subcutaneous administration of RTU glucagon just before exercise, with or without a 50% reduction in basal rate insulin, compared to a 50% basal rate insulin reduction alone prevents the occurrence of hypoglycemia (i.e., blood glucose <70 mg/dL) measured by blood glucose meter during and after moderate-to-high intensity aerobic exercise by adult subjects with T1D in an outpatient setting. In June 2020, we reported positive results from the outpatient stage of this Phase 2 study. Over this time when individually compared to standard of care alone, the number of EIH episodes was significantly less with RTU Glucagon + standard of care and with Open Label RTU Glucagon. RTU Glucagon + standard of care resulted in an approximately 70% lower rate of EIH when compared to standard of care alone. Additionally, Open Label RTU Glucagon resulted in an approximately 54% lower rate of EIH when compared to standard of care alone. The difference in the incidence rates of EIH between the two RTU Glucagon arms was not statistically significant.

Across all outpatient stage exercise sessions, the nominal use of oral glucose tablets during and after exercise, in order to treat hypoglycemia, was greater in the standard of care arm compared to RTU Glucagon + standard of care and Open Label RTU Glucagon. Consequently, the nominal incidence of hyperglycemia episodes (blood glucose > 180 mg/dl) was observed to be 2.4 fold greater in the standard of care arm when compared to RTU Glucagon + standard of care arm. RTU Glucagon did not appear to individually contribute to hyperglycemia. When hyperglycemia events did occur, the time duration and severity of events did not differ between treatment arms.

In both phases of the study, mini doses of RTU glucagon were safe and well tolerated, and no serious adverse events occurred.

Based on FDA interactions and expectations for a registrational program to support a mini-dose indication for Glucagon RTU in EIH, we submitted an IND in February 2022. We received FDA clearance in March 2022 and are actively planning to initiate a new phase 2 clinical program by the end of 2022 to further address the management of EIH in people with diabetes who use insulin.

Non-Glucagon Programs

Ready-to-Use Product for Endocrinology (Levothyroxine; XP-8121)

We are currently in Phase 1 development with product candidate XP-8121, an early-stage program designed to address maintenance therapy in patients with congenital or acquired hypothyroidism who require thyroid hormone replacement.

Levothyroxine and Hypothyroidism

The thyroid gland is responsible for the synthesis, storage, and release of metabolic hormones including thyroxine (T4) and triiodothyronine (T3). These hormones are crucial in the regulation of critical metabolic processes and are vital for normal growth and development during fetal life, infancy, and childhood.

Therapeutically, levothyroxine is administered when the body is deficient in the endogenous hormone. The goal of therapy is restoration of the euthyroid state which can reverse the clinical manifestations of hypothyroidism and significantly improve quality of life. The treatment of choice for correction of hypothyroidism is levothyroxine, which is the mainstay of thyroid hormone replacement therapy. It is one of the most widely prescribed drug products in the United States, but the complexity of maintaining biochemical and clinical euthyroidism in patients undergoing treatment with oral levothyroxine cannot be underestimated. It has been reported that nearly 40% of patients undergoing treatment with oral levothyroxine are either over- or under-treated due to factors that include, but are not limited to, drug formulation, use of the drug with food, adherence to the drug, use of concomitant medications, and pre-existing medical conditions. Many patients failing to reach target TSH levels are generally managed by simply increasing their levothyroxine daily dose. However, levothyroxine is a drug with a narrow therapeutic index, meaning that relatively small deviations from the proper dose can cause a clinically meaningful shift in pharmacological effects when administered to a patient; thus, the titration of levothyroxine oral drug may be a tailored and incremental process.

XP-8121 Overview

XP-8121 is a novel formulation for subcutaneous administration that could potentially mitigate many of the challenges associated with oral formulations, such as identification of an ideal dose due to absorption variation and medication adherence for patients who have

difficulty maintaining a stable, therapeutic serum level. Preclinical studies of SC XP-8121 showed a sustained plasma exposure profile and similar Cmax when compared with equivalent doses of the oral formulation. We are currently conducting a Phase 1 study of XP-8121 to evaluate the pharmacokinetics, safety and tolerability, and potential for weekly dosing in the treatment of hypothyroidism.

The Phase 1 clinical study is a single ascending dose crossover design in 30 healthy participants to compare matching doses of oral levothyroxine (Synthroid®) and subcutaneous XP-8121. The primary endpoints of the study are to characterize the absorption and elimination kinetics of XP-8121 and compare bioavailability of XP-8121 to oral levothyroxine. Secondary endpoints are safety and tolerability of XP-8121.

Market Opportunity

There are more than 100 million prescriptions written for oral levothyroxine per year, making it one of the most prescribed therapies in the United States. Non-adherence to daily therapy, resistant hypothyroidism, and limited GI absorption are some of the major reasons for treatment failure or suboptimal treatment with oral levothyroxine. We believe these challenges could be mitigated by XP-8121, if approved, and translate into the long-term health benefit of achieving a euthyroid state for patients. It is estimated that 47% of patients have an associated GI condition o 15% experience inadequate control of symptoms. Assuming 56 million weekly doses per year and $30 per dose comparable to branded orals, this represents a $1 to $2 billion market opportunity.

XeriSol Pramlintide-Insulin Co-formulation (XP-3924)

Xeris Pharma has developed a novel, investigational fixed-ratio co-formulation of pramlintide and regular human insulin (XP-3924) to improve glycemic control in adult and pediatric patients with diabetes mellitus (T1D and T2D). Xeris' proprietary formulation technology (XeriSol™) enables the 2 peptides (pramlintide and insulin), which require different aqueous pH environments for optimal stability, to be co-formulated in a stable ready-to-use solution. The current formulation patent exists through at least Q4 2032, expected to extend to 2036 with successful prosecution of the currently pending continuation application, and through 2041-2042 with the ongoing formulation development work

XP-3924 Market Opportunity

We believe XP-3924 has the opportunity to serve a large unmet need in patients on mealtime insulin, with the market opportunity estimated at $3-4 billion in the United States. It is estimated that ~1/3 of patients on mealtime insulin are not achieving their A1C goals despite optimized insulin therapy. Additional therapeutic options for patients with advanced diabetes not well-controlled on mealtime insulin are limited. The only pharmacological therapy indicated for such patients is pramlintide (Symlin®). We have an open IND for XP-3924, recently completed a Phase 2 clinical trial in adults with Type 1 Diabetes and obtained FDA feedback on the clinical development and regulatory requirements for submitting a 351(a) stand-alone BLA. We are currently seeking partners to license the development and commercialization rights to XP-3924 in the US.

Ready-to-Use Diazepam (XP-0863)

XP-0863 is a liquid formulation of diazepam for intramuscular injection being studied for the treatment of ARS. Xeris' patent protected technology XeriSol™ has been used to develop a room-temperature stable, ready-to-use, small-volume solution of diazepam for intramuscular injection delivered by an auto-injector, which will provide patients and caregivers an alternative to rectal and nasal administrations of benzodiazepines. XP-0863 is designed to address variable absorption, and suboptimal PK profiles of the currently marketed formulations of benzodiazepines, by offering a longer duration of action, consistent absorption of drug delivered through intramuscular administration, and a convenient and reliable form factor of the autoinjector. XP-0863 has been granted an orphan designation by the FDA for the treatment of ARS and Dravet syndrome in patients with epilepsy. Approximately 160,000 people in the United States experience ARS.

Injectable and rectal gel formulations of diazepam are the current standard of care for the emergency treatment of epileptic seizures. In 2018, diazepam formulations generated total U.S. sales of approximately $86 million, of which Diastat® Rectal Gel and its generic formulations comprised $74 million. Diastat requires a multi-step procedure which makes it more difficult to administer while a patient is experiencing seizures. Additionally, the use of rectal gel in both middle school children and young adults with ARS is reduced because of social stigma. These characteristics are limitations that may diminish the specific demand for rectal diazepam products. Due to this limitation, we believe the market for diazepam in ARS is underpenetrated. We believe that a ready-to-use diazepam injectable rescue pen would improve patient quality of life and drive adoption of diazepam to treat ARS. We believe that, if approved, XP-0863 would have the opportunity to fill the unmet need in ARS for a reliable, user-friendly treatment option with adequate onset of action and durable effect sufficient to break the seizure cluster and prevent recurrence. The market opportunity is estimated at ~$650-1.3B.

We have completed a Phase 1a and a Phase 1b single dose studies in healthy subjects vs. Diastat® which demonstrated Cmax comparable to and Tmax longer than Diastat®, comparable partial AUCs across early timepoints, increased overall exposure (AUC0-∞) when compared to Diastat®, and dose proportionality. XP-0863 was safe and well-tolerated with minimal sedation, minimal injection site reactions and no serious adverse events. In addition to the orphan designation, the FDA has granted Fast Track designation and aligned on the proposed clinical development plan of a single Phase 3, single arm safety study in patients with epilepsy as well as a 505(b)(2) submission. A primary container and device partner has been identified to develop a pre-filled syringe

and/or rescue autoinjector. We are currently seeking partners to license the development and commercialization rights to XP-0863 in the US.

Manufacturing and Supply

We currently contract with third parties for the manufacture, assembly, testing, packaging, storage and distribution of our products. In our experience, third party contract manufacturing organizations ("CMOs") are generally cost-efficient, high quality and reliable, and we currently have no plans to build our own manufacturing or distribution infrastructure. Our technical team has extensive pharmaceutical development, manufacturing, analytical, quality and distribution experience and is qualified and capable of managing supply chain operations across multiple CMOs. Our Quality System, Standard Operating Procedures and CMO interfaces are designed to promote the FDA's current Good Manufacturing Practice requirements ("CGMP") compliance and effective regulatory communications. We selected our CMOs for specific competencies, and they have met our development, manufacturing, quality and regulatory requirements and have all been involved in manufacturing our clinical supplies, commercial registration batches, and commercial product.

Glucagon is the active pharmaceutical ingredient ("API") used in Gvoke and our ready-to-use glucagon product candidates. Bachem Americas, Inc., ("Bachem") is our primary commercial source for API. Bachem holds a U.S. drug master file for glucagon produced at its facility in Switzerland, and its manufacturing process is fully validated. We have entered into a non-exclusive supply agreement with Bachem. While we believe that Bachem has sufficient capacity to satisfy our long-term glucagon API requirements for Gvoke and other ready-to-use glucagon product candidates, we are evaluating alternate sourcing options.

Manufacturing drug product for Gvoke requires an aseptic fill/finish facility capable of handling solvents and a cyclic olefinic polymer syringe. Pyramid Laboratories, Inc. ("Pyramid") has been actively involved in the development of Gvoke and our ready-to-use glucagon product candidates. Its facility in California is our primary source for drug product. We have entered into a non-exclusive supply agreement with Pyramid. While we believe that Pyramid has sufficient capacity to satisfy our demand requirements for at least three to five years, we are evaluating alternate sourcing options.

The auto-injector used to deliver drug product in Gvoke HypoPen is a proprietary multi-product device platform developed by SHL Medical AG, SHL Pharma LLC, and SHL Pharma (collectively "SHL"). SHL produces device sub-assemblies as its facilities in Taiwan and performs final drug product/device assembly operations at its facility in Florida. We have entered into a non-exclusive supply agreement with SHL.

We have a supply agreement with Taro Pharmaceuticals U.S.A., Inc. ("Taro") to produce Keveyis. The supply agreement may extend beyond the orphan exclusivity period unless terminated by either party pursuant to the terms of the agreement. If the supply agreement is terminated by Taro at the conclusion of the orphan exclusivity period, we have the right to manufacture the product on our own or have the product manufactured by a third party on our behalf.

Levoketoconazole is the API used in Recorlev. Regis Technologies, Inc. ("Regis") has been actively involved in the development of levoketoconazole and its facility in Illinois is our sole source for API. We have entered into a supply agreement with Regis. We believe that Regis has sufficient capacity to satisfy our demand requirements for at least three to five years.

Manufacturing Recorlev drug product requires a conventional solid oral dosage form manufacturing facility. Xcelience, LLC. ("Lonza") has been actively involved in the development of Recorlev and its facility in Florida is our sole source for drug product. We have entered into a supply agreement with Lonza. We believe that Lonza has sufficient capacity to satisfy our demand requirements for at least three to five years.

We believe that a number of CMOs can provide suitable secondary packaging services for Gvoke and Recorlev, and we have entered into commercial supply agreements with one vendor. A number of third-party logistic providers can provide commercial order processing and finished goods distribution services to U.S. specialty pharmacies and wholesale customers, and we have a commercial distribution agreement with one such vendor for Gvoke, Keveyis and Recorlev.

To date, we and our suppliers and third-party manufacturing partners have been able to continue to supply our products to our patients and currently do not anticipate any interruptions in supply. Our third-party contract manufacturing partners continue to operate at or near normal levels, with enhanced safety measures intended to prevent the spread of the coronavirus. While we currently do not anticipate any interruptions in our manufacturing process, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our third-party suppliers and contract manufacturing partners' ability to supply and/or manufacture our products.

Competition

Our industry is characterized by intense competition and a strong emphasis on proprietary products. While we believe that our employees, product and product candidate platform, development expertise and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies. Many of our potential competitors have substantially greater financial, technical and human resources than we do, as well as more experience in the development of product candidates, obtaining FDA and other regulatory approvals of products, and the commercialization of those products.

- **Gvoke:** Four emergency glucagon kits are currently available to treat severe hypoglycemia: Eli Lilly's GEK, Novo Nordisk's GlucaGen HypoKit, Fresenius Kabi's Glucagon Emergency Kit and Amphastar's generic Glucagon for Injection Emergency Kit. Each kit is sold as a vial of lyophilized, glucagon powder with an exposed syringe/needle that contains a liquid diluent. The glucagon powder must be combined with the liquid diluent at the time of use and drawn into a syringe in accordance with a complex multi-step reconstitution and dose calibration procedure. Additionally, once reconstituted, the glucagon must be used immediately. We believe that the drawbacks of traditional kits and the lack of conversations regarding glucagon limit their adoption. Three innovative glucagon products are currently available to treat severe hypoglycemia, including our Gvoke, Eli Lilly's intranasal glucagon dry powder, Baqsimi, and Zealand Pharma's dasiglucagon auto-injector, Zegalogue.

  In our market research, respondents ranked the importance of successful full-dose delivery and ability to tell if the full dose was administered significantly higher than the attribute "needleless". Caregivers and people with diabetes associated Gvoke HypoPen with efficacious and successful dose delivery, as well as ease of ability to tell if the full dose was administered. Similarly, healthcare professionals indicated that one of the most appealing attributes of Gvoke is the greater likelihood of successful dose delivery.

- **Keveyis:** Keveyis is the first and only FDA approved therapy for PPP. Acetazolamide, an oral carbonic anhydrase inhibitor, is used frequently off-label for the prophylactic and sometimes acute treatment of PPP. Potassium supplements are indicated for use in hypokalemic periodic paralysis in the United States and are frequently used either chronically or for emergency treatment of episodes in the form of PPP. Several other types of drugs have been reported to have benefits for chronic or acute use in one or more than one PPP variant, including potassium-sparing diuretics, beta receptor agonists, mexelitine and other sodium channel blockers, and others. We are not aware of drugs currently in development for prophylactic chronic treatment of PPP.

- **Recorlev:** A number of therapies are currently approved or in various stages of development for endogenous Cushing's syndrome. Currently, there are no therapies broadly marketed for the treatment of endogenous Cushing's syndrome patients in the U.S. Korlym (mifepristone) is indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery. Signifor (pasireotide) and Signifor LAR are marketed by Recordati in the United States and are indicated for the treatment of adult patients with Cushing's disease (a subset of Cushing's syndrome) for whom pituitary surgery is not an option or has not been curative. Isturisa (osilodrostat) is a cortisol synthesis inhibitor indicated for adult patients with Cushing's disease (a subset of Cushing's syndrome) for whom pituitary surgery is not an option or has not been curative is marketed by Recordati. A number of products, including ketoconazole, metyrapone, cabergoline, mitotane and etomidate are used off-label for the treatment of Cushing's Syndrome in the U.S. Ketoconazole, metyrapone and mitotane are marketed by HRA Pharma in certain European countries. Products in development include relacorilant (CORT125134), a selective glucocorticoid receptor antagonist, currently in Phase 3 for Cushing's syndrome by Corcept Therapeutics. AstraZeneca PLC. is developing AZD-4017 inhibitor of 11 beta-hydroxysteroid dehydrogenase 1 (11BHSD1), currently in Phase 2. Sparrow Pharmaceuticals is developing SPI-62, a HSD-1 inhibitor, currently in Phase 2. Synchronicity Pharma Inc. is developing SHP-1705, which acts by modulating cryptochrome (Cry) receptor activity, currently in Phase 1. Sosei Heptares is developing HTL-0030310 a selective somatostatin receptor 5 agonist, currently in Phase 1. Crinetics has initiated a double-blind, randomized, placebo-controlled Phase 1 study of this orally administered, nonpeptide small molecule drug candidate in healthy volunteers. This study will assess the safety and tolerability of single and multiple doses of CRN04894 and will measure the effect of CRN04894 on suppression of cortisol, cortisol precursors, and adrenal androgens following exogenous ACTH stimulation.

Intellectual Property

Proprietary Protection

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our products and product candidates, manufacturing and process discoveries and other know-how, to operate without infringing the proprietary rights of others, and to prevent others from infringing our proprietary rights. We have been building and continue to build our intellectual property portfolio relating to our product candidates and technology. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also intend to rely on trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us or our partners in the future will be commercially useful in protecting our technology.

Patent Rights

We currently own 141 patents issued globally, including a composition of matter patent covering our ready-to-use glucagon formulation that expires in 2036. Upon completion of the acquisition of Strongbridge, we control the patents of Xeris Pharma and those of Strongbridge Dublin Limited, the latter of which has 53 granted patents globally including those related to proprietary formulations of levoketoconazole (the active pharmaceutical ingredient in Recorlev®) and the uses of such formulations in treating certain endocrine-related diseases and syndromes. This includes US Patent No. 11,020,393, which was granted on June 1, 2021, and which provides patent protection through 2040 for the use of Recorlev in the treatment of certain patients with persistent or recurrent Cushing's syndrome.

Trade Secrets and Other Protection

In addition to patented intellectual property, we also rely on trade secrets and proprietary know-how to protect our technology and maintain our competitive position, especially when we do not believe that patent protection is appropriate or can be obtained. Our policy is to require each of our employees, consultants and advisors to execute a confidentiality and inventions assignment agreement before beginning their employment, consulting or advisory relationship with us. The agreements generally provide that the individual must keep confidential and not disclose to other parties any confidential information developed or learned by the individual during the course of the individual's relationship with us except in limited circumstances. These agreements generally also provide that we own all inventions conceived and/or reduced to practice by the individual in the course of their employment with us or rendering services to us.

Other Intellectual Property Rights

We file trademark applications and pursue registrations in the United States and abroad when appropriate. We own registered trademarks for the mark Xeris Pharmaceuticals in the U.S., for the marks GVOKE, GVOKE HYPOPEN and HYPOPEN in the US and several ex-US countries, the registered trademark for OGLUO in the EU and the UK, and the registered trademarks for XERISOL and XERIJECT in Australia, the EU and the UK. We also own pending trademark applications for XERISOL and XERIJECT in the U.S. and a number of ex-US countries, and for the marks GVOKE and GVOKE HYPOPEN in a number of ex-U.S. countries, all for use in connection with our pharmaceutical research and development and products, as well as trade names that could be used with our product candidates.

From time to time, we may find it necessary or prudent to obtain licenses from third-party intellectual property holders.

Regulation

Government Regulation

United States Drug and Biological Product Development

In the United States, the FDA regulates drugs, medical devices and combinations of drugs and devices, or combination products, under the FDCA and its implementing regulations and biologics under the FDCA and the Public Health Service Act ("PHSA") and their implementing regulations. Drugs, biologics, medical devices and combination products are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, requests for voluntary product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Certain of our products and product candidates are subject to regulation as combination products, which means that they are composed of both a drug product and device product. If our drug products, along with our combination product, marketed individually, each component would be subject to different regulatory pathways and reviewed by different centers within the FDA. A combination product, however, is assigned to a center that will have primary jurisdiction over its regulation based on a determination of the combination product's primary mode of action, which is the single mode of action that provides the most important therapeutic action. In the case of Gvoke and some of our product candidates, the primary mode of action is attributable to the drug component of the product, or biological component of the product, which means that the FDA's Center for Drug Evaluation and Research ("CDER") or FDA's Center for Biologics Evaluation and Research ("CBER") has primary jurisdiction over the premarket development, review and approval of the combination product. Accordingly, we plan to continue to investigate our products through the IND framework and seek approval through the NDA or BLA pathway. Based on our discussions with the FDA to date, we do not anticipate that the FDA will require a separate medical device authorization for the device component of our combination products, but this could change during the course of its review of any marketing application that we may submit. The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests, animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice ("GLP") regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB"), representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with an applicable IND and other clinical study related regulations, sometimes referred to as FDA's Clinical Practices ("GCPs") regulations, to establish the safety and efficacy of the proposed drug or biologic for its proposed indication;
- submission to the FDA of an NDA or BLA;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with the FDA's CGMP regulations;
- potential FDA inspection of Xeris, the clinical trial sites, or other vendors that generated the data in support of the NDA or BLA;
- payment of associated user fees;
- review by an FDA advisory committee, where appropriate or if applicable;
- FDA review and approval of the NDA or BLA prior to any commercial marketing or sale; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy ("REMS") and the potential requirement to conduct post-approval studies.

Once a pharmaceutical product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity, formulation, and stability, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND. An IND is an exemption from the FDCA that allows an unapproved product to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. The sponsor must also include a protocol detailing, among other things, the objectives of the initial clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the initial clinical trial lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions related to a proposed clinical trial and places the trial on a clinical hold within that 30-day period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns or non-compliance and may be imposed on all drug or biological products within a certain class of drugs or biologics. The FDA also can impose partial clinical holds, for example, prohibiting the initiation of clinical trials of a certain duration or for a certain dose.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. These regulations include the requirement that all research subjects provide informed consent in writing before their participation in any clinical trial. Further, an IRB must review and approve the plan for any clinical trial before it commences at any institution, and the IRB must conduct continuing review and reapprove the study at least annually. An IRB considers, among other things, whether the risks to individuals participating in the clinical trial are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the clinical trial and the consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

Each new clinical protocol and any amendments to the protocol must be submitted for FDA review and to the IRBs for approval. Protocols detail, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The product is initially introduced into a small number of healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product is suspected or known to be unavoidably toxic, the initial human testing may be conducted in patients.
- Phase 2. Involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage and schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit relationship of the product and provide an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the

FDA may mandate the performance of Phase 4 trials. Companies that conduct certain clinical trials are also required to register them and post the results of completed clinical trials on a government-sponsored database, such as ClinicalTrials.gov in the United States, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events, findings from other studies that suggest a significant risk to humans exposed to the product, findings from animal or in vitro testing that suggest a significant risk to human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product has been associated with unexpected serious harm to patients. 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 provides authorization for whether a trial may move forward at designated check points based on access to certain data from the study. The clinical trial sponsor may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with CGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life. In addition, for certain combination products it may be necessary to conduct Human Factors studies prior to NDA or BLA submission to ascertain the usability of the product by patients in real-world settings.

FDA Review Process

The results of product development, preclinical studies, Human Factors studies (when required), and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the drug or biologic, proposed labeling and other relevant information, are submitted to the FDA as part of an NDA or BLA, requesting approval to market the product. An NDA for a new drug must contain proof of the drug's safety and efficacy. A BLA is a request for approval to market a biologic for one or more specified indications and must contain proof of the biologic's safety, purity, and potency. Under federal law, most NDAs or BLAs must be accompanied by a significant application user fee to the FDA. There also are continuing user fee requirements, under which the FDA assesses an annual program fee for each product identified in an approved NDA or BLA. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses which we utilized for Gvoke.

The FDA reviews all NDAs and BLAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA or BLA for filing. The FDA typically makes a decision on accepting an NDA or BLA for filing within 60 days of receipt. The decision to accept the NDA or BLA for filing means that the FDA has made a threshold determination that the application is sufficiently complete to permit a substantive review. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act ("PDUFA"), the FDA's goal to complete its substantive review and respond to the applicant is ten months from the receipt of a standard NDA or ten months from the filing date of an NDA for a new molecular entity or original BLA. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification and may go through multiple review cycles.

After the NDA or BLA submission is accepted for filing, the FDA reviews the NDA or BLA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with CGMPs to assure and preserve the product's identity, strength, quality, and purity. The FDA may refer applications for novel drug or biological products or drug or biological products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and us during the review process. The review and evaluation of an NDA or BLA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving an NDA or BLA, the FDA may conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with CGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with CGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA or BLA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process, and manufacturing

facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug or biologic with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all the specific deficiencies in the NDA or BLA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, nonclinical studies, or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA or BLA, addressing all the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a product for marketing in the United States, and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, or precautions be included in the product labeling or may condition the approval of the NDA or BLA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 clinical trials to further assess drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a REMS to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription, or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on at least two adequate and well-controlled clinical studies and must contain substantial evidence of the safety and effectiveness of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is authorized, however, to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and effectiveness for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternative and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application ("ANDA") to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug ("RLD").

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is the same as the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to an RLD if the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the RLD. Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic

equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity ("NCE") is a drug that contains no active moiety, which is the molecule or ion responsible for the physiological or pharmacological action of the drug substance, that has previously been approved by the FDA in any other NDA. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, which states that the proposed drug will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Pursuant to the Food and Drug Administration Reauthorization Act of 2017, the FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitive generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Marketing Exclusivity for Biological Products

An abbreviated approval pathway for biological products shown to be biosimilar to or interchangeable with an FDA-licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009 ("BPCI Act"). This amendment to the PHSA, in part, attempts to minimize duplicative testing. Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a biological product be biosimilar to the reference product and that the product can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times to an individual, that the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product without such alternation or switch.

A reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. ''First licensure'' typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA, including a 505(b)(2) NDA, or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant relies on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not provide a Paragraph IV certification against the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or the 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired.

Regulation of Combination Products in the United States

Certain products may be comprised of components, such as drug components and device components, that would normally be regulated under different types of regulatory authorities, and frequently by different centers at the FDA. These products are known as combination products. Specifically, under regulations issued by the FDA, a combination product may be:

- a product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products;
- a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, or device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or
- any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

Under the FDCA and its implementing regulations, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The designation of a lead center generally eliminates the need to receive approvals from more than one FDA component for combination products, although it does not preclude consultations by the lead center with other components of FDA. The determination of which center will be the lead center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a drug-device combination product is attributable to the drug product, the FDA center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA also has established an Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute.

A combination product with a drug primary mode of action generally would be reviewed and approved pursuant to the drug approval processes under the FDCA. In reviewing the NDA or 505(b)(2) application for such a product, however, FDA reviewers in the drug center could consult with their counterparts in the device center to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. In addition, under FDA regulations, combination products are subject to CGMP requirements applicable to both drugs and devices, including the Quality System ("QS") regulations applicable to medical devices.

Drug-device combination products present unique challenges for competitors seeking approval of an ANDA for generic versions of combination products. Generally, FDA reviews both the drug and device constituents of a proposed generic product to determine whether it is the same as the innovator product, including whether the basic design and operating principles of the device component

are the same and whether minor differences require significant differences in labeling for safe and effective use. If FDA determines that the device component of the proposed generic product is not the same in terms of performance and critical design, or that the labeling is not the same, it generally will not approve the ANDA. Likewise, if FDA determines that certain clinical studies, such as clinical usability or human factors studies, are necessary to demonstrate the safety and/or effectiveness of the device component, FDA generally will not accept or approve an ANDA for a combination product and will instead require the submission of a full NDA or 505(b)(2) application.

Post-Marketing Requirements

Any products for which we receive FDA approval are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse events with the product, providing the applicable regulatory authorities with updated safety and efficacy information, and product sampling and distribution requirements in accordance with the Prescription Drug Marketing Act ("PDMA"), a part of the FDCA, as well as the Drug Supply Chain Security Act ("DSCSA"). The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCSA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market. Moreover, each component of a combination product retains its regulatory status (as a drug or device, for example) and is subject to the requirements established by the FDA for that type of component. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market.

Prescription drug and biologic advertising is subject to federal, state and foreign regulations. In the United States, the FDA regulates prescription drug and biologic promotion and advertising, including direct-to-consumer advertising. Prescription drug and biologic promotional materials must be submitted to the FDA in conjunction with their first use. In addition, a pharmaceutical company must comply with restrictions on promoting drugs and biologics for uses or in patient populations that are not described in the drug’s or biologic's approved labeling (known as “off-label use”), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs or biologics for off-label uses, manufacturers are prohibited from marketing or promoting such off-label uses.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that combination products be manufactured in specific approved facilities and in accordance with CGMPs applicable to drugs, biologics and devices, including certain QS requirements. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with CGMP regulations. CGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from CGMP. Drug and biologics manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with CGMPs and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain CGMP compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA or BLA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to CGMPs, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA or BLA, including, among other things, recall or withdrawal of the product from the market.

The FDA also may require post-marketing testing, known as Phase 4 testing or REMS and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, untitled or warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product’s approved labeling, including the addition of new warnings and contraindications, and may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA’s policies may change, which could delay or prevent regulatory approval of our products under development and impact approved products already on the market.

Other Regulatory Matters

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, voluntary recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals,

exclusion from federal healthcare programs, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or effectiveness of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the voluntary recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Orphan Designation and Exclusivity

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States. Alternatively, orphan drug designation may be available if the disease or the condition affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different conditions. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another product with the same drug for the same condition under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity cannot assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, as amended, an NDA or supplement thereto 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. A sponsor who is planning to submit a marketing application for a drug product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan ("PSP") within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers if certain criteria are met. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials, and/or other clinical development programs. The requirements for pediatric data generally do not apply to drugs or biologics for an indication for which orphan designation has been granted.

Pediatric exclusivity is another type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent five-year and three-year and orphan exclusivity. This six-month exclusivity may be granted if an NDA or BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of FDA-requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Expedited Review and Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate the FDA's review and approval of new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for that disease or condition. For a Fast Track product, the FDA may consider sections of the NDA or BLA for

review on a rolling basis before the complete application is submitted if relevant criteria are met. In October 2020, we were granted Fast Track designation by the FDA for our novel formulation of diazepam.

A product candidate may also qualify for priority review, under which the FDA generally sets the target date for FDA action on the NDA or BLA that is subject to PDUFA goals at six months after the FDA accepts the application for filing, or for drugs that are not new chemical entities, six months after the FDA receives the application. Priority review is granted when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA PDUFA review period of ten months after the FDA accepts the application for filing, or for drugs that are not new chemical entities, ten months after FDA receives the application. Priority review designation does not change the scientific or medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve an NDA or BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after regulatory approvals are generally required to verify the drug or biologic's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. Drugs or biologics granted accelerated approval may be subject to expedited withdrawal procedures if the product sponsor fails to conduct the required post-marketing studies, or if such post-marketing studies fail to verify a clinical benefit.

The FDA also may designate a product candidate as a Breakthrough Therapy if it is intended, either 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. Breakthrough Therapy designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy designation is a distinct status from both accelerated approval and priority review, which also can be granted to the same drug or biologic if relevant criteria are met. If a product is designated as Breakthrough Therapy, the FDA will work to expedite the development and review of such product.

Fast Track designation, Breakthrough Therapy designation and priority review do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Regulations and Procedures Governing Approval of Medicinal Products in the European Union

In order to market any product outside the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety, and efficacy and governing, among other things, clinical trials, marketing authorization, pricing, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU generally follows the same lines as in the United States. It entails satisfactory completion of pharmaceutical development, preclinical studies, and adequate and well-controlled clinical trials to establish the safety and efficacy of the medicinal product for each proposed indication. It also requires the submission to the relevant competent authorities for clinical trials authorization and to the EMA for an MAA and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU. Similar requirements are necessary to conduct clinical trials in the United Kingdom, with the submission of an MAA to the CHMP for marketing authorization.

Clinical Trial Approval

In April 2014, the EU adopted the new Clinical Trials Regulation (EU) No 536/2014 (CTR), which replaced the Clinical Trials Directive. The CTR entered into application on January 31, 2022. The transitory provisions of the CTR offer sponsors the possibility to choose between the requirements of the previous Clinical Trials Directive and the CTR if the request for authorization of a clinical trial is submitted in the year after the CTR became applicable. If the sponsor chooses to submit under the Clinical Trials Directive, the clinical trial continues to be governed by the Clinical Trial Directive until three years after the CTR became applicable. If a clinical trial continues for more than three years after the CTR became applicable, the CTR will at that time begin to apply to the clinical trial. The CTR overhauls the current system of approvals for clinical trials in the EU. Specifically, the new legislation, which is directly applicable in all EU Member States (meaning no national implementing legislation in each Member State is required), aims at simplifying and streamlining the approval of clinical trials in the EU, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. For instance, the CTR provides for a streamlined application procedure via a single-entry point and strictly defined deadlines for the assessment of clinical trial applications. Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

Marketing Authorization

To obtain a marketing authorization for a product under EU regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid throughout the EU, and in the additional Member States of the European Economic Area (Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines), and products with a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions, and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

Under the centralized procedure, the CHMP is responsible for conducting the initial assessment of a product and for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days, excluding clock stops, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

National marketing authorizations, which are issued by the competent authorities of the Member States of the EU and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in a Member State of the EU, this national authorization can be recognized in other Member States through the mutual recognition procedure. If the product has not received a national authorization in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized marketing authorizations (under the Northern Ireland Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a current centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare Products Regulatory Agency (MHRA), the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required. The MHRA also has the power to have regard to marketing authorizations approved in EU Member States through decentralized or mutual recognition procedures with a view to more quickly granting a marketing authorization in the UK or Great Britain.

Data and Market Exclusivity

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. Data exclusivity, if granted, prevents applicants for authorization of generics or biosimilars of these innovative products from referencing the innovator's pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU, during a period of eight years from the date on which the reference product was first authorized in the EU. During an additional two-year period of market exclusivity, a generic or biosimilar MAA can be submitted and authorized, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Orphan Designation and Exclusivity

In the EU, the EMA's Committee for Orphan Medicinal Products ("COMP") grants orphan designation to promote the development of products that: (1) are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition: (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the necessary

investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention, or treatment of such condition has been authorized for marketing in the EU or, if such method exists, the product would be of a significant benefit to those affected by that condition. The application for orphan designation must be submitted before the application for marketing authorization.

In the EU, orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers, and 10 years of market exclusivity is granted following medicinal product approval. During the ten-year market exclusivity period, the EMA cannot accept an MAA, or grant a marketing authorization, or accept an application to extend a marketing authorization, for the same therapeutic indication, in respect of 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. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Market exclusivity would not prevent the approval of a similar medicinal product that is shown to be safer, more effective or otherwise clinically superior.

Regulation of Combination Products

The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. EU guidance has been published to help manufacturers select the right regulatory framework. In the case of drug-delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product, the medicinal product is regulated in accordance with the aforementioned rules while the device part is regulated as a medical device and will have to comply with all the requirements set by Regulation 2017/745, or the Medical Devices Regulation (which became applicable on 26 May 2021 and repealed the EU Council Directive 93/42/EEC, or the Medical Devices Directive). Where the medical device and medicinal product form a single integrated product (e.g. pre-filled inhalers), if the principal intended action is achieved by the medicine, the product is considered a medicinal product that includes a medical device and the entire product is regulated under the EU pharmaceutical legislation. However, the MAA for the product should include a CE certificate for the device in accordance with the Medical Devices Regulation or, if not CE marked but would need to be certified if marketed separately, the applicant must include an opinion from a notified body on conformity of device (except for Class I devices). This is a requirement under the new Medical Devices Regulation.

The characteristics of non-integral devices used for the administration of medicinal products may impact the quality, safety and efficacy profile of the medicinal products. To the extent that administration devices are co-packaged with the medicinal product or, in exceptional cases, where the use of a specific type of administration device is specifically provided for in the product information of the medicinal product, additional information may need to be provided in the MA application for the medicinal product on the characteristics of the medical device(s) that may impact on the quality, safety and/or efficacy of the medicinal product. The requirements regarding quality aspects for integral drug-device combination products, including devices that are co-packaged with medicinal products, are outlined in an EMA guideline which came into effect on January 1, 2022.

The EU requires that all medical devices placed on the market in the EU must meet the relevant general safety and performance requirements laid down in Annex I of the Medical Devices Regulation. The most fundamental requirement is that a medical device must be designed and manufactured in such a way that it will not compromise the clinical condition or safety of patients, or the safety and health of users and others. In addition, the device must achieve the performances intended by the manufacturer and be designed, manufactured, and packaged in a suitable manner. To demonstrate compliance with the general safety and performance requirements laid down in Annex I to the Medical Devices Regulation, medical device manufacturers must undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. Conformity assessment procedures require an assessment of available clinical evidence, literature data for the product, and post-market experience in respect of similar products already marketed. Except for low-risk medical devices (Class I non-sterile, non-measuring devices), where the manufacturer can self-declare the conformity of its products with the general safety and performance requirements (except for any parts which relate to sterility or metrology), a conformity assessment procedure requires the intervention of a Notified Body. Notified Bodies are independent organizations designated by EU countries to assess the conformity of devices before being placed on the market. If satisfied that the relevant product conforms to the relevant general safety and performance requirements, the Notified Body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE Mark to the device, which allows the device to be placed on the market throughout the EU.

As a general rule, demonstration of conformity of medical devices and their manufacturers with the general safety and performance requirements must be based, among other things, on the evaluation of clinical data supporting the safety and performance of the products during normal conditions of use. Specifically, a manufacturer must demonstrate that the device achieves its intended performance during normal conditions of use, that the known and foreseeable risks, and any adverse events, are minimized and acceptable when weighed against the benefits of its intended performance, and that any claims made about the performance and safety of the device are supported by suitable evidence.

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

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the UK voted in favor of leaving the EU, commonly referred to as Brexit, and the UK formally left the EU on January 31, 2020. There was a transition period during which EU pharmaceutical laws continued to apply to the UK, which

expired on December 31, 2020. However, the EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework will continue to apply in Northern Ireland). The regulatory regime in Great Britain therefore largely aligns with current EU regulations, however it is possible that these regimes will diverge in future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation.

Other Healthcare Laws and Compliance Requirements

In addition to FDA restrictions on the marketing of pharmaceutical products and medical devices, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. Although we do not provide healthcare services, submit claims for third-party reimbursement, or receive payments directly from Medicare, Medicaid or other third-party payors for our products, we are subject to broadly applicable healthcare fraud and abuse regulation and enforcement by federal and state governments, which could significantly impact our business. Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including the Centers for Medicare & Medicaid Services ("CMS"), other divisions of the Department of Health and Human Services ("HHS"), the Department of Justice ("DOJ"), the Drug Enforcement Administration ("DEA"), the Consumer Product Safety Commission ("CPSC"), the Federal Trade Commission ("FTC"), the Occupational Safety & Health Administration ("OSHA"), the Environmental Protection Agency ("EPA"), and state and local governments. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by the federal government and the states in which we conduct our business as well as in foreign jurisdictions in which we may conduct trials or where we may otherwise be subject to local regulation. The laws that may affect our ability to operate include:

- Anti-Kickback Statute ("AKS"). The federal AKS makes it illegal for any person or entity (including a prescription drug manufacturer or a party acting on its behalf) to knowingly and willfully solicit, offer, receive or pay remuneration, directly or indirectly, in cash or in kind, in exchange for or intended to induce or reward either the referral of an individual for, or the purchase, order, prescription or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, they are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. A person or entity can be found guilty of violating the AKS without actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties statute. Violations of the AKS carry potentially significant civil and criminal penalties, including imprisonment, fines, administrative civil monetary penalties, and exclusion from participation in federal healthcare program;
- The federal civil and criminal false claims and civil monetary penalties laws, including the federal False Claims Act ("FCA"), prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using or causing to be made or used a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Companies that submit claims directly to payors also may be liable under the FCA for the direct submission of such claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;
- the anti-inducement law prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a federal or state governmental program;

- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH") and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, 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, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. In addition, HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or 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, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to HHS information regarding any payment or other "transfer of value" made or distributed to healthcare professionals (currently defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the healthcare professionals and their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners.
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics in an accurate and timely manner to government programs;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- The Foreign Corrupt Practices Act ("FCPA"), which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment.

Additionally, we may be subject to state and non-U.S. equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare services reimbursed by any source, not just governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements, and if we fail to comply with an applicable state law requirement, we could be subject to penalties. Finally, there are state and non-U.S. laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws.

Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including penalties, fines, disgorgement, imprisonment and/or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government. In addition, private individuals have the ability to bring actions on behalf of the U.S. government under the federal False Claims Act as well as under the false claims laws of several states.

Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our current and future business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our arrangements with physicians and other healthcare providers, some

of whom receive stock options as compensation for services provided, may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our drug candidates outside the United States also will likely subject us to non-U.S. equivalents of the healthcare laws mentioned above, among other non-U.S. laws.

If any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, which also may adversely affect our business.

We may be subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

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

In the U.S., to help patients afford our approved product, we may utilize programs to assist them, including patient assistance programs (PAPs) and co-pay coupon programs for eligible patients. PAPs are regulated by and subject to guidance from CMS OIG. In addition, at least one insurer has directed its network pharmacies to no longer accept co-pay coupons for certain specialty drugs the insurer identified. Our co-pay coupon programs could become the target of similar insurer actions. In addition, in November 2013, the CMS issued guidance to the issuers of qualified health plans sold through the ACA's marketplaces encouraging such plans to reject patient cost-sharing support from third parties and indicating that the CMS intends to monitor the provision of such support and may take regulatory action to limit it in the future. The CMS subsequently issued a rule requiring individual market qualified health plans to accept third-party premium and cost-sharing payments from certain government-related entities. In September 2014, the OIG of the HHS issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and/or civil monetary penalty laws if they do not take appropriate steps to exclude Part D beneficiaries from using co-pay coupons. Accordingly, companies exclude these Part D beneficiaries from using co-pay coupons.

On December 2, 2020, the HHS published 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 (PBMs), unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between PBMs and manufacturers. Implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and PBM service fees are currently under review by the current U.S. presidential administration and may be amended or repealed. Further, on December 31, 2020, CMS published a new rule, effective January 1, 2023, requiring manufacturers to ensure the full value of co-pay assistance is passed on to the patient or these dollars will count toward the Average Manufacturer Price and Best Price calculation of the drug. On May 21, 2021, PhRMA sued the HHS in the U.S. District Court for the District of Columbia, to stop the implementation of the rule claiming that the rule contradicts federal law surrounding Medicaid rebates. It is unclear how the outcome of this litigation will affect the rule. We cannot predict how the implementation of and any further changes to this rule will affect our business.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. For example, in March 2010, the ACA was enacted in the United States. The ACA includes measures that have significantly changed, and are expected to continue to significantly change, the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA of greatest importance to the pharmaceutical industry are that the ACA:

- Made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs to 23.1% of average manufacturer price, or AMP, and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP.
- Imposed a requirement on manufacturers of branded drugs to provide a 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discount off the negotiated price of branded drugs dispensed to Medicare Part D beneficiaries in the coverage gap (i.e., "donut hole") as a condition for a manufacturer's outpatient drugs being covered under Medicare Part D.
- Extended a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations.
- Expanded the entities eligible for discounts under the 340B Drug Discount Program.
- Established a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected.
- Imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs, apportioned among these entities according to their market share in certain government healthcare programs.
- Established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products. The ACA established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business. Prior to the Biden administration, on October 13, 2017, former President Trump signed an Executive Order which terminated the cost sharing subsidies that reimburse insurers under the ACA. The former Trump administration concluded that cost-sharing reduction, or CSR, payments to insurance companies required under the ACA have not received necessary appropriations from Congress and announced that it will discontinue these payments immediately until those appropriations are made. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. On August 14, 2020, the U.S. Court of Appeals for the Federal Circuit ruled in two separate cases that the federal government is liable for the full amount of unpaid CSRs for the years preceding and including 2017. For CSR claims made by health insurance companies for years 2018 and later, further litigation will be required to determine the amounts due, if any. Further, on June 14, 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued the payments were owed to them. On April 27, 2020, the United States Supreme Court reversed the U.S. Court of Appeals for the Federal Circuit's decision and remanded the case to the U.S. Court of Federal Claims, concluding the government has an obligation to pay these risk corridor payments under the relevant formula. It is unclear what impact these rulings will have on our business.

In addition, other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted:

- On August 2, 2011, the U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the temporary suspension, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022.
- On January 2, 2013, the U.S. American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.
- On April 13, 2017, CMS published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.
- On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.
- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.
- On December 20, 2019 former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the Cadillac tax, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At a federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021 CMS rescinded the Most Favored Nations rule. Additionally, on November 30, 2020, HHS published 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 new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that additional foreign, federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our products or product candidates, once approved, or additional pricing pressures.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidate for which we obtain regulatory approval. In the United States and markets in other countries, sales of any product candidates for which we receive regulatory approval for commercial sale will depend, in part, on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. A decision by a third-party payor not to cover our products or product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In addition, coverage and reimbursement for products can differ significantly from payor to payor. One third-party payor's decision to cover a particular pharmaceutical drug product or service does not ensure that other payors will also provide coverage for the pharmaceutical drug product or service or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of pharmaceutical drug products and services, in addition to their safety and efficacy. In order to obtain and maintain coverage and reimbursement for any product, we may need to conduct expensive clinical trials in order to demonstrate the medical necessity and cost-effectiveness of such product, in addition to the costs required to obtain regulatory approvals. Our products may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 ("ACA") contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must 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 formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

In addition, there have been several changes to the 340B drug pricing program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain health care facilities. On December 27, 2018, the District Court for the District of Columbia invalidated a reimbursement formula change under the 340B drug pricing program, and CMS subsequently altered the FYs 2019 and 2018 reimbursement formula on specified covered outpatient drugs ("SCODs"). The court ruled this change was not an "adjustment" which was within the Secretary's discretion to make but was instead a fundamental change in the reimbursement calculation. However, most recently, on July 31, 2020, the U.S. Court of Appeals for the District of Columbia Circuit overturned the district court's decision and found that the changes were within the Secretary's authority. On September 14, 2020, the plaintiffs-appellees filed a Petition for Rehearing En Banc (i.e., before the full court), but was denied on October 16, 2020. Plaintiffs-appellees filed a petition for a writ of certiorari at the Supreme Court on February 10, 2021. On Friday July 2, 2021, the Supreme Court granted the petition. It is unclear how these developments could affect covered hospitals who might purchase our future products and affect the rates we may charge such facilities for our approved products in the future, if any.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by HHS, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our drugs, if any such drug or the condition that they are intended to treat are the subject of a trial. It also is possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of our drugs after approval. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

These laws and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our products or product candidates for which we may obtain regulatory approval or the frequency with which any such product is prescribed or used.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. We expect that an increasing emphasis on cost containment measures in the United States will continue to increase the pressure on pharmaceutical pricing. 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 of our products or product candidates for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, the pricing of pharmaceutical products and medical devices is subject to governmental control in many countries. For example, in the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular therapy to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. Other countries may allow companies to fix their own prices for products but monitor and control product volumes and issue guidance to physicians to limit prescriptions. Efforts to control prices and utilization of pharmaceutical products and medical devices likely will continue as countries attempt to manage healthcare expenditures.

Human Capital Resources

As of December 31, 2021, we had 294 full-time employees in the United States, 164 of whom were primarily engaged in sales and marketing, 85 of whom were primarily engaged in general administration, and 45 of whom were primarily engaged in product development and research.

We believe our success will depend on, among other things, our ability to continue to hire and retain the necessary qualified personnel across all departments in our organization, as we expand the commercialization of our products. Our President and Chief Operating Officer and Vice President, Human Resources are responsible for developing and executing our human capital strategy. This includes the attraction, acquisition, development and engagement of talent to deliver on the Company's strategy. the executive management team regularly updates our board of directors and its committees on the operation and status of our human capital trends and activities.

Diversity, Equity and Inclusion

We are committed to building a company that provides an inclusive environment where we invite and encourage diverse perspectives, ideas, and people. With that goal in mind, we have established a committee comprised of employees and sponsored by key executive team members to build a strategy designed to promote a diverse and inclusive work environment. We believe these initiatives and a workforce with diverse backgrounds, experiences and viewpoints will continue to bring innovative solutions to the Company. In addition, we have sought to implement recruiting practices and to work with recruiting partners who can help us best identify and attract diverse candidates. We continue to expand our systems to track key human capital metrics such as demographics, diversity, compensation and benefits, and engagement and to think of new ways to best support our female and underrepresented employees to help advance their careers.

Training and Talent Development

We believe that our employees are the key to our success, and we believe their development is what drives our growth and prosperity as a company. To support employee development, as well as plan for short and long term business success, we review and update a company succession plan regularly and we offer a number of development opportunities for our employees through various methods. Our succession plan is reviewed with the board annually. In addition, upon joining the company, all new employees are required to become familiar with our policies, including our Code of Business Conduct and Ethics and Employee Handbook, and complete compliance training, and existing employees are required to acknowledge current policies annually.

Compensation and Benefits

An important part of attracting and retaining key talent is competitive pay and benefits. To ensure our compensation and benefits programs are competitive, we engage nationally recognized outside compensation and benefits consulting firms to independently evaluate the effectiveness of our programs and to provide benchmarking against our peers within the industry. Our pay for

performance philosophy seeks to motivate and reward employees while accomplishing the Company's short and long-term strategic goals. As part of a robust performance management process, employees are evaluated both on what they accomplished and how they demonstrated our values. Annual salary increases and incentive bonuses are based on both individual and corporate performance factors.

As a long-term incentive, to encourage our employees to think like owners and share in the Company's long-term success, employees are granted equity in the form of stock options or restricted stock units and can elect to participate in our employee stock purchase plan. Employees are generally eligible for health insurance, paid and unpaid leaves including paid parental leave, paid caregiver leave, retirement plans with an employer contribution match, life and disability/accident coverage, parking or commuter assistance, an employee assistance program providing mental health, legal and financial health resources, and access to convenient COVID-19 testing.

Health and Safety

We are committed to the safety of our employees and the communities we serve. We provide regular health and safety training programs for employees, which includes, upon on-boarding, an overview during new hire orientation, as well as ongoing training throughout the year.. Employees are trained on workplace safety, including security and inspection, work related injuries and emergency protocols as applicable for their role and work location. In addition, special health and safety training is conducted for laboratory staff.

Also, in response to the COVID-19 pandemic, we quickly implemented policies to protect our employees and provide solutions to enable our employees to manage their work and personal responsibilities. In addition, a Pandemic Response Team was established, comprised of senior leaders, to help guide and direct activities associated with local governance and business requirements during the COVID-19 pandemic. Refer to "Impact of COVID-19" included in Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" for information on Human Capital Management actions taken by the Company in response to the COVID-19 pandemic.

Corporate Information

We were incorporated under the laws of the State of Delaware in 2005. Our principal offices are located at 180 N. LaSalle Street, Suite 1600, Chicago, Illinois 60601, and our telephone number is (844) 445-5704. We completed our initial public offering of common stock in June 2018, and our common stock is listed on The Nasdaq Global Select Market under the symbol "XERS." Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report on Form 10-K.

Available Information

Our website address is www.xerispharma.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended ("Exchange Act") are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at *http://www.sec.gov*. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Our code of conduct, corporate governance guidelines and the charters of our Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are available through our website at www.xerispharma.com.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. Careful consideration should be given to the following risk factors, in evaluating us and our business. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks summarized and described below are not intended to be exhaustive and are not the only risks facing us. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.

Risks Related to the Impact of the COVID-19 Pandemic

Our business may be adversely affected by the ongoing coronavirus pandemic.

Our business could be adversely affected by health epidemics in regions where we have business activities and could cause significant disruption in the operations of third-party manufacturers and contract research organizations ("CROs") upon whom we rely, and for which we may not have adequate insurance coverage. For example, beginning in late 2019, the outbreak of a novel strain of virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes coronavirus disease 2019, or COVID-19, evolved into a global pandemic. The coronavirus spread globally, and the impact of the outbreak is continually evolving, particularly in light of new variants of COVID-19.

As a result of the ongoing COVID-19 pandemic, we may experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- We believe that the COVID-19 pandemic has had, and may continue to have, an adverse impact on demand for certain of our products due to government-imposed quarantines, stay-at-home orders, travel restrictions, mandated business closures and other public health safety measures which may result in patients not visiting their healthcare providers or their pharmacies to get their prescriptions filled. Initially, we suspended in-person interactions by our sales and marketing personnel in healthcare settings. We were engaging with these customers remotely, via webinar programs and virtual meetings, as we sought to continue to support healthcare professionals and patient care. As parts of the country reopened, some of our sales and marketing personnel began to reengage with a limited number of in-person interactions. With the emergence of variants and, in some areas, lack of acceptance of vaccines, some areas implement or reintroduce restrictions, which may impact our sales and marketing personnel's access to customers. Remote interactions may be less effective as in-person interactions. In addition, several conferences and other programs at which we intended to market our products have been postponed, canceled and/or transitioned to virtual meetings. In addition, due to the prioritization of healthcare resources toward pandemic efforts, even remote interactions may not be possible.
- We currently rely on third-party suppliers and contract manufacturing organizations ("CMOs") for the manufacturing of Gvoke, Keveyis, and Recorlev, as well as to perform third-party logistics functions, including warehousing and distribution of Gvoke, Keveyis, and Recorlev. In addition, we rely on third parties to perform quality testing and supply other goods and services to run our business. If any such third party in our supply chain for materials is adversely impacted by restrictions resulting from the COVID-19 pandemic or supply chain issues, including staffing shortages, production slowdowns and disruptions in delivery systems, our supply chain may be disrupted, limiting our ability to manufacture commercial quantities.
- In March 2020, we closed our offices and requested that most of our personnel, including all of our administrative employees, work remotely, restricted on-site staff to only those personnel and contractors who must perform essential activities that must be completed on-site and limited the number of staff in any given location. We have since reopened our offices on a voluntary basis and have implemented safety measures designed to comply with applicable federal, state and local guidelines in response to the COVID-19 pandemic. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. Further, this could increase our cybersecurity risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, research or clinical trial sites and other important agencies and contractors.
- Although essential personnel in our laboratory currently remain on-site, they and other employees and contractors conducting research and development activities on our behalf may not be able to access our laboratory or conduct such activities for an extended period of time in the event of the closure of our offices or the offices of our contractors and/or the possibility that governmental authorities further modify current restrictions. As a result, this could delay timely completion of preclinical activities.

- Health regulatory agencies globally may experience disruptions in their operations as a result of the coronavirus pandemic. The FDA and comparable foreign regulatory agencies may have slower response times or be under-resourced to continue to monitor our clinical trials and, as a result, review, inspection, and other timelines may be materially delayed. It is unknown how long these disruptions could continue, were they to occur. Any elongation or deprioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates. For example, regulatory authorities may require that we not distribute a product candidate lot until the relevant agency authorizes its release. Such release authorization may be delayed as a result of the coronavirus pandemic and could result in delays to our clinical trials.
- The trading prices for our common shares and other biopharmaceutical companies have been highly volatile as a result of the coronavirus pandemic. As a result, we may face difficulties raising further capital through sales of our common shares or convertible debt or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the spread of the coronavirus could materially and adversely affect our business and the value of our common shares.

Since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have received Emergency Use Authorization by the FDA and two of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials and/or commercial product, which could lead to delays in these trials and/or issues with our commercial supply.

The coronavirus pandemic continues to rapidly evolve. The ultimate impact of the coronavirus pandemic on our business operations is highly uncertain and subject to change and will depend on future developments, which cannot be accurately predicted, including the duration of the pandemic, the emergence of new variants, the acceptance and availability of vaccines in various geographies, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19 and the actions taken to contain coronavirus or address its impact in the short and long term, among others. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, our research programs, healthcare systems or the global economy. We will continue to monitor the situation closely.

Risks Related to our Financial Position and Need for Financing

Risks Related to Our Operating History

As a company, we have a limited operating history and limited experience commercializing pharmaceutical products and have incurred significant losses since inception. We expect to incur losses over the next few years and may not be able to achieve or sustain revenues or profitability in the future.

Historically, we have funded our operations primarily through private placements of convertible preferred stock, public offerings of common stock and convertible notes, and debt issuances. We commercially launched Gvoke PFS in November 2019, Gvoke HypoPen in July 2020 and Recorlev in January 2022. Strongbridge commercially launched Keveyis in April 2017. We are in the early stages of commercializing our biopharmaceutical products and have a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies prior to and at the early stages of commercialization of any product candidates, especially biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully commercializing biopharmaceutical products. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to successfully execute our commercialization strategy and may not be successful in doing so. We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We have incurred significant losses in every fiscal year since inception. For the year ended December 31, 2021 and 2020, we reported a net loss of $122.7 million and $91.1 million, respectively. In addition, our accumulated deficit as of December 31, 2021 was $460.1 million. Substantially all of our operating losses have resulted from costs incurred in connection with research and development, clinical and regulatory initiatives to obtain approvals for our product candidates and preparation for commercialization of Gvoke.

We expect to continue to incur significant operating expenses as we continue the commercialization of Gvoke, Keveyis and Recorlev, develop, enhance and commercialize new products (including Recorlev), and incur additional operational and reporting costs associated with being a public company. In particular, we anticipate that we will continue to incur significant expenses as we:

- execute our Gvoke, Keveyis and Recorlev commercial strategies in the U.S.;
- continue our research and development efforts;
- seek regulatory approval for new product candidates and product enhancements;

- integrate the combined company; and
- continue to operate as a public company.

Gvoke was approved by the FDA for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages two years and above on September 10, 2019. In February 2021 the European Commission ("EC") granted marketing authorization and in April 2021 the United Kingdom's Medicines and Healthcare products Regulatory Agency approved Ogluo for the treatment of severe hypoglycemia in adults, adolescents, and children aged two years and over with diabetes mellitus. On July 19, 2021, we announced that we had entered into an exclusive agreement with Tetris Pharma Limited ("Tetris") for the commercialization of Ogluo in the European Economic Area, United Kingdom, and Switzerland (the "Territory"). Under the terms of the applicable agreements, Xeris will be responsible for product supply and Tetris will be responsible for commercialization of Ogluo in the Territory. Tetris launched Ogluo in the United Kingdom in December 2021. Our ability to generate revenue from Gvoke, Keveyis and Recorlev and our product candidates and to transition to profitability and generate positive cash flows is uncertain and depends on the successful commercialization of Gvoke, Keveyis and Recorlev and any of our product candidates for which we obtain marketing approval. Many of our product candidates are still in development. Successful development and commercialization will require achievement of key milestones, including completing clinical trials and obtaining marketing approval for our product candidates, manufacturing, marketing and selling those products for which we, or any of our future collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues, and if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If we continue to suffer losses as we have in the past, investors may not receive any return on their investment and may lose their entire investment.

Although we generate revenue from Gvoke, Keveyis and Recorlev, we have not yet generated revenue from any of our current or future product candidates, and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. Our ability to generate revenue from Gvoke, Keveyis and Recorlev, and our product candidates, if successfully developed and approved, depends on a number of factors, including, but not limited to, our ability to:

- obtain commercial quantities of our products at acceptable cost levels;
- achieve an adequate level of market acceptance of our products in the medical community and with third-party payors, including placement in accepted clinical guidelines for the conditions for which our product candidates are intended to target;
- obtain and maintain third-party coverage and adequate reimbursement for our products;
- launch and commercialize our products utilizing our own sales force or by entering into partnership or co-promotion arrangements with third parties; and
- successfully develop and obtain marketing approval for our product candidates.

We have incurred and expect to continue to incur significant sales and marketing costs as we commercialize Gvoke, Keveyis and Recorlev. Regardless of these expenditures, our products and our product candidates, if approved, may not be commercially successful. Although we generate revenue from Gvoke, Keveyis and Recorlev, if we are unable to generate sufficient product revenue, we will not become profitable and may be unable to continue operations without continued funding.

Risks Related to Future Financial Condition

We may require additional capital to sustain our business, and this capital may cause dilution to our stockholders and might not be available on terms favorable to us, or at all, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

Biopharmaceutical development is a time consuming, expensive and uncertain process that takes years to complete. We are incurring significant commercialization expenses related to product sales, marketing, manufacturing, packaging and distribution of Gvoke, Keveyis and Recorlev and expect to continue to incur such expenses for our products, as well as for any of our product candidates, if approved. We expect to require additional capital to complete the clinical trials associated with our product candidates and begin commercialization efforts, if approved. Accordingly, we may need additional funding in connection with our continuing operations. In the future, if we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our research and development programs and/or sales and marketing activities. Market volatility resulting from the ongoing COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed.

We may be required to or choose to obtain further funding through public equity offerings, debt financings, royalty-based financing arrangements, collaborations and licensing arrangements or other sources. If we raise additional funds through further issuances of equity or convertible debt securities, our existing stockholders could suffer significant dilution, and any new equity securities we issue could have rights, preferences and privileges superior to those of holders of our common stock. Any debt financing obtained by us would be senior to our common stock, would likely cause us to incur interest expense, and could involve restrictive covenants relating to our capital raising activities and other financial and operational matters, which may increase our expenses and make it more difficult for us to obtain additional capital and to pursue business opportunities, including potential acquisitions and in-licensing opportunities. Under our existing credit facility, the Amended and Restated Loan and Security Agreement dated September 10, 2019 (as amended, supplemented or otherwise modified from time to time, including by that certain First Amendment to the Amended and Restated Loan and Security Agreement dated April 21, 2020, that certain Second Amendment to Amended and Restated Loan and Security Agreement dated June 30, 2020, that certain Third Amendment to Amended and Restated Loan and Security Agreement dated August 5, 2020, that certain Fourth Amendment to the Amended and Restated Loan and Security Agreement dated October 23, 2020, that certain Fifth Amendment to Amended and Restated Loan and Security Agreement dated May 3, 2021, that certain Consent under Loan and Security Agreement dated May 24, 2021, and that certain Joinder and Sixth Amendment to Amended and Restated Loan and Security Agreement dated October 5, 2021, collectively, the “Amended Loan Agreement”) with Oxford Finance LLC, as the collateral agent and a lender, and Silicon Valley Bank, as a lender, Xeris Biopharma Holdings, Inc., Xeris Pharmaceuticals, Inc. and Strongbridge U.S. Inc., we are restricted in our ability to incur additional indebtedness and to pay dividends but, in connection with our public notes offering, the Lenders consented to the Convertible Notes (defined below) offering as permitted convertible indebtedness. Any additional debt financing that we may secure in the future could include similar or more restrictive covenants relating to our capital raising activities, buying or selling assets and other financial and operational matters, which may make it more difficult for us to obtain additional capital, manage our business and pursue business opportunities. We may also be required to secure any such debt obligations with some or all of our assets. For example, our Amended Loan Agreement is secured by substantially all of our property and assets, including our intellectual property assets, subject to certain exceptions.

If we raise additional funds through collaborations or marketing, distribution or licensing, or royalty-based financing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. Securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management’s ability to oversee the commercialization of our products and development and commercialization, if approved, of our product candidates. It is also possible that we may allocate significant amounts of capital toward solutions or technologies for which market demand is lower than anticipated and, as a result, abandon such efforts. Any of these negative developments could have a material adverse effect on our business, operating results, financial condition and common stock price.

We may not have cash available to us in an amount sufficient to enable us to make interest or principal payments on our indebtedness when due, or repurchase our Convertible Notes for cash following a fundamental change, and our existing and future indebtedness may limit our ability to repurchase the Convertible Notes.

On June 30, 2020, we completed a public offering of $86.3 million aggregate principal amount of our 5.00% Convertible Senior Notes due 2025 (the "Convertible Notes"), including $11.3 million pursuant to the underwriters' option to purchase additional notes which was exercised in July 2020. A total principal amount of $39.1 million of Convertible Notes converted into equity in the second half of 2020. As of December 31, 2021, the outstanding balance of Convertible Notes was $47.2 million. The Convertible Notes are governed by the terms of a base indenture for senior debt securities dated June 30, 2020 (the “Base Indenture”), as supplemented by the first supplemental indenture thereto dated June 30, 2020 and the second supplemental indenture thereto dated October 5, 2021 ("the Supplemental Indentures" and together with the Base Indenture, the "Indenture"), each between us and U.S. Bank National Association, as trustee. Failure to satisfy our current and future debt obligations under the Indenture could result in an event of default and, as a result, all of the amounts outstanding could immediately become due and payable. In the event of an acceleration of amounts due under the Indenture as a result of an event of default, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness.

Noteholders may require us to repurchase their Convertible Notes following a fundamental change at a cash repurchase price generally equal to the principal amount of the Convertible Notes to be repurchased, plus accrued and unpaid interest, if any. A fundamental change includes certain acquisition transactions and the failure of our common stock to be listed on the Nasdaq Global Select Market or certain similar national securities exchanges. We may not have enough available cash or be able to obtain financing at the time we are required to repurchase the Convertible Notes. In addition, applicable law, regulatory authorities and the agreements governing our existing and future indebtedness may restrict our ability to repurchase the Convertible Notes. Our failure to repurchase the Convertible Notes when required will constitute a default under the Indenture that governs the Convertible Notes. A default under the Indenture or the fundamental change itself could also lead to a default under agreements governing our other existing or future indebtedness, which may result in that other indebtedness becoming immediately payable in full. For instance, a fundamental change without lender consent would constitute an event of default under our Amended Loan Agreement. We may not have sufficient funds to satisfy all amounts due under the other indebtedness and the Convertible Notes.

In addition, we have $43.5 million outstanding under our Amended Loan Agreement as of December 31, 2021. All obligations under our Amended Loan Agreement are secured by substantially all of our property and assets, including our intellectual property assets, subject to certain limited exceptions. The term loans and the Convertible Notes may create additional financial risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations at maturity. Failure to satisfy our current and future debt obligations under our Amended Loan Agreement could result in an event of default and, as a result, our lenders could accelerate all amounts due. Events of default also include our failure to comply with customary affirmative and negative covenants as well as a default under any indenture or other agreement governing convertible indebtedness permitted by the Amended Loan Agreement, including the Indenture. Affirmative covenants include the maintenance of a minimum cash balance of $5.0 million in an account with Silicon Valley Bank and, in the event that we also maintain one or more permitted accounts at other institutions, an additional amount equal to the outstanding obligations. Negative covenants include prohibition on the payment of dividends and distributions, certain mergers and change of control events, and restrictions on the incurrence of additional debt. In addition, the occurrence of material adverse changes in our business, including our prospect of repayment of our obligations, could result in an event of default. In the event of an acceleration of amounts due under our Amended Loan Agreement as a result of an event of default, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness. In addition, our lenders could seek to enforce their security interests in any collateral securing such indebtedness.

Our PPP Loan, which we repaid in full in June 2020, was subject to the terms and conditions applicable to loans administered by the SBA under the CARES Act, and we may be subject to an audit or enforcement action related to the PPP Loan.

On April 21, 2020, we entered into the U.S. Small Business Administration (the "SBA") PPP Note (the "Note") with Silicon Valley Bank (the “PPP Lender”) for a loan in the amount of $5.1 million (the “PPP Loan”) enabled by the Coronavirus Aid, Relief and Economic Security Act of 2020 (the "CARES Act"). We received the full amount of the PPP Loan on April 22, 2020. On May 4, 2020, we repaid $0.9 million of the PPP Loan. In June 2020, we repaid the remaining amount outstanding under the PPP Loan in connection with the concurrent Convertible Notes and equity offerings.

We may be subject to CARES Act-specific lookbacks and audits that may be conducted by other federal agencies, including several oversight bodies created under the CARES Act. These bodies have the ability to coordinate investigations and audits and refer matters to the Department of Justice for civil or criminal enforcement and other actions. Complying with such SBA audit could divert management resources and attention and require us to expend significant time and resources, which could have an adverse effect on our business, financial condition and results of operations.

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

Risks Related to Commercialization and Marketing

Our business depends entirely on the commercial success of our products and product candidates. Even if approved, our product candidates may not be accepted in the marketplace and our business may be materially harmed.

To date, we have expended significant time, resources and effort on the development of our product candidates, and a substantial portion of our resources recently has been and will continue to be focused on launching, marketing and commercializing our products, Gvoke, Keveyis and Recorlev, in the United States. Our business and future success are substantially dependent on our ability to generate and increase product revenues in the near term. Our estimates of the potential market opportunity for Gvoke, Keveyis, Recorlev and our product candidates include several key assumptions of the current market size and current pricing for commercially available products and are based on industry and market data obtained from industry publications, studies conducted by us, our industry knowledge, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, if any of these assumptions proves to be inaccurate, the actual market for our product and product candidates could be smaller than our estimates of our potential market opportunity. Our product candidates are in various stages of development and subject to the risks of failure inherent in developing drug products. Any delay or setback in the regulatory approval, product launch, commercialization or distribution of any of our product candidates will adversely affect our business. There is no guarantee that the infrastructure, systems, processes, policies, relationships and materials we have built for the commercialization of Gvoke, Keveyis and Recorlev will be sufficient for us to achieve success at the levels we expect. Further, our products may contain undetected manufacturing defects, including mislabeling, which might require product replacement, re-labeling or product recalls, which could further harm our business. See the section entitled, "*Business — Coverage and Reimbursement*".

Even if all regulatory approvals are obtained, the commercial success of our products and product candidates will depend on gaining market acceptance among physicians, patients, patient advocacy groups, healthcare payors and the medical community. The degree of market acceptance of our products and product candidates will depend on many factors, including:

- the scope of regulatory approvals, including limitations or warnings contained in a product's regulatory-approved labeling;
- our ability to produce, through a validated process, sufficiently large quantities of our products to permit successful commercialization;
- our ability to establish and maintain commercial manufacturing arrangements with third-party manufacturers;
- our ability to build and maintain sales, distribution and marketing capabilities sufficient to launch commercial sales of our products;
- the acceptance in the medical community of the potential advantages of the products, including with respect to our efforts to increase adoption of our products by patients and healthcare providers;
- the incidence, prevalence and severity of adverse side effects of our products;
- the willingness of physicians to prescribe our products and of the target patient population to try these therapies;
- the price and cost-effectiveness of our products;
- the availability of sufficient third-party coverage and reimbursement, including the extent to which each product is approved for use at, or included on formularies of, hospitals and managed care organizations;
- any negative publicity related to our or our competitors' products or other formulations of products that we administer, including as a result of any related adverse side effects;
- alternative treatment methods and potentially competitive products;
- the potential advantages of our products over existing and future treatment methods; and
- the strength of our sales, marketing and distribution support.

Additionally, if, after marketing approval of any of our products or product candidates, we or others later identify undesirable or unacceptable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product, require us to take our approved product off the market or ask us to voluntarily remove the product from the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- regulatory authorities may impose conditions under a risk evaluation and mitigation strategy ("REMS") including distribution of a medication guide to patients outlining the risks of such side effects or imposing distribution or use restrictions;
- we may be required to change the way a product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- we may be subject to litigation or products liability claims; and
- our reputation may suffer.

If our product candidates are approved but do not achieve an adequate level of acceptance by physicians, patients and third-party payors, we may never generate significant revenue from these products, and our business, financial condition and results of operations may be materially harmed. Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new therapeutics are introduced that are more favorably received than our products or that render our products obsolete, or if significant adverse events occur. If our products do not achieve and maintain market acceptance, we will not be able to generate sufficient revenue from product sales to attain profitability.

If we are unable to establish or do not maintain sufficient marketing, sales and distribution capabilities or enter into agreements with third parties to market, sell and distribute our products on terms acceptable to us, we may not be able to generate product revenues and our business, results of operations, and financial condition will be materially adversely affected.

We have developed our commercial infrastructure for the sales, marketing and distribution of Gvoke, Keveyis, and Recorlev. In order to successfully commercialize our product candidates, we will need to maintain and may need to expand our marketing, sales, distribution, managerial and other non-technical capabilities and/or make arrangements with third parties to perform some or all of these services. We have established and recently expanded our sales force to market our products in the United States. There are significant expenses and risks involved with establishing our own sales and marketing capabilities, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, obtain access to an adequate number of physicians and persuade them to prescribe our products and any product candidates that receive regulatory approval, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in our ability to maintain or expand, if needed, our internal sales, marketing and distribution capabilities would adversely impact the commercialization of Gvoke, Keveyis and Recorlev and the launch and commercialization of our product candidates, if approved.

We cannot be sure that we will be able to recruit, hire and retain a sufficient number of sales representatives or that they will be effective at promoting our products. In addition, we will need to commit significant additional management and other resources to establish and grow our sales organization. We may not be able to achieve the necessary development and growth in a cost-effective manner or realize a positive return on our investment. We will also have to compete with other companies to recruit, hire, train and retain sales and marketing personnel.

In the event that we are unable to effectively deploy our sales organization or distribution strategy on a timely and efficient basis, if at all, the commercialization of our product candidates could be delayed which would negatively impact our ability to generate product revenues. For example, as a result of the COVID-19 pandemic, we have had to limit in-person interactions and engage with many healthcare professionals remotely, which may be less effective. In addition, due to the prioritization of healthcare resources toward pandemic efforts, even remote interactions may not be possible.

We intend to leverage the sales and marketing capabilities that we are establishing for Gvoke to commercialize additional product candidates for the management of other hypoglycemic conditions, if approved by the FDA, in the United States. If we are unable to do so for any reason, we would need to expend additional resources to establish commercialization capabilities for those product candidates, if approved.

In addition, we intend to establish collaborations to commercialize our product candidates outside the United States, if approved by the relevant regulatory authorities. Therefore, our future success will depend, in part, on our ability to enter into and maintain collaborative relationships for such efforts, the collaborator’s strategic interest in the product and such collaborator’s ability to successfully market and sell the product. We may not be able to establish or maintain such collaborative arrangements, or if we are able to do so, such collaborators may not have effective sales forces. To the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, and such efforts may not be successful.

Risks Related to Third-Parties Actions and Market Acceptance

Our reliance on third-party suppliers, including single-source suppliers, and a limited number of options for alternate sources for Gvoke, Keveyis, and Recorlev or our product candidates could harm our ability to develop our product candidates or to commercialize Gvoke, Keveyis, Recorlev or any product candidates that are approved.

We do not currently own or operate any manufacturing facilities for the production of Gvoke, Keveyis, Recorlev for commercial supply or our product candidates for use in clinical trials. We rely on third-party suppliers to manufacture and supply our products and our product candidates. For Gvoke, we currently rely on a number of single-source suppliers, such as Bachem Americas, Inc. ("Bachem") for active pharmaceutical ingredient ("API"), Pyramid Laboratories Inc. ("Pyramid") for drug product and SHL Pharma, LLC ("SHL Pharma") for auto-injector and final product assembly, and we have entered into several supply agreements including with Bachem, Pyramid and SHL Pharma. Taro Pharmaceuticals U.S.A., Inc. ("Taro") produces all of our requirements for Keveyis. The agreement with Taro may extend beyond the orphan exclusivity period unless terminated by either party pursuant to the terms of the agreement. If terminated by Taro at the conclusion of the orphan exclusivity period, we will need to find a new third party to manufacture Keveyis or manufacture the product ourselves. Similarly for Recorlev, we rely on a number of single-source suppliers, such as Regis Technologies, Inc. for API and Xcelience, LLC (“Lonza”) for finished drug product. We rely on other third parties to manufacture our product candidates for use in clinical trials. If any of these vendors is unable or unwilling to meet our future requirements, we may not be able to manufacture and/or supply our products in a timely manner. Our current arrangements with these manufacturers are terminable by such manufacturers, subject to certain notice provisions.

Our third-party suppliers may not be able to produce sufficient inventory to meet commercial demand in a timely manner, or at all. Our third-party suppliers may not be required to provide us with any guaranteed minimum production levels or have dedicated capacity for our products. As a result, there can be no assurances that we will be able to obtain sufficient quantities of products, components or other key materials in the future, which could have a material adverse effect on our business as a whole. For example, the extent to which the COVID-19 pandemic impacts our and our suppliers’ ability to procure sufficient supplies for the manufacture of our commercial products or our product candidates continues to evolve and there can be no assurances that there will not be disruptions to supply in the future. Any disruption to the facilities or operations of our third-party suppliers resulting from weather-related events, epidemics, including the global health concerns such as the COVID-19 pandemic, fire, acts of terrorism, political instability or any other cause could materially impair our ability to manufacture our products and to distribute our products to customers. For example, we have a global supply chain and manufacture some components of our products outside the United States, including without limitation, Taiwan. Any interruption in the production or delivery of our supplies could reduce sales of our products and increase our costs and any negative impact of such matters on our third-party suppliers and manufacturers may also have an adverse impact on our results of operations or financial condition.

Gvoke and some of our product candidates are drug-device combination products that are regulated under the drug regulations of the Federal Food, Drug, and Cosmetic Act (the “FDCA”) based on their primary mode of action as a drug. Third-party manufacturers may not be able to comply with the current Good Manufacturing Practice ("CGMP") regulatory requirements applicable to drug-device combination products, including applicable provisions of the FDA’s drug CGMP regulations, device CGMP requirements embodied in the Quality System Regulations ("QSRs") or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of our products and product candidates, re-labeling or re-packaging of our products, operating restrictions and criminal prosecutions, any of which could significantly affect the supply of our products and product candidates. The facilities used by our contract manufacturers to manufacture our products and product candidates must be approved by the FDA pursuant to inspections conducted by the FDA. The FDA and other foreign regulatory authorities require manufacturers to register manufacturing facilities. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with CGMPs and QSRs. Contract manufacturers may face manufacturing or quality control problems causing drug substance or device component production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable CGMP or QSR requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications, CGMP and/or QSRs and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or such foreign regulatory authorities do not approve these facilities for the manufacture of our products or product candidates or if they withdraw any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to market our products or develop, obtain regulatory approval for or market our product candidates, if approved.

There are a limited number of third-party suppliers that are compliant with CGMP and/or QSRs, as required by the FDA, the EU, and other regulatory authorities, and that also have the necessary expertise and capacity to manufacture our materials and products. As a result, it may be difficult for us to locate third-party suppliers for our anticipated future needs, and our anticipated growth could strain the ability of our current third-party suppliers to deliver products, raw materials and components to us. If we are unable to arrange for third-party suppliers for our materials and products, or to do so on commercially reasonable terms, we may not be able to complete development of or market our products.

The introduction of new CGMP or QSR regulations or product specific requirements by a regulatory body may require that we source alternative materials, modify existing manufacturing processes or implement design changes to our products that are subject to prior approval by the FDA or other regulatory authorities. We may also be required to reassess a third-party supplier's compliance with all applicable new regulations and guidelines, which could further impede our ability to manufacture and supply products in a timely manner. As a result, we could incur increased production costs, experience supply interruptions, suffer damage to our reputation and experience an adverse effect on our business and financial results.

In addition, our reliance on third-party suppliers involves a number of additional risks, including, among other things:

- our suppliers may fail to comply with regulatory requirements or make errors in manufacturing raw materials, components or products that could negatively affect the efficacy or safety of our products or cause delays in shipments of our products;
- we may be subject to price fluctuations due to terms within long-term supply arrangements with suppliers or lack of long-term supply arrangements for key materials and products;
- our suppliers may lose access to critical services or sustain damage to a facility, including losses due to natural disasters, geo-political events, or epidemics that may result in a sustained interruption in the manufacture and supply of our products;
- fluctuations in demand for our products or a supplier's demand from other customers may affect their ability or willingness to deliver materials or products in a timely manner or may lead to long-term capacity constraints at the supplier;
- we may not be able to find new or alternative sources or reconfigure our products and manufacturing processes in a timely manner if necessary raw materials or components become unavailable;
- our suppliers may encounter financial or other hardships unrelated to our demand for materials, products and services, which could inhibit their ability to fulfill our orders and meet our requirements; and
- the possibility of breach or termination of a manufacturing agreement or purchase order by the third party.

In addition, we could be forced to secure new materials or develop alternative third-party suppliers, which can be difficult given our product complexity, long development lead-times and global regulatory review processes.

If any CMOs with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials or commercial distribution could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our products or product candidates. In addition, in the case of the CMOs that supply our products or product candidates, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. Additionally, under the CARES Act, we must have in place a risk management plan that identifies and evaluates the risks to the supply of approved drugs for certain serious diseases or conditions for each establishment where the drug or API is manufactured. The risk management plan will be subject to FDA review during an inspection. If we experience shortages in the supply of our marketed products, our results could be materially impacted.

Reimbursement decisions by third-party payors and consolidation within the healthcare industry and among competitors more generally may have an adverse effect on pricing and market acceptance. If there is not sufficient reimbursement for our products, it is less likely that they will be widely used and pricing pressure may impact our ability to sell our products at prices necessary to support our current business strategies.

Our future revenues and profitability will be adversely affected if U.S. and foreign governmental, private third-party insurers and payors and other third-party payors, including Medicare and Medicaid, do not agree to defray or reimburse the cost of our products on behalf of patients. If these entities fail to provide coverage and reimbursement with respect to our products or provide an insufficient level of coverage and reimbursement, our products may be too costly for some patients to afford and physicians may not prescribe them. In addition, limitations on the amount of reimbursement for our products may also reduce our profitability. In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, actions and proposals to control and reduce healthcare costs. There have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval for our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any of our products or product candidates for which we obtain marketing approval. As the healthcare industry consolidates, competition to provide products and services to industry participants has become more intense and may intensify as the potential purchasers of our products or third-party payors use their purchasing power to exert competitive pricing pressure. We expect that market demand, government regulation, third-party coverage and reimbursement policies and societal pressures will continue to change the healthcare industry worldwide, resulting in further business consolidations and alliances among our potential purchasers. If competitive forces drive down the prices we are able to charge for our products, our profit margins will shrink, which will adversely affect our ability to invest in and grow our business. See the sections entitled, "*Business — Coverage and Reimbursement"* and "*Business — Healthcare Reform*".

Government and other third-party payors are also challenging the prices charged for healthcare products and increasingly limiting, and attempting to limit, both coverage and level of reimbursement for prescription drugs.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products, and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare, and private payors tend to follow CMS to a substantial degree. Factors payors consider in determining reimbursement are based on whether the product is (i) a covered benefit under its health plan; (ii) safe, effective and medically necessary; (iii) appropriate for the specific patient; (iv) cost-effective; and (v) neither experimental nor investigational.

New requirements by third-party payors include: (i) 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 that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States; (ii) third-party payors are increasingly requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement; and (iii) many pharmaceutical manufacturers must calculate and report certain price metrics to the government, such as average manufacturer price, or AMP, and Best Price. Penalties may apply when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

The United States and several other jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could negatively affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of our products that we develop due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs. While we cannot predict what impact on federal reimbursement policies this legislation will have in general or on our business specifically, the ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect market acceptance of our products and our product candidates.

Some patients may require health insurance coverage to afford our products or product candidates, and if we are unable to obtain adequate coverage and reimbursement by third-party payors, our ability to successfully commercialize our products or product candidates may be adversely impacted. Any limitation on the use of our products or any decrease in the price of our products will have a material adverse effect on our ability to achieve profitability.

The success of Gvoke, Keveyis, Recorlev and our other product candidates will be dependent on its proper use by patients, healthcare practitioners and caregivers.

While we have designed our products to be operable by patients, caregivers and healthcare practitioners, we cannot control the successful use of the product by patients, caregivers and healthcare practitioners. Even though our products were used correctly by individuals in our human factors studies, there is no guarantee that these results will be replicated by users in the future. If we are not successful in promoting the proper use of our products by patients, healthcare practitioners and caregivers, we may not be able to achieve market acceptance or effectively commercialize our products. In addition, even in the event of proper use of our products, individual devices may fail. Increasing the scale of production inherently creates increased risk of manufacturing errors, and we may not be able to adequately inspect every device that is produced, and it is possible that individual devices may fail to perform as designed. Manufacturing errors could negatively impact market acceptance of any of our products, result in negative press coverage, or increase the risk that we may be sued.

Risks Related to our Dependence on Third Parties

We depend on third parties to conduct the clinical trials for our product candidates, and any failure of those parties to fulfill their obligations could harm our development and commercialization plans.

We depend on independent clinical investigators, CROs, academic institutions and other third-party service providers to conduct clinical trials with and for our product candidates. Although we rely heavily on these parties for successful execution of our clinical trials, we are ultimately responsible for the results of their activities and many aspects of their activities are beyond our control. For example, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial, but the independent clinical investigators may prioritize other projects over ours or may fail to timely communicate issues regarding our products to us. Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory requirements or our stated protocols. Further, conducting clinical trials in foreign countries, as we have done and may do for certain of our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. The delay or early termination of any of our clinical trial arrangements, the failure of third parties to comply with the regulations and requirements governing clinical trials, or our reliance on results of trials that we have not directly conducted or monitored could hinder or delay the development, approval and commercialization of our product candidates and would adversely affect our business, results of operations and financial condition.

We maintain compliance programs related to our clinical trials through our clinical operations and development personnel. Our clinical trial vendors are required to monitor and report to us issues with the conduct of our clinical trials, and we monitor our clinical trial vendors through our clinical, regulatory and quality assurance staff and other service providers. However, we cannot assure you that our clinical trial vendors or personnel will timely and fully discover and report any fraud or abuse or other issues that may occur in connection with our clinical trials to us. Such fraud or abuse or other issues, if they occur and are not successfully remediated, could have a material adverse effect on our research, development, and commercialization activities and results.

Risks Related to the Product Development and Regulatory Approval of Our Product Candidates

Risks Related to Regulatory Approval

We cannot be certain that our product candidates will receive marketing approval. Without marketing approval, we will not be able to commercialize our product candidates.

We have devoted significant financial resources and business efforts to the development of our product candidates. We cannot be certain that any of our product candidates will receive marketing approval.

The development of a product candidate and issues relating to its approval and marketing are subject to extensive regulation by the FDA in the United States and by comparable regulatory authorities in other countries. We are not permitted to market our product candidates in the United States until we receive approval of a New Drug Application ("NDA") or Biologics License Application ("BLA") from the FDA. The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions.

NDAs and BLAs must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. NDAs and BLAs must also include significant information regarding the chemistry, manufacturing and controls for the product. Obtaining approval of an NDA or BLA is a lengthy, expensive and uncertain process, and we may not be successful in obtaining approval. Any delay or setback in the regulatory approval or commercialization of any of our product candidates will adversely affect our business.

The FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. For example, the FDA:

- < could determine that we cannot rely on the Section 505(b)(2) regulatory pathway or other pathways we have selected, as applicable, for our product candidates;
- < could determine that the information provided by us was inadequate, contained clinical deficiencies or otherwise failed to demonstrate the safety and effectiveness of our product candidates for any indication;
- < may not find the data from bioequivalence studies and/or clinical trials sufficient to support the submission of an NDA or to obtain marketing approval in the United States, including any findings that the clinical and other benefits of our product candidates outweigh their safety risks;
- < may disagree with our trial design or our interpretation of data from preclinical studies, bioequivalence studies and/or clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our trials;
- < may determine that we have identified the wrong listed drug or drugs or that approval of our Section 505(b)(2) application for any of our product candidates is blocked by patent or non-patent exclusivity of the listed drug or drugs or of other previously approved drugs with the same conditions of approval as any of our product candidates (as applicable);
- < may identify deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for the manufacturing of our product candidates;
- < may audit some or all of our clinical research and human factors study sites to determine the integrity of our data and may reject any or all of such data;
- < may approve our product candidates for fewer or more limited indications than we request, or may grant approval contingent on the performance of costly post-approval clinical trials;
- < may change its approval policies or adopt new regulations; or
- < may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates.

Even if a product is approved, the FDA may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials and/or reporting as conditions of approval. Regulators of other countries and jurisdictions have their own procedures for approval of product candidates with which we must comply prior to marketing in those countries or jurisdictions.

Obtaining regulatory approval for marketing of a product candidate in one country does not ensure that we will be able to obtain regulatory approval in any other country. In addition, delays in approvals or rejections of marketing applications in the United States or other countries may be based upon many factors, including regulatory requests for additional analyses, reports, data, preclinical studies and clinical trials, regulatory questions regarding different interpretations of data and results, changes in regulatory policy during the period of product development and the emergence of new information regarding our product candidates or other products. Also, regulatory approval for any of our product candidates may be withdrawn.

Clinical failure may occur at any stage of clinical development, and the results of our clinical trials may not support our proposed indications for our product candidates. If our clinical trials fail to demonstrate efficacy and safety to the satisfaction of the FDA or other regulatory authorities, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate.

We cannot be certain that existing clinical trial results will be sufficient to support regulatory approval of our product candidates. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and preclinical testing. Moreover, success in clinical trials in a particular indication does not ensure that a product candidate will be successful in other indications. A number of companies in the pharmaceutical industry have suffered significant setbacks in clinical trials, even after promising results in earlier preclinical studies or clinical trials or successful later-stage trials in other related indications. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. The results of preclinical and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical and initial clinical trials. A failure of a clinical trial to meet its predetermined endpoints would likely cause us to abandon a product candidate and may delay development of any of our product candidates. Any delay in, or termination of, our clinical trials will delay the submission of the applicable NDA or BLA to the FDA, the Marketing Authorization Application ("MAA") to the European Medicines Agency ("EMA") or other similar applications with other relevant foreign regulatory authorities and, ultimately, our ability to commercialize our product candidates and generate revenue.

We intend to utilize the 505(b)(2) pathway for the regulatory approval of certain of our product candidates. If the FDA does not conclude that such product candidates meet the requirements of Section 505(b)(2), final marketing approval of our product candidates by the FDA or other regulatory authorities may be delayed, limited, or denied, any of which would adversely affect our ability to generate operating revenues.

We are pursuing a regulatory pathway pursuant to Section 505(b)(2) of the FDCA for the approval of certain of our product candidates, which allows us to rely on submissions of existing clinical data for the drug. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments, and permits the submission of an NDA where at least some of the information required for approval comes from preclinical studies or clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The FDA interprets Section 505(b)(2) of the FDCA to permit the applicant to rely upon the FDA's previous findings of safety and efficacy for an approved product. The FDA requires submission of information needed to support any changes to a previously approved drug, such as published data or new studies conducted by the applicant or clinical trials demonstrating safety and efficacy. The FDA could require additional information to sufficiently demonstrate safety and efficacy to support approval.

If the FDA determines that our product candidates do not meet the requirements of Section 505(b)(2), we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for regulatory approval. In March 2010, former President Obama signed into law legislation creating an abbreviated pathway for approval under the Public Health Service Act, or PHS Act, of biological products that are similar to other biological products that are approved under the PHS Act. The legislation also expanded the definition of biological product to include proteins such as insulin. The law contains transitional provisions governing protein products such as insulin, that, under certain circumstances, might permit companies to seek approval for their insulin products as biologics under the PHS Act. Specifically, on March 23, 2020, a small subset of "biological products" approved under the Federal Food, Drug, and Cosmetic Act, such as insulin, which historically were approved as drugs, transitioned to being regulated as biological products. Being regulated as biological products enables transition products to serve as the reference product for biosimilar or interchangeable products approved through the abbreviated licensure pathway. The transition is a regulatory action in which the approved drug application for a transition biological product will be "deemed" to be a biologics license application. Thus our XeriSol pramlintide-insulin co-formulation which would have previously been reviewed through a 505(b)(2) NDA is instead now required to be approved under the PHS Act. If our other product candidates do not meet the requirements of Section 505(b)(2) or are otherwise ineligible or become ineligible for approval via the Section 505(b)(2) pathway, the time and financial resources required to obtain FDA approval for these product candidates, and the complications and risks associated with these product candidates, would likely substantially increase. Moreover, an inability to pursue the Section 505(b)(2) regulatory pathway would likely result in new competitive products reaching the market more quickly than our product candidates, which would likely materially adversely impact our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization.

Some pharmaceutical companies and other actors have objected to the FDA's interpretation of Section 505(b)(2) to allow reliance on the FDA's prior findings of safety and effectiveness. If the FDA changes its interpretation of Section 505(b)(2), or if the FDA's interpretation is successfully challenged in court, this could delay or even prevent the FDA from approving any Section 505(b)(2) application that we submit. Moreover, the FDA has adopted an interpretation of the three-year exclusivity provisions whereby a 505(b)(2) application can be blocked by exclusivity even if it does not rely on the previously approved drug that has exclusivity (or any safety or effectiveness information regarding that drug). Under the FDA's interpretation, the approval of one or more of our

product candidates may be blocked by exclusivity awarded to a previously-approved drug product that shares certain innovative features with our product candidates, even if our 505(b)(2) application does not identify the previously-approved drug product as a listed drug or rely upon any of its safety or efficacy data. Any failure to obtain regulatory approval of our product candidates would significantly limit our ability to generate revenues, and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenues.

Additional time may be required to obtain regulatory approval for certain of our product candidates because they are combination products.

Certain of our product candidates are drug and device combination products that require coordination within the FDA and similar foreign regulatory agencies for review of their device and drug components. Medical products containing a combination of new drugs, biological products or medical devices may be regulated as "combination products" in the United States and Europe. A combination product generally is defined as a product comprised of components from two or more regulatory categories (e.g., drug/device, device/biologic, drug/biologic). Each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a new drug, biologic or device. In order to facilitate pre-market review of combination products, the FDA designates one of its centers to have primary jurisdiction for the pre-market review and regulation of the overall product based upon a determination by the FDA of the primary mode of action of the combination product. Where approval of the drug and device is sought under a single application, there could be delays in the approval process due to the increased complexity of the review process and the lack of a well-established review process and criteria. The EMA has a parallel review process in place for combination products, the potential effects of which in terms of approval and timing could independently affect our ability to market our combination products in Europe.

Gvoke, Keveyis, Recorlev and our product candidates may have undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require them to include safety warnings, require them to be taken off the market or otherwise limit their sales.

Undesirable side effects that may be caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. The range and potential severity of possible side effects from systemic therapies are significant. The results of future clinical trials may show that our product candidates cause undesirable or unacceptable side effects, which could interrupt, delay or halt clinical trials, and result in delay of, or failure to obtain, marketing approval from the FDA and other regulatory authorities, or result in marketing approval from the FDA and other regulatory authorities with restrictive label warnings. Recent developments in the pharmaceutical industry have prompted heightened government focus on safety reporting during both pre- and post-approval time periods and pharmacovigilance. Global health authorities may impose regulatory requirements to monitor safety that may burden our ability to commercialize our drug products.

To date, patients treated with our ready-to-use glucagon have experienced drug-related side effects typically observed with glucagon products, including nausea, vomiting and headaches. In our clinical trials of Recorlev, the most common adverse reactions (incidence > 20%) were nausea/vomiting, hypokalemia, hemorrhage/contusion, systemic hypertension, headache, hepatic injury, abnormal uterine bleeding, erythema, fatigue, abdominal pain/dyspepsia, arthritis, upper respiratory infection, myalgia, arrhythmia, back pain, insomnia/sleep disturbances, and peripheral edema the most common adverse reactions (incidence > 20%) were nausea/vomiting, hypokalemia, hemorrhage/contusion, systemic hypertension, headache, hepatic injury, abnormal uterine bleeding, erythema, fatigue, abdominal pain/dyspepsia, arthritis, upper respiratory infection, myalgia, arrhythmia, back pain, insomnia/sleep disturbances, and peripheral edema. These adverse events can be dose-dependent and may increase in frequency and severity if we increase the dose to increase efficacy. It is possible that there may be side effects associated with our product candidates' use. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential products liability claims. They could also adversely affect physician or patient acceptance of our product candidates. Any of these occurrences may harm our business, financial condition and prospects.

Even if our product candidates receive marketing approval, if we or others later identify undesirable or unacceptable side effects caused by such products:

- regulatory authorities may require the addition of labeling statements, including “black box” warnings, contraindications or dissemination of field alerts to physicians and pharmacies;
- we may be required to change instructions regarding the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- regulatory authorities may require us to take our approved product off the market;
- we may be subject to litigation or products liability claims; and
- our reputation may suffer.

Any of these events could also prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from the sale of our products.

We have received orphan drug designation for Keveyis, Recorlev and certain of our product candidates with respect to certain indications and may pursue such designation for others, but we may be unable to obtain such designation or to maintain the benefits associated with orphan drug status, including market exclusivity, even if that designation is granted.

We have received orphan drug designation from the FDA for four indications for our product candidates, which are our ready-to-use glucagon for PBH and Congenital Hyperinsulinism ("CHI") and our ready-to-use diazepam for acute repetitive seizures and Dravet syndrome. We have also received orphan drug designation from the EMA for our ready-to-use glucagon for CHI and Noninsulinoma Pancreatogenous Hypoglycaemia Syndrome ("NIPHS") which includes patients with PBH. We may pursue such designation for others in specific orphan indications in which there is an unmet medical need. We will continue to rely on orphan drug exclusivity in the marketing and sales of Keveyis until it expires on August 7, 2022 and intend to rely on orphan drug exclusivity and, if granted, new chemical entity (“NCE”) exclusivity in the marketing and sale of Recorlev. Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Although we may seek orphan drug designation for certain additional indications, we may never receive such designation. Moreover, obtaining orphan drug designation for one indication does not mean we will be able to obtain such designation for another indication.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve any other applications, including an NDA, to market the same drug for the same indication for seven years, except in limited circumstances such as if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Similarly, the FDA can subsequently approve a drug with the same active moiety for the same condition during the exclusivity period if the FDA concludes that the later drug is clinically superior, meaning the later drug is safer, more effective or makes a major contribution to patient care. In assessing whether we can demonstrate that our drug provides a “major contribution to patient care” over and above the currently approved drugs, which is evaluated by the FDA on a case-by-case basis, there is no one objective standard and the FDA may, in appropriate circumstances, consider such factors as convenience of treatment location, duration of treatment, patient comfort, reduced treatment burden, advances in ease and comfort of drug administration, longer periods between doses, and potential for self-administration. However, such a demonstration to overcome the seven-year market exclusivity may be difficult to establish with limited precedents and there can be no assurance that we will be successful in these efforts. Even with respect to the indications for which we have received orphan designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products, and thus approval of our product candidates could be blocked for seven years if another company previously obtained approval and orphan drug exclusivity for the same drug and same condition. If we do obtain exclusive marketing rights in the United States, they may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of the relevant patients. Further, exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition, the same drugs can be approved for different indications and might then be used off-label in our approved indication, and different drugs for the same condition may already be approved and commercially available.

In Europe, the period of orphan drug exclusivity is ten years, although it may be reduced to six years if, at the end of the fifth year, it is established that the criteria for orphan drug designation are no longer met, in other words, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity. We have received orphan drug designation from the EMA for our ready-to-use glucagon for the treatment of CHI and NIPHS, which includes patients with PBH.

Even with the FDA approval of Gvoke, Keveyis and Recorlev in the United States and the EMA and MHRA approval of Ogluo in the European Union and the United Kingdom, we may not be able to obtain or maintain foreign regulatory approvals to market our products in other countries.

We do not have any products other than Gvoke, Keveyis and Recorlev approved for sale in the United States, nor any products or product candidates other than Ogluo approved for sale in any international markets, and we do not have experience in obtaining regulatory approval in international markets outside of the European Union and the United Kingdom. In order to market products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy. Approval by the FDA in the United States does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval or certification by one foreign regulatory authority does not ensure approval or certification by regulatory authorities in other foreign countries or by the FDA. International jurisdictions require separate regulatory approvals and compliance with numerous and varying regulatory requirements. The approval procedures vary among countries and may involve requirements for additional testing, and the time required to obtain approval may differ from country to country and from that required to obtain clearance or approval in the United States.

In addition, some countries only approve or certify a product for a certain period of time, and we are required to re-approve or re-certify our products in a timely manner prior to the expiration of our prior approval or certification. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals or certifications and may not receive necessary approvals to commercialize our products in any market. If we fail to receive necessary approvals or certifications to commercialize our products in foreign jurisdictions on a timely basis, or at all, or if we fail to have our products re-approved or re-certified, our business, results of operations and financial condition could be adversely affected. The foreign regulatory approval or certification process may include all of the risks associated with obtaining FDA clearance or approval. In addition, the clinical standards of care may differ significantly such that clinical trials conducted in one country may not be accepted by healthcare providers, third-party payors or regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any drug we develop will be unrealized.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our products and product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products or product candidates for which we obtain marketing approval. See the section entitled, "*Business — Healthcare Reform*".

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

The cost of prescription pharmaceuticals in the United States has also been the subject of considerable debate, and members of Congress have indicated that they will address such costs through new legislative measures. To date, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, improve transparency in drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare, and reform government program reimbursement methodologies for drug products. There has recently been intense publicity regarding the pricing of pharmaceutical products generally, including publicity and pressure resulting from the prices charged for new products as well as price increases for older products that the government and public deem excessive. We may experience downward pricing pressure on the price of our products due to social or political pressure to lower the cost of drugs, which could reduce our revenue and future profitability. Many companies in our industry have received governmental requests for documents and information relating to drug pricing and patient support programs, including Strongbridge, which is cooperating with these voluntary requests for information. We could incur significant expense and experience reputational harm as a result of these or other similar future inquiries, as well as reduced market acceptance and demand for our products, which could harm our ability to market our products in the future. These factors could also result in changes in our product pricing and distribution strategies, reduced demand for our products and/or reduced reimbursement of products, including by federal health care programs such as Medicare and Medicaid and state health care programs.

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these other countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost

effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for approved products. In addition, there have been several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare and reform government program reimbursement methodologies for drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our products and product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval of those product candidates for which we seek marketing approval, as well as subject us to more stringent labeling and post-marketing testing and other requirements.

Risks Related to Product Development

Our failure to successfully identify, develop and market additional product candidates, or acquire additional product candidates or enter into collaborations or other commercial agreements could impair our ability to grow.

As part of our growth strategy, we intend to identify, develop and market additional product candidates leveraging our formulation technology platforms, and evaluate other commercial relationships through collaborations or other strategic agreements. We are exploring various therapeutic opportunities for our pipeline programs. We may spend several years completing our development of any particular current or future internal product candidates, and failure can occur at any stage. The product candidates to which we allocate our resources may not ***end*** up being successful. Gvoke, which delivers ready-to-use glucagon via a pre-filled syringe or auto-injector, was approved by the FDA on September 10, 2019 for the treatment of severe hypoglycemia in pediatric (aged two years and above) and adult patients with diabetes. While we have identified several additional potential applications of our ready-to-use glucagon, there is no guarantee that we will be able to utilize our formulation technology platforms to obtain approval of additional product candidates.

In the future, we may be dependent upon pharmaceutical companies, academic scientists and other researchers to sell or license product candidates, approved products or the underlying technology to us. The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates and approved products. In addition, we expect to seek one or more collaborators for the development and commercialization of one or more of our products or product candidates, particularly with respect to our pipeline product candidates or foreign geographies. We face significant competition in seeking appropriate collaborators. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies or enter into collaborations or other strategic arrangements and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all.

In addition, future acquisitions may entail numerous operational and financial risks, including:

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

Further, any product candidate that we identify internally or acquire would require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and other regulatory authorities.

Risks Related to our Industry and Ongoing Legal and Regulatory Requirements

Risks Related to Ongoing Regulatory Obligations

Even after approval of our products and product candidates, we may still face future development and regulatory difficulties. If we fail to comply with continuing U.S. and non-U.S. regulations or new adverse safety data arise, we could lose our marketing approvals and our business would be seriously harmed.

Our approved products and product candidates, if approved, will also be subject to ongoing regulatory requirements for manufacturing, distribution, sale, labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information. Approved products, third-party suppliers and their facilities are required to comply with extensive FDA requirements and requirements of other similar agencies even after approval, including ensuring that quality control and manufacturing procedures conform to CGMPs and applicable QSRs and applicable product tracking and tracing requirements. As such, we and our third-party suppliers are subject to continual review and periodic inspections, both announced and unannounced, to assess compliance with CGMPs and QSRs. Accordingly, we and our third-party suppliers must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and other similar agencies and to comply with certain requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. Accordingly, we may not promote our approved products for indications or uses for which they are not approved.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. These unknown problems could be discovered as a result of any post-marketing follow-up studies, routine safety surveillance or other reporting required as a condition to approval.

Regulatory agencies may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice ("DOJ"), closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use, and if we, or any future collaborators, do not market any of our products for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing, government investigations, or litigation. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws. On August 14, 2020, we received an untitled letter from FDA's Office of Prescription Drug Promotion regarding a promotional television advertisement for Gvoke PFS. The letter raised concerns that the advertisement did not include sufficient risk information, made misleading claims as to the product's ease of use, and omitted information about the seriousness of the condition for which Gvoke PFS is indicated and the circumstances when it is appropriate to administer Gvoke PFS. The television advertisement cited in the untitled letter was discontinued in March of 2020. We submitted a response to the FDA regarding our plan to revise the advertisement at issue. The FDA completed evaluation of our response and confirmed that we have addressed all the violations contained in the untitled letter.

If our products or product candidates fail to comply with applicable regulatory requirements, or if a problem with one of our products or third-party suppliers is discovered, a regulatory agency may:

- restrict the marketing or manufacturing of such products;
- restrict or require modification of or revision to the labeling of a product;
- issue warning letters or untitled letters which may require corrective action;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us to enter into a consent decree or permanent injunction, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- impose other administrative or judicial civil or criminal penalties including fines, imprisonment and disgorgement of profits;
- suspend or withdraw regulatory approval;
- refuse to approve pending applications or supplements to approved applications filed by us;
- close the facilities of our third-party suppliers;
- suspend ongoing clinical trials;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or recommend or require a product recall.

The FDA's and foreign regulatory agencies' policies are subject to change, and additional federal, state, local or non-U.S. governmental regulations may be enacted that could affect our ability to maintain compliance. We cannot predict the likelihood, nature or extent of adverse governmental regulation that may arise from future legislation or administrative action, either in the United States or abroad.

Our relationships with customers and payors 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, administrative burdens and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with investigators, healthcare practitioners, consultants, third-party payors and customers, if any, will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws and regulations may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute any products for which we obtain marketing approval. See the section entitled, "*Business — Other Healthcare Laws and Compliance Requirements*".

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our arrangements with physicians and other healthcare providers, some of whom may receive stock options as compensation for services provided, may not comply with current or future statutes, regulations, agency guidance 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, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, and imprisonment, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and our financial results. Defending against any such actions can be costly and time consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Third party patient assistance programs that receive financial support from companies have become the subject of enhanced government and regulatory scrutiny. Government enforcement agencies have shown increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. The U.S. government has established guidelines that suggest that it is lawful for pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are bona fide charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria and do not link aid to use of a donor's product. However, donations to patient assistance programs have received some negative publicity and have been the subject of multiple government enforcement actions, related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives. Specifically, in recent years, there have been multiple settlements resulting out of government claims challenging the legality of their patient assistance programs under a variety of federal and state laws. It is possible that we may make grants to independent charitable foundations that help financially needy patients with their premium, co-pay, and co-insurance obligations. If we choose to do so, and if we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, we could be subject to damages, fines, penalties, or other criminal, civil, or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies, and procedures will be sufficient to protect against acts of our employees, business partners, or vendors that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could impact our business practices, harm our reputation, divert the attention of management, increase our expenses, and reduce the availability of foundation support for our patients who need assistance. Further, it is possible that changes in insurer policies regarding co-pay coupons and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, and therefore could have a material adverse effect on our sales, business, and financial condition. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the current U.S. presidential administration may reverse or otherwise change these measures, both the current U.S. presidential administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs. We cannot predict how the implementation of and any further changes to this rule will affect our business.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside the United States and require us to develop and implement costly compliance programs.

We currently have operations in the United States, and we maintain relationships with CMOs in certain parts of Europe, Asia and the United States for the manufacture of our products and product candidates. The Foreign Corrupt Practices Act ("FCPA") prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any

foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the DOJ. The Securities and Exchange Commission ("SEC") is involved with enforcement of the books and records provisions of the FCPA and may suspend or bar issuers from having its securities traded on U.S. exchanges for violations of the FCPA's accounting provisions.

Various laws, regulations and executive orders also restrict the use and dissemination outside 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. As we expand our presence outside the United States, we are required to dedicate additional resources to comply with laws and regulations in each new jurisdiction in which we are operating or plan to operate, and these laws may preclude us from developing, manufacturing, or selling certain drugs and product candidates outside the United States, which could limit our growth potential and increase our development costs.

The creation and implementation of international business practices compliance programs, particularly FCPA compliance, are costly and such programs are difficult to enforce, especially in countries in which corruption is a recognized problem and where reliance on third parties is required. In addition, the FCPA presents particular challenges in the pharmaceutical industry because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor.

Accordingly, our failure to comply with the FCPA or other export control, anti-corruption, anti-money laundering and anti-terrorism laws or regulations and other similar laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under such laws would have a negative impact on our operations and harm our reputation and ability to procure government contracts. We cannot assure you that our compliance policies and procedures are or will be sufficient or that our directors, officers, employees, representatives, consultants and agents have not engaged and will not engage in conduct for which we may be held responsible, nor can we assure you that our business partners have not engaged and will not engage in conduct that could materially affect their ability to perform their contractual obligations to us or even result in our being held liable for such conduct.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, such as the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution or arbitrage between low-priced and high-priced countries can further reduce prices. To obtain reimbursement or pricing approval in some countries, we, or any future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies, which is time consuming and costly. If reimbursement of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

Risks Related to Industry Competition

We operate in a competitive business environment and, if we are unable to compete successfully against our existing or potential competitors, our sales and operating results may be negatively affected and we may not successfully commercialize our products or product candidates, even if approved.

The pharmaceutical and biotechnology industries are characterized by intense competition and significant and rapid technological change as researchers learn more about diseases and develop new technologies and treatments. Any product candidates that we successfully develop and commercialize will compete with existing drugs and new drugs that may become available in the future. While we believe that our product and product candidate platform, development expertise and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Many of our current and potential competitors are major pharmaceutical companies that have substantially greater financial, technical and marketing resources than we do, and they may succeed in developing products that would render our products obsolete or noncompetitive. Our ability to compete successfully will depend on our ability to develop future products that reach the market in a timely manner, are well adopted by patients and healthcare providers and receive adequate coverage and reimbursement from third-party payors. Because of the size of the potential market, we anticipate that companies will dedicate significant resources to developing products competitive to our product candidates.

For example, Gvoke has numerous competitors in the severe hypoglycemia market, which currently include Eli Lilly's Baqsimi®, an intranasal glucagon dry powder, Eli Lilly's GEK, Novo Nordisk's GlucaGen HypoKit and Fresenius Kabi's glucagon emergency kit for low blood sugar. Amphastar's ANDA for generic Glucagon for Injection Emergency Kit was approved by the FDA on December 29, 2020 for the treatment of severe hypoglycemia. Zealand Pharma received approval by the FDA of its dasiglucagon auto-injector Zegalogue® in March 2021 and launched in June 2021. At any time, these or other industry participants may develop alternative treatments, products or procedures for the treatment of severe hypoglycemia that compete directly or indirectly with Gvoke. Competitors may also develop and patent processes or products earlier than we can or obtain regulatory clearance or approvals for competing products more rapidly than we can, which could impair our ability to develop and commercialize similar processes or products. If alternative treatments are, or are perceived to be, superior to our products, sales of our products or product candidates, if approved, could be negatively affected and our results of operations could suffer.

The widespread acceptance of currently available therapies with which our product candidates will compete may limit market acceptance of Gvoke or our product candidates even if approved and commercialized. For example, traditional glucagon kits currently available for hypoglycemia are widely accepted in the medical community and have a long history of use. These treatments compete with Gvoke and may limit the potential for Gvoke to receive widespread acceptance.

In addition, Keveyis is an oral carbonic anhydrase inhibitor, that was approved in the United States to treat hyperkalemic, hypokalemic and related variants of PPP. Acetazolamide, another oral carbonic anhydrase inhibitor, is used frequently off-label for the prophylactic and sometimes acute treatment of PPP. Potassium supplements, are indicated for use in hypokalemic periodic paralysis in the United States and are frequently used either chronically or for emergency treatment of episodes in that form of PPP. Several other types of drugs have been reported to have benefits for chronic or acute use in one or more than one PPP variant, including potassium-sparing diuretics, beta receptor agonists, mexelitine and other sodium channel blockers, and others. We are not aware of drugs currently in development for prophylactic chronic treatment of PPP.

We are currently aware of various companies that are marketing existing drugs that may compete with Recorlev such as Corcept Therapeutics and Recordati. The treatment of endogenous Cushing's syndrome patients who fail or are ineligible for surgery in the United States and Europe are: Korlym (mifepristone) marketed by Corcept Therapeutics in the United States; Signifor LAR (pasireotide) and Isturisa (osilodrostat), all marketed by Recordati in the United States and European Union; and ketoconazole, metyrapone and mitotane marketed by HRA in the European Union. Corcept is developing relacorilant, a second-generation glucocorticoid receptor modulator; currently in Phase 3. Ketoconazole is used off-label for treatment of Cushing's syndrome in the United States. Regulatory approval of ketoconazole for the treatment of endogenous Cushing's syndrome in the United States, which is not currently being sought by any sponsor to our knowledge, could significantly increase competition for Recorlev due to the similar mechanisms of action between the drug products.

If the FDA or other applicable regulatory authorities approve generic products that compete with any of our products or product candidates, the sales of our product candidates, if approved, could be adversely affected.

Once an NDA, including a Section 505(b)(2) application, is approved, the product covered becomes a "listed drug" which can be cited by potential competitors in support of approval of an abbreviated new drug application ("ANDA"). FDA regulations and other applicable regulations and policies provide incentives to manufacturers to create modified versions of a drug to facilitate the approval of an ANDA or other application for similar substitutes. If these manufacturers demonstrate that their product has the same active ingredient(s), dosage form, strength, route of administration, and conditions of use, or labeling, as our products or product candidates, they might only be required to conduct a relatively inexpensive study to show that their generic product is absorbed in the body at the same rate and to the same extent as, or is bioequivalent to, our products or product candidates. In some cases, even this limited bioequivalence testing can be waived by the FDA. Laws have also been enacted to facilitate the development of generic drugs and biologics based off recently approved NDAs and BLAs. The Creating and Restoring Equal Access to Equivalent Samples Act ("CREATES Act") was enacted in 2019 requiring sponsors of approved NDAs and BLAs to provide sufficient quantities of product samples on commercially reasonable, market-based terms to entities developing generic drugs and biosimilar biological products. The law establishes a private right of action allowing developers to sue application holders that refuse to sell them product samples needed to support their applications. If we are required to provide product samples or allocate additional resources to responding to such requests or any legal challenges under this law, our business could be adversely impacted. Competition from generic equivalents to our products or product candidates could substantially limit our ability to generate revenues and therefore to obtain a return on the investments we have made in our products or product candidates. For example, Amphastar's ANDA for generic Glucagon for Injection Emergency Kit was approved by the FDA on December 29, 2020 for the treatment of severe hypoglycemia. We will continue to rely on orphan drug exclusivity in the marketing and sales of Keveyis through expiration of orphan drug exclusivity in August, 2022 and intend to rely on orphan drug exclusivity and NCE, if available, exclusivity in the marketing and sale of Recorlev. While we applied for NCE exclusivity for Recorlev under section 505(u) of the FDCA, the FDA may determine that the Recorlev application does not meet the eligibility criteria under 505(u) for NCE exclusivity.

Risks Related to Our Intellectual Property

Risks Related to Protecting Our Intellectual Property

Our success depends on our ability to protect our intellectual property and proprietary technology, as well as the ability of our collaborators to protect their intellectual property and proprietary technology.

Our success depends in large part on our ability to obtain and maintain patent protection and trade secret protection in the United States and other countries with respect to the use, formulation and structure of our proprietary product candidates, the methods used to manufacture them, the related therapeutic targets and associated methods of treatment as well as on successfully defending these patents against potential third-party challenges. Our ability to protect our products and product candidates from unauthorized making, using, selling, offering to sell or importing by third parties is dependent on the extent to which we have rights under valid and enforceable patents that cover these activities. If we do not adequately protect our intellectual property rights, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel product candidates that are important to our business; we may in the future also license or purchase patents or applications owned by others. The patent application and approval process is expensive and time consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Moreover, obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

If the scope of the patent protection we or our potential licensors obtain is not sufficiently broad, we may not be able to prevent others from developing and commercializing technology and products similar or identical to ours. The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect our current and future product candidates or otherwise provide any competitive advantage. In addition, to the extent that we license intellectual property in the future, we cannot assure you that those licenses will remain in force. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally twenty years after it is filed. Various extensions may be available; however, the life of a patent and the protection it affords are limited. 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.

Even if they are unchallenged, our patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our patents by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to one or more of our products or product candidates but that uses a formulation and/or a device that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our products or product candidates is not sufficiently broad to exclude such competition, our ability to successfully commercialize our products or product candidates could be negatively affected, which would harm our business. Although we currently own all of our patents and our patent applications, similar risks would apply to any patents or patent applications that we may in-license in the future.

We, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position.

It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our partners, collaborators, licensees or licensors fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees or licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it may be used to invalidate a patent or may prevent a patent from issuing from a pending patent application. For example, such patent filings may be subject to a third-party pre-issuance submission of prior art to the USPTO and/or to other patent offices around the world.

Alternately or additionally, we may become involved in post-grant review procedures, oppositions, derivations proceedings, reexaminations, inter partes review or interference proceedings, in the United States or elsewhere, challenging patents or patent applications in which we have rights, including patents on which we rely to protect our business. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to exclude others from using or commercializing similar or identical technology and products, or may limit the duration of the patent protection of our technology and products.

Pending and future patent applications may not result in patents being issued which protect our business, in whole or in part, or which effectively prevent others from commercializing competitive products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, patent laws in various jurisdictions, including significant commercial markets such as Europe, restrict the patentability of methods of treatment of the human body more than United States law does.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any future development partners will be successful in protecting our product candidates by obtaining, maintaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;
- patents that may be issued may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, and sell our potential product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates in such countries.

Issued patents that we have or may in the future obtain or license may not provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our or our future licensors' patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that patents owned or in the future licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

We have entered into a license agreement with a third party (and may, in the future, enter into additional such license agreements with other third parties) pursuant to which they have the right, but not the obligation, in certain circumstances to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents. Even if we are permitted to pursue such enforcement or defense, we will require the cooperation of those licensors and cannot guarantee that we would receive it and on what terms. We cannot be certain that those licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. If we cannot obtain patent protection or enforce existing or future patents against third parties, our competitive position and our financial condition could suffer.

In addition, we rely on the protection of our trade secrets and proprietary know-how. Although we take steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, our business may be harmed.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to develop and manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may harm our business.

The patent positions of pharmaceutical, biotechnology and other life sciences companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Further, the determination that a patent application or patent claim meets all of the requirements for patentability is a subjective determination based on the application of law and jurisprudence. The ultimate determination by the USPTO or by a court or other trier of fact in the United States, or corresponding foreign national patent offices or courts, on whether a claim meets all requirements of patentability cannot be assured. We have not conducted searches for third-party publications, patents and other information that may affect the patentability of claims in our various patent applications and patents, so we cannot be certain that all relevant information has been identified. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patent applications and patents, in any future licensed patents or patent applications or in third-party patents.

We cannot provide assurances that any claim(s) in any of our patent applications will be found to be patentable, including over our own prior art patents, or that any such patent applications will issue as patents. Neither can we make assurances as to the scope of any claims that may issue from our pending and future patent applications nor to the outcome of any proceedings instituted by any potential third parties that could challenge the patentability, validity or enforceability of our patents and patent applications in the United States or foreign jurisdictions. Any such challenge, if successful, could limit patent protection for our products and product candidates and/or materially harm our business.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we may not be able to generate sufficient data to support full patent applications that protect the entire breadth of developments in one or more of our programs;
- it is possible that one or more of our pending patent applications will not become an issued patent or, if issued, that the patent(s) will not: (a) be sufficient to protect our technology, (b) provide us with a basis for commercially viable products and/or (c) provide us with any competitive advantages;
- if our pending applications issue as patents, they may be challenged by third parties as not infringed, invalid or unenforceable under U.S. or foreign laws; or
- if issued, the patents under which we hold rights may not be valid or enforceable.

In addition, to the extent that we are unable to obtain and maintain patent protection for one of our products or product candidates or in the event that such patent protection expires, it may no longer be cost-effective to extend our portfolio by pursuing additional development of a product or product candidate for follow-on indications.

We also may rely on trade secrets to protect our technologies or products, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisers may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third-party entity illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.

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. Where available, we will seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available and may refuse to grant

extensions to our patents or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

Our unpatented trade secrets, know-how, confidential and proprietary information, and technology may be inadequately protected.

We rely in part on unpatented trade secrets, know-how and technology. This intellectual property is difficult to protect, especially in the pharmaceutical industry, where much of the information about a product must be submitted to regulatory authorities during the regulatory approval process. We seek to protect trade secrets, confidential information and proprietary information, in part, by entering into confidentiality and invention assignment agreements with employees, consultants, and others. These parties may breach or terminate these agreements, and we may not have adequate remedies for such breaches. Furthermore, these agreements may not provide meaningful protection for our trade secrets or other confidential or proprietary information or result in the effective assignment to us of intellectual property and may not provide an adequate remedy in the event of unauthorized use or disclosure of confidential information or other breaches of the agreements. Despite our efforts to protect our trade secrets and our other confidential and proprietary information, we or our collaboration partners, board members, employees, consultants, contractors, or scientific and other advisors may unintentionally or willfully disclose our proprietary information to competitors.

Thus, there is a risk that our trade secrets and other confidential and proprietary information could have been, or could, in the future, be shared by any of our former employees with, and be used to the benefit of, any company that competes with us.

If we fail to maintain trade secret protection or fail to protect the confidentiality of our other confidential and proprietary information, our competitive position may be adversely affected. Competitors may also independently discover our trade secrets. Enforcement of claims that a third party has illegally obtained and is using trade secrets is expensive, time consuming and uncertain. If our competitors independently develop equivalent knowledge, methods and know-how, we would not be able to assert our trade secret protections against them, which could have a material adverse effect on our business.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During the trademark registration process, we may receive Office Actions from the USPTO objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Intellectual Property Litigation

The pharmaceutical industry is characterized by frequent patent litigation, and we could become subject to litigation that could be costly, result in the diversion of management's time and efforts, require us to pay damages or prevent us from marketing our existing or future products.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our products that have been approved for sale, and to use our proprietary technology without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the USPTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we will market products and are developing product candidates. Some claimants, who may include our competitors in both the United States and abroad, may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our products and product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

We cannot be sure that we know of each and every patent and pending application in the United States and abroad that is relevant or necessary to the commercialization of Gvoke, Keveyis Recorlev, or our product candidates. Generally, we do not conduct independent reviews of patents issued to third parties. The large number of patents, the rapid rate of new patent issuances, the complexities of the technology involved, and uncertainty of litigation increase the risk of business assets and management's attention being diverted to patent litigation. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents upon which our products or product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our products or product candidates, any compositions formed

during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product or product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product or product candidate unless we obtained a license or until such patent expires or is finally determined to be invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful. Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement lawsuits, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to exclude the other party from making, using or selling the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to exclude the other party from making, using or selling the invention at issue on the grounds that our patent claims do not cover the invention or the other party's manufacture, use or sale of it. An adverse outcome in a litigation or proceeding involving one or more of our patents could limit our ability to assert those patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are unenforceable, that the alleged infringing mark does not infringe our trademark rights, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this last instance, we could ultimately be forced to cease use of such trademarks.

Others may challenge inventorship or claim an ownership interest in our intellectual property which could expose it to litigation and have a significant adverse effect on its prospects.

A third party or former employee or collaborator may claim an ownership interest in one or more of our patents or other proprietary or intellectual property rights. A third party could bring legal actions against us and seek monetary damages and/or enjoin clinical testing, manufacturing and marketing of the affected product or products. While we are presently unaware of any claims or assertions by third parties with respect to our patents or other intellectual property, we cannot guarantee that a third party will not assert a claim or an interest in any of such patents or intellectual property. If we become involved in any litigation, it could consume a substantial portion of our resources and cause a significant diversion of effort by our technical and management personnel.

If any of these actions are successful, in addition to any potential liability for damages, we could be required to obtain a license to continue to manufacture or market the affected product, in which case we may be required to pay substantial royalties or grant cross-licenses to our patents. We cannot, however, assure you that any such license will be available on acceptable terms, if at all. Furthermore, any potential intellectual property litigation also could force us to do one or more of the following:

- stop selling products or using technology that contains the allegedly infringing intellectual property;
- lose the opportunity to license our technology to others or to collect royalty payments based upon successful protection and assertion of our intellectual property rights against others;
- incur significant legal expenses;
- pay substantial damages to the party whose intellectual property rights we may be found to be infringing;
- redesign those products that contain the allegedly infringing intellectual property, which could be costly, disruptive and/or infeasible; or
- attempt to obtain a license to the relevant intellectual property from third parties, which may not be available on reasonable terms or at all.

The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of any adverse party. This is especially true in intellectual property cases that may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree. Any litigation or claim against us, even those without merit, may cause us to incur substantial costs and could place a significant strain on our financial resources, divert the attention of management from our core business, and harm our reputation.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of our competitors or are in breach of non-competition or non-solicitation agreements with our competitors.

We may also be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of our competitors or are in breach of non-competition or non-solicitation agreements with our competitors. Many of our employees were previously employed at other pharmaceutical companies, including our competitors or potential competitors, in some cases until recently. We may be subject to claims that we or our employees have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of these former employers or competitors. In addition, we have been and may in the future be

subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defense to those claims fails, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Any litigation or the threat thereof may adversely affect our ability to hire employees. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our products and product candidates, which could have an adverse effect on our business, results of operations and financial condition.

An NDA submitted under Section 505(b)(2) subjects us to the risk that we may be subject to a patent infringement lawsuit that would delay or prevent the review or approval of our product candidates.

We expect to submit NDAs under Section 505(b)(2) of the FDCA for most of our product candidates. Section 505(b)(2) permits the submission of an NDA where at least some of the information required for approval comes from preclinical studies and/or clinical trials that were not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference. An NDA under Section 505(b)(2) would enable us to reference published literature and/or the FDA's previous findings of safety and effectiveness for a previously approved drug. For NDAs submitted under Section 505(b)(2), the patent certification and related provisions of the Hatch-Waxman Act apply.

Accordingly, if we rely for approval on the safety or effectiveness information for a previously approved drug, referred to as a listed drug, we will be required to include patent certifications in our 505(b)(2) application regarding any patents covering the listed drug. If there are patents listed in the FDA publication Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book, for the listed drug, and we seek to obtain approval prior to the expiration of one or more of those patents, we will be required to submit a Paragraph IV certification indicating our belief that the relevant patents are invalid or unenforceable or will not be infringed by the manufacture, use or sale of the product that is the subject of our 505(b)(2) application. Otherwise, our 505(b)(2) application cannot be approved by the FDA until the expiration of any patents listed in the Orange Book for the listed drug. While we did not submit any Paragraph IV certifications in connection with our 505(b)(2) NDA for Gvoke, and do not expect to submit any Paragraph IV certifications for our other current product candidates, there can be no assurance that we will not be required to submit a Paragraph IV certification in respect of any future product candidates for which we seek approval under Section 505(b)(2).

However, an NDA submitted under Section 505(b)(2) subjects us to the risk that we may be subject to a patent infringement lawsuit that would delay or prevent the review or approval of our product candidates.

If we submit any Paragraph IV certification that may be required, we will be required to provide notice of that certification to the NDA holder and patent owner shortly after our 505(b)(2) application is accepted for filing. Under the Hatch-Waxman Act, the patent owner may file a patent infringement lawsuit after receiving such notice. If a patent infringement lawsuit is filed within 45 days of the patent owner's or NDA holder's receipt of notice (whichever is later), a one-time, automatic stay of the FDA's ability to approve the 505(b)(2) NDA is triggered, which typically extends for 30 months unless patent litigation is resolved in favor of the Paragraph IV filer or the patent expires before that time. Accordingly, we may invest a significant amount of time and expense in the development of one or more product candidates only to be subject to significant delay and patent litigation before such product candidates may be commercialized, if at all.

In addition, a 505(b)(2) application will not be approved until any non-patent exclusivity listed in the Orange Book for the listed drug, or for any other drug with the same protected conditions of approval as our product, has expired. The FDA also may require us to perform one or more additional clinical trials or measurements to support the change from the listed drug, which could be time consuming and could substantially delay our achievement of regulatory approval. The FDA also may reject any future 505(b)(2) submissions and require us to submit traditional NDAs under Section 505(b)(1), which would require extensive data to establish safety and effectiveness of the product for the proposed use and could cause delay and additional costs. In addition, the FDA could reject any future 505(b)(2) application and require us to submit an ANDA if, before the submission of our 505(b)(2) application, the FDA approves an application for a product that is pharmaceutically equivalent to ours. These factors, among others, may limit our ability to commercialize our product candidates successfully.

We may not be able to enforce our intellectual property rights throughout the world.

We may not be able to enforce our intellectual property rights throughout the world. Filing, prosecuting, enforcing and defending patents on our products and product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products and product candidates.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third

parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop and market their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Agreements through which we may license patent rights may not give us sufficient rights to permit us to pursue enforcement of those licensed patents or defense of any claims asserting the invalidity of these patents or the ability to control enforcement or defense of such patent rights in all relevant jurisdictions as requirements may vary.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Moreover, such proceedings could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely affect the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Risks Related to Intellectual Property Laws

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and are therefore costly, time consuming and inherently uncertain. Changes in patent statutes, regulations promulgated under them, and court holdings interpreting the statutes and regulations could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Further, for a patent with an effective filing date of March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine-month window from issuance of the patent. Alternatively, a petition for inter partes review can be filed after the nine-month period for filing a post-grant review petition has expired. Post-grant review proceedings can be brought on any ground of invalidity, whereas inter partes review proceedings can only raise an invalidity challenge based on published prior art and patents. In these adversarial actions, the USPTO reviews patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts and uses a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier and less costly for a competitor or third party to have a U.S. patent invalidated in a USPTO post-grant review or inter partes review proceeding than in a litigation in a U.S. federal court. If any of our patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that we will be successful in defending the patent, which could result in a loss of the challenged patent right to us.

Risks Related to Employee Matters, Managing Growth and Ongoing Operations

Risks Related to Ongoing Operations

Disruptions at the FDA, the SEC and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

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

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold due to the COVID-19 pandemic, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches for evaluating public health. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be appropriate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. During the COVID-19 public health emergency, the FDA has worked to ensure timely reviews of applications for medical products in line with its user fee performance goals and conduct mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Risks Relating to the Integration of the Combined Company

We may not be able to successfully integrate and combine the businesses of Xeris and Strongbridge following the completion of the Transactions and we may not realize the anticipated benefits from the Transactions.

On October 5, 2021, we completed the previously announced acquisition and merger between Xeris Pharma and Strongbridge as contemplated by the Transaction Agreement, dated as of May 24, 2021, by and among us, Xeris, Strongbridge and Wells MergerSub, Inc. (the "Transaction Agreement"). We entered into the Transaction Agreement with the expectation that the Transactions will result in various benefits, including certain cost savings and operational efficiencies or synergies. To realize these anticipated benefits, the businesses of Xeris and Strongbridge must be successfully integrated. Historically, Xeris and Strongbridge have been independent companies. The integration process to date has been complex and time consuming and may require substantial additional resources and effort. If the companies are not successfully integrated, the anticipated benefits of the Transactions may not be realized fully (or at all) or may take longer to realize than expected. A variety of factors may adversely affect our ability to fully realize the expected operating synergies, savings and other benefits of the Transactions, including, without limitation:

- latent impacts resulting from the diversion of management team's attention from ongoing business concerns as a result of the devotion of management's attention to the Transactions;
- difficulties in achieving anticipated cost savings, synergies, business opportunities and growth prospects;
- the possibility of faulty assumptions underlying expectations regarding the integration process, including with respect to the intended tax efficient transactions;

- unanticipated issues, costs and strained resources in integrating information technology, communications programs, financial procedures and operations, and other systems, procedures and policies;
- difficulties in managing a larger combined company, addressing differences in business culture and retaining key personnel and employees;
- unanticipated changes in applicable laws and regulations;
- uncertainty that employees may experience about their roles within the combined company, which may have an additional adverse effect on our ability to attract or retain key management personnel and other key employees;
- coordinating geographically separate organizations; and
- failure to otherwise integrate Xeris' and Strongbridge's respective businesses.

Some of these factors will be outside of our control and any one of them could result in increased costs and diversion of management's time and energy, as well as decreases in the amount of expected revenue which could materially impact our business, financial conditions and results of operations. The integration process and other disruptions resulting from the Transactions may also adversely affect our relationships with employees, suppliers, customers, licensors and others, and difficulties in integrating the separate businesses or regulatory functions could harm the reputation of the combined company. If we are not able to adequately address integration challenges, we may be unable to successfully integrate our operations or realize the anticipated benefits of the Transactions.

Risks Related to Employment Matters

Our business could suffer if we lose the services of key members of our senior management or if we are not able to attract and retain other key employees and consultants.

We are dependent upon the continued services of key members of our executive management and a limited number of key advisors and personnel. In particular, we are highly dependent on the skills and leadership of our executive management team, including Paul Edick, our Chief Executive Officer, Steven Pieper, our Chief Financial Officer, Steven Prestrelski, our Chief Scientific Officer and Co-Founder, John Shannon, our President and Chief Operating Officer, Ken Johnson, our Senior Vice President, Global Development and Medical Affairs, and Beth Hecht, our Chief Legal Officer and Corporate Secretary. The loss of any one of these individuals could disrupt our operations or our strategic plans. Our industry has experienced a high rate of turnover of management personnel in recent years. Any of our personnel may terminate their employment at will. If we lose one or more of our executive officers or other key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully.

Additionally, our future success will depend on, among other things, our ability to continue to hire and retain the necessary qualified scientific, technical and managerial personnel, for whom we compete with numerous other companies, academic institutions and organizations. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

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 other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to commercialize our products and to develop and commercialize our product candidates will be limited.

Risks Related to Our Common Stock

Risks Related to Investment in Securities

Our stock price has been and will likely continue to be volatile, and you may not be able to resell shares of our common stock at or above the price you paid.

The trading price of our common stock historically has been highly volatile and could continue to be subject to large fluctuations in response to the risk factors discussed in this section, and others beyond our control, including:

- our ability to successfully commercialize Gvoke, Keveyis and Recorlev;
- regulatory actions with respect to our products and product candidates;
- regulatory actions with respect to our competitors' products and product candidates;
- the success of existing or new competitive products or technologies;
- results of clinical trials of product candidates of our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- the timing and results of clinical trials of our pipeline product candidates;
- commencement or termination of collaborations for our development programs;
- the results of our efforts to develop additional product candidates or products;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure or discontinuation of any of our development programs;
- the pricing and reimbursement of Gvoke, Keveyis or any of our product candidates that may be approved;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions;
- global health concerns, such as the COVID-19 pandemic; and
- the other factors described in this "Risk Factors" section.

In recent years, the stock markets, and particularly the stock of smaller pharmaceutical and biotechnology companies, at times have experienced price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of affected companies. Broad market and industry factors may significantly affect the market price of our common stock unrelated to our actual operating performance. Since shares of our common stock were sold in our IPO in June 2018 at a price of $15.00 per share, our stock price has fluctuated significantly.

In addition, in the past, class action litigation has often been instituted against companies whose securities have experienced periods of volatility in market price. Securities litigation brought against us following volatility in our stock price, regardless of the merit or ultimate results of such litigation, could result in substantial costs, which would hurt our financial condition and operating results and divert management's attention and resources from our business.

The conversion of any of the Convertible Notes or other convertible securities into shares of common stock could have a dilutive effect that could cause our share price to go down.

We have a number of convertible securities outstanding, including CVRs, Convertible Notes and warrants, and the conversion of such securities into shares of our common stock could have a dilutive effect that could cause our share price to go down.

The Convertible Notes are convertible into shares of common stock at any time at the option of the holder subject to certain conditions. We have reserved a sufficient number of shares of common stock for issuance upon conversion of the Convertible Notes, CVRs and warrants. During the second half of 2020, $39.1 million in principal amount of Convertible Notes were converted into 13,171,791 shares of our common stock. As of December 31, 2021, the outstanding balance of Convertible Notes was $47.2 million. If any more or all of the Convertible Notes are converted into shares of common stock, our existing shareholders will experience

immediate dilution of voting rights and the price of shares of our common stock may decline. Furthermore, the perception that such dilution could occur may cause the market price of our common stock to decline. At any time before the close of business on the second scheduled trading day immediately before the maturity date, holders of Convertible Notes may convert their Convertible Notes at their option into shares of our common stock, together, if applicable, with cash in lieu of any fractional share, at the then-applicable conversion rate. The conversion rate for the Convertible Notes will initially be 326.7974 shares of our common stock per $1,000 principal amount of Convertible Notes, which represents an initial conversion price of approximately $3.06 per share of common stock, and is subject to adjustment under the terms of the Convertible Notes. In the event of certain circumstances, we will increase the conversion rate, provided that the conversion rate will not exceed 367.6470 shares of our common stock per $1,000 principal amount of Convertible Notes. Because the conversion rates of the Convertible Notes adjust upward upon the occurrence of certain events, our existing shareholders may experience more dilution if any or all of the Convertible Notes are converted into shares of common stock after the adjusted conversion rate became effective.

The CVRs represent contingent additional consideration of up to $1.00 for each CVR, payable to CVR holders, to satisfy future performance milestones, settleable in cash, common stock, or a combination of cash and common stock, at our sole election. If the performance milestones are met and we elect to pay the CVR consideration in common stock, it could have a dilutive effect to our earnings per share and cause our share price to go down.

Upon completion of the Acquisition, each outstanding and unexercised Strongbridge warrant (except private placement warrants) was assumed by the Company such that, upon exercise, the applicable holders will have the right to have delivered to them the reference property (as such term is defined in the Strongbridge assumed warrants). Each outstanding and unexercised Strongbridge private placement warrant was assumed by the Company such that the applicable holders will have the right to subscribe for the Company's Shares, in accordance with certain terms of the Strongbridge private placement warrants. The conversion of these warrants into shares of our common stock could have a dilutive effect that could cause our share price to go down.

We do not anticipate paying any cash dividends in the foreseeable future, and accordingly, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

We do not anticipate declaring any cash dividends to holders of our common stock in the foreseeable future. In addition, under our Amended Loan Agreement, we are restricted from paying any dividends or making any distributions on account of our capital stock. Our ability to pay cash dividends also may be prohibited by future loan agreements. Consequently, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investment. Investors seeking cash dividends should not invest in our common stock.

Risks Related to Tax

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2021, we had federal net operating loss carryforwards of $475.7 million and various state net operating loss carryforwards of $309.7 million. If not utilized, the federal net operating losses generated in taxable years beginning on or before December 31, 2017 will expire at various dates between 2025 and 2037, and these net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Federal net operating losses generated in taxable years beginning after December 31, 2017 can be carried forward indefinitely; however, such net operating losses may only offset up to 80% of taxable income in taxable years beginning after December 31, 2021. As of December 31, 2021, we had $5.4 million and $2.5 million of federal and state income tax credits, respectively, to reduce future tax liabilities. If not utilized, the $5.4 million in federal income tax credits will begin to expire in 2025, and the $2.5 million of state research and development credits will begin to expire in 2022, and these tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended ("Code") and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. Our existing net operating losses or credits may be subject to limitations arising from previous ownership changes, and if we undergo future ownership changes, many of which may be outside of our control, our ability to utilize our net operating losses or credits could be further limited by Sections 382 and 383 of the Code. Accordingly, we may not be able to utilize a material portion of our net operating losses or credits.

Changes in tax law may adversely affect us or our investors.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service ("IRS") and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made, and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form or with what effective dates tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law.

Risks Related to our Indenture for our Convertible Notes, Charter and Bylaws

Provisions in the Indenture for our Convertible Notes and corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us.

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 you might otherwise receive a premium for your 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 the members of 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:

- establish a classified board of directors such that all members of the board are not elected at one time; allow the authorized number of our directors to be changed only by resolution of our board of directors; and limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- 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 a special meeting of stockholders;
- 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;
- require the approval of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws; and
- provide that the Court of Chancery of the State of Delaware will be the exclusive forum for any state law derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty by one or more of our directors, officers or employees, any action asserting a claim against us pursuant to the Delaware General Corporation Law, or any action asserting a claim against us that is governed by the internal affairs doctrine, and that the United States District Court for the District of Illinois will be the exclusive forum for claims arising under the Securities Act of 1933, as amended (the "Securities Act").

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, 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. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders. This could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in our stockholders’ best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

In addition, certain provisions in the Indenture governing our Convertible Notes could make a third-party attempt to acquire us more difficult or expensive. For example, if a takeover constitutes a fundamental change, then noteholders will have the right to require us to repurchase their notes for cash. In addition, if a takeover constitutes a make-whole fundamental change, then we may be required to temporarily increase the conversion rate. In either case, and in other cases, our obligations under the notes and the indenture could increase the cost of acquiring us or otherwise discourage a third party from acquiring us or removing incumbent management, including in a transaction that noteholders or holders of our common stock may view as favorable.

Our bylaws designate certain courts as the sole and exclusive forums for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees and may discourage such lawsuits with respect to such claims.

Our amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claim for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of or based on a fiduciary duty owed by any of our current or former directors, officers and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein (the “Delaware Forum Provision”). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Securities Exchange Act of 1934, as amended. In addition, our amended and restated bylaws further provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the “Federal Forum Provision”).

This forum selection provision may limit a shareholder's ability to bring a claim in a judicial forum that it finds favorable or cost-efficient for disputes with us or any of our directors, officers, employees or agents, which may discourage such lawsuits, or increase the costs to a shareholder of bringing such lawsuits, against us and such persons.

The enforceability of forum selection provisions in other companies' articles of incorporation, bylaws or similar governing documents has been challenged in legal proceedings, and it is possible that in connection with any action a court could find the forum selection provisions contained in our bylaws to be inapplicable or unenforceable in such action. If a court were to find these forum selection provisions inapplicable or unenforceable, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely impact our operating or financial condition or performance.

General Risk Factors

If we experience significant disruptions in our information technology systems, our business may be adversely affected.

We depend on our information technology systems for the efficient functioning of our business, including accounting, data storage, compliance, purchasing and inventory management. Our current systems are not fully redundant. While we will attempt to mitigate interruptions, we may experience difficulties in implementing some upgrades which would impact our business operations or experience difficulties in operating our business during the upgrade, either of which could disrupt our operations, including our ability to timely ship and track product orders, project inventory requirements, manage our supply chain and otherwise adequately service our customers. In the event we experience significant disruptions of our information technology systems, we may not be able to repair our systems in an efficient and timely manner. Accordingly, such events may disrupt or reduce the efficiency of our entire operation and have a material adverse effect on our results of operations and cash flows.

We are increasingly dependent on sophisticated information technology for our infrastructure. Our information systems require an ongoing commitment of significant resources to maintain, protect and enhance existing systems. Despite our implementation of security measures, our information systems, like those of other companies, are vulnerable to damages from computer viruses, natural disasters, unauthorized access, cyber attack, including ransomware, and other similar disruptions. Any system failure, accident or security breach could result in disruptions to our operations. For example, third parties may attempt to hack into systems and may obtain our proprietary information or other sensitive information, which could cause significant damage to our reputation, lead to claims against the Company and ultimately harm our business.

If products liability lawsuits are brought against us, our business may be harmed, and we may be required to pay damages that exceed our insurance coverage.

We may face liability claims related to the use or misuse of our products and product candidates. These claims may be expensive to defend and may result in large judgments against us. During the course of treatment, patients using our products and product candidates could suffer adverse medical effects for reasons that may or may not be related to our products and product candidates. Our products which are commercialized face greater risks and therefore, our risk will increase upon any commercialization by us of our product candidates. Any of these events could result in a claim of liability. Any such claims against us, regardless of their merit, could result in significant costs to defend or awards against us that could materially harm our business, financial condition or results of operations. In addition, any such claims against us could result in a distraction to management, decreased demand for our products, an adverse effect on our public reputation, and/or difficulties in commercializing our products. To date, we have not received notice of any products liability claims against us. We maintain total products liability insurance coverage of $15.0 million.

Although we maintain products liability insurance for claims arising from the use of our products after FDA approval and for claims arising from the use of our product candidates in clinical trials prior to FDA approval at levels that we believe are appropriate, we may not be able to maintain our existing insurance coverage or obtain additional coverage on commercially reasonable terms for the use of our other products and product candidates in the future. Also, our insurance coverage and resources may not be sufficient to satisfy any liability resulting from products liability claims, which could materially harm our business, financial condition or results of operations. In addition, we have in the past and may in the future agree to indemnify the counterparties from losses arising from claims relating to the products, processes or services made, used, sold or performed.

Should our obligation under an indemnification provision exceed applicable insurance coverage or if we were denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage and the collaborator does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

Products liability claims could result in an FDA or other regulatory authority investigation of the safety or efficacy of our products, our manufacturing processes and facilities, our marketing programs, our internal safety reporting systems or our staff conduct. A regulatory authority investigation could also potentially lead to a recall of our products or more serious enforcement actions, limitations on the indications for which they may be used, or suspension or withdrawal of approval. Products liability claims could also result in investigation, prosecution or enforcement action by the DOJ or other federal or state government agencies.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis, and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an “emerging growth company” under the Jumpstart Our Business Startups Act ("JOBS Act") enacted in April 2012, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act. We could be an “emerging growth company” for up to five years from the date of our IPO. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

As a result of being a public company, we will continue to incur significant additional costs which may adversely affect our operating results and financial condition.

We expect to continue to incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, as well as rules implemented by the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, or the Dodd-Frank Act, the SEC and The Nasdaq Global Select Market. These rules and regulations have increased our accounting, legal and financial compliance costs and make some activities more time consuming and costly. In addition, we will continue to incur costs associated with our public company reporting requirements, and we expect those costs may increase in the future. For example, we have devoted and expect to continue to devote significant resources to complete the assessment and documentation of our internal controls over financial reporting under Section 404 of the Sarbanes-Oxley Act, including assessment of the design and effectiveness of our internal controls related to our information systems.

During the course of our ongoing review and testing of our internal controls, we may identify deficiencies and may incur significant costs to remediate such deficiencies, including material weaknesses, if any, that we identify through these efforts. We cannot predict or estimate the amount of additional costs we may incur or the timing of such costs.

New laws and regulations, as well as changes to existing laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act, the Dodd-Frank Act and rules adopted by the SEC and The Nasdaq Global Select Market, would likely result in increased costs to us as we respond to their requirements, which may adversely affect our operating results and financial condition.

Securities analysts may publish inaccurate or unfavorable research or reports about our business or may publish no information at all, which could cause our stock price or trading volume to decline.

The trading market for our common stock is influenced by the research and reports that industry or financial analysts publish about us and our business. We do not control these analysts. Analysts who publish information about our common stock may have relatively little experience with our company, which could affect their ability to accurately forecast our results and could make it more likely that we fail to meet their estimates. If any of the analysts who cover us provide inaccurate or unfavorable research or issue an adverse opinion regarding our stock price, our stock price could decline. If one or more of these analysts cease coverage of our company or fail to publish reports covering us regularly, we could lose visibility in the market, which in turn could cause our stock price or trading volume to decline.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we face this type of litigation, it could result in substantial costs and a diversion of management’s attention and resources, which could harm our business.

We are an “emerging growth company” and a "smaller reporting company," and the reduced disclosure requirements applicable to “emerging growth companies” and "smaller reporting companies" may make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012 ("JOBS Act"), and we have elected to take advantage of certain exemptions and relief from various reporting requirements that are applicable to other public companies that are not “emerging growth companies.” In particular, while we are an “emerging growth company,” (i) we will not be

required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, (ii) we will be exempt from any rules that may be adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotations or a supplement to the auditor's report on financial statements, (iii) we will be subject to reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (iv) we will not be required to hold nonbinding advisory votes on executive compensation or stockholder approval of any golden parachute payments not previously approved.

As a result, our public filings may not be comparable to companies that are not "emerging growth companies". We may remain an "emerging growth company" until the fiscal year-end following the fifth anniversary of the completion of our IPO, though we may cease to be an "emerging growth company" earlier under certain circumstances, including (i) if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any June 30, in which case we would cease to be an "emerging growth company" as of the following January 1, (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous three years, or (iii) if our gross revenue exceeds $1.07 billion in any fiscal year.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. In addition, we qualify as a "smaller reporting company," which allows us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. Even after we no longer qualify as an "emerging growth company," we may still qualify as a "smaller reporting company" if the market value of our common stock that is held by non-affiliates is below $250 million (or $700 million if our annual revenue is less than $100 million) as of June 30 in any given year, which would allow us to continue to take advantage of these exemptions.

Investors may find our common stock less attractive if we rely on these exemptions and relief granted by the JOBS Act. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may decline and/or become more volatile.

Our data collection and processing activities are governed by restrictive regulations governing the use, processing and, in certain jurisdictions, cross-border transfer of personal information.

We may be subject to European, UK, US federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). We have personnel located in Ireland and have conducted and may in the future conduct clinical trials in the European Union ("EU") and/or the United Kingdom ("UK") subjecting us to additional privacy restrictions and data protection requirements. The collection and use of personal health data in the EU are governed by the provisions of the General Data Protection Regulation ("GDPR"), as well as other national data protection legislation in force in relevant Member States (including the UK GDPR and the Data Protection Act 2018 in the UK). These laws impose a broad range of strict requirements on companies subject to the GDPR, such as including requirements relating to having legal bases for processing personal data relating to identifiable individuals and transferring such information outside the European Economic Area, or EEA (or in the case of the UK GDPR, outside of the UK), providing details to those individuals regarding the processing of their personal data, implementing safeguards to keep personal data secure, having data processing agreements with third parties who process personal data, providing information to individuals regarding data processing activities, responding to individuals' requests to exercise their rights in respect of their personal data, obtaining consent of the individuals to whom the personal data relates, reporting security and privacy breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. The GDPR may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. This may be onerous and adversely affect our business, financial condition, results of operations and prospects. Although the UK is regarded as a third country under the EU's GDPR, the European Commission has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

To enable the transfer of personal data outside of the EEA or the UK, adequate safeguards must be implemented in compliance with European and UK data protection laws. On June 4, 2021, the EC issued new forms of standard contractual clauses for data transfers from controllers or processors in the EU/EEA (or otherwise subject to the GDPR) to controllers or processors established outside the EU/EEA (and not subject to the GDPR). The new standard contractual clauses replace the standard contractual clauses that were adopted previously under the EU Data Protection Directive. The UK is not subject to the European Commission's new standard contractual clauses but has published a draft version of a UK-specific transfer mechanism, which, once finalized, will enable transfers from the UK. Following a ruling from the Court of Justice of the European Union, in Data Protection Commissioner v Facebook Ireland Limited and Maximillian Schrems ('Schrems II'), Case C-311/18 ("Schrems II"), companies relying on standard contractual clauses to govern transfers of personal data to third countries (in particular the United States) will need to assess whether the data importer can ensure sufficient guarantees for safeguarding the personal data under GDPR. This assessment includes assessing whether third party vendors can also ensure these guarantees. We will be required to implement these new safeguards when conducting restricted data transfers under the EU and UK GDPR and doing so will require significant effort and cost.

If we are investigated by a European data protection authority, we may face fines and other penalties, including bans on processing and transferring personal data. EU data protection authorities have the power to impose administrative fines for violations of the GDPR of up to a maximum of €20 million or 4% of the data controller's or data processor's total worldwide global turnover for the preceding fiscal year, whichever is higher, and violations of the GDPR may also lead to damages claims by data controllers and data subjects. Such penalties are in addition to any civil litigation claims by data controllers, clients, and data subjects. As such, we will need to take steps to cause our processes to continue to be compliant with the applicable portions of the GDPR, but we cannot assure you that we will be able to implement changes in a timely manner or without significant disruption to our business, or that such steps will be effective, and we may face the risk of liability under the GDPR.

Similarly, non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher.

Although the EU GDPR and the UK GDPR currently impose substantially similar obligations, it is possible that over time the UK GDPR could become less aligned with the EU GDPR. This lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and cost to our handling of EU personal information and our privacy and data security compliance programs and could require us to implement different compliance measures for the UK and the European Union.

Many jurisdictions outside of Europe where we may do business or conduct trials in the future are also considering and/or have enacted comprehensive data protection legislation. In addition, we also continue to see jurisdictions imposing data localization laws. These and similar regulations may interfere with our intended business activities, inhibit our ability to expand into those markets, require modifications to our products or services or prohibit us from continuing to offer services or conduct trials in those markets without significant additional costs.

Our employees, independent contractors, consultants, collaborators and CROs may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm to our reputation.

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and CROs may engage in fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, to provide accurate information to the FDA or comparable non-U.S. regulatory authorities, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, to report financial information or data accurately or to disclose unauthorized activities to us. Such misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of product materials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Global economic uncertainty and weakening product demand caused by political instability, changes in trade agreements and conflicts, such as the conflict between Russia and Ukraine, could adversely affect our business and financial performance.

Economic uncertainty in various global markets caused by political instability and conflict and economic challenges caused by the COVID-19 pandemic has resulted, and may continue to result, in weakened demand for our products. Political developments impacting government spending and international trade, including potential government shutdowns and trade disputes and tariffs, may negatively impact markets and cause weaker macro-economic conditions. The effects of these events may continue due to potential U.S. government shutdowns and the transition in administrations, and the United States' ongoing trade disputes with China and other countries. In addition, the current military conflict between Russia and Ukraine could disrupt or otherwise adversely impact our operations and related sanctions, export controls or other actions that may be initiated by nations including the U.S., the European Union or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.) could adversely affect our business and/or our supply chain or those of our third party service providers. The continuing effect of any or all of these events could adversely impact demand for our products, harm our operations and weaken our financial results.

ITEM 1B. UNRESOLVED STAFF COMMENTS

We have no unresolved written comments regarding our periodic or current reports from the staff of the U.S. Securities and Exchange Commission ("SEC").

ITEM 2. PROPERTIES

Our principal office is located in Chicago, Illinois and occupies approximately 41,000 square feet of leased space. The lease term expires on June 30, 2031. Our research and development laboratory site is also located in Chicago and occupies approximately 10,887 square feet of leased space under a 156-month lease through December 2033. We currently believe that our offices are suitable and adequate to meet our needs.

ITEM 3. LEGAL PROCEEDINGS

We are not currently subject to any material legal proceedings. From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this report, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

ITEM 4. MINE SAFETY DISCLOSURES

Not Applicable.

PART II

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

Market Information

The common stock of Xeris Biopharma Holdings, Inc. (the “Company”) is listed The Nasdaq Global Select Market (“Nasdaq”) under the symbol “XERS”. Prior to October 6, 2021, the common stock of Xeris Pharmaceuticals, Inc. (“Xeris Pharma”) (the predecessor company) was listed on Nasdaq under the symbol “XERS” since June 21, 2018. Prior to that time, there was no public market for our common stock. On October 5, 2021, pursuant to the Transaction Agreement (defined in Item 1A), Xeris Pharma completed its acquisition of Strongbridge Biopharma plc (“Strongbridge”). Immediately following the Transactions (defined in Item 1A), both Xeris Pharma and Strongbridge became wholly owned subsidiaries of the Company. The common stock of Xeris Pharma and the ordinary shares of Strongbridge were de-registered after completion of the Transactions.

Holders of Record

On March 4, 2022, there were approximately 248 stockholders of record of our common stock and the closing price of our common stock was $2.32 per share as reported by Nasdaq. Since many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Recent Sales of Unregistered Securities

We did not sell any of our unregistered securities during the year ended December 31, 2021.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not purchase any of our registered equity securities during the year ended December 31, 2021.

ITEM 6. RESERVED

Not Applicable.

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

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve significant risks and uncertainties. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those set forth in Part I, Item 1A. Risk Factors, of this Annual Report on Form 10-K.

Overview

Unless otherwise indicated, references to "Xeris," the "Company," "we," "our" and "us" in this Annual Report on Form 10-K refer to Xeris Pharmaceuticals, Inc. ("Xeris Pharma") when referring to periods prior to the acquisition of Strongbridge Biopharma plc, an Irish public limited company ("Strongbridge") (discussed below) on October 5, 2021 and to Xeris Biopharma Holdings, Inc. when referring to periods on or subsequent to October 5, 2021. Also, throughout this document, unless otherwise noted, references to Gvoke® include Gvoke PFS, Gvoke HypoPen® and Ogluo® (glucagon).

We are a biopharmaceutical company committed to developing and commercializing innovative solutions to enhance the lives of people with life-threatening diseases. Our primary focus is on therapies for patient populations in endocrinology, neurology, and gastroenterology. We currently have three commercially available products, Gvoke, a ready-to-use liquid glucagon for the treatment of severe hypoglycemia, Keveyis, the first and only U.S. Food and Drug Administration ("FDA") approved therapy for primary periodic paralysis ("PPP") and Recorlev, approved by the FDA in December 2021 for the treatment of endogenous hypercortisolemia in adult patients with Cushing's Syndrome. We also have a pipeline of development programs to extend our current marketed products into new indications and uses or bring new products forward using our proprietary formulation technology platforms, XeriSol™ and XeriJect™.

Acquisition of Strongbridge

On May 24, 2021, Xeris Pharma and Strongbridge entered into the Transaction Agreement together with Xeris Biopharma Holdings, Inc., a Delaware corporation ("the Company"), and Wells MergerSub, Inc., a Delaware corporation ("MergerSub") (the "Transaction Agreement") whereby we would acquire Strongbridge (the "Acquisition") pursuant to a scheme of arrangement (the "Scheme") under Irish law. Under the terms of the Transaction Agreement, (i) the Company acquired Strongbridge by means of the Acquisition pursuant to the Scheme and (ii) MergerSub merged with and into Xeris Pharma, with Xeris Pharma as the surviving corporation in the merger (the "Merger," and the Merger together with the Acquisition, the "Transactions"). As a result of the Transactions, both Xeris Pharma and Strongbridge became wholly owned subsidiaries of the Company. the Company acquired all of the outstanding Strongbridge ordinary shares ("Strongbridge Shares") in exchange for (i) 0.7840 of a share of the Company's common stock ("Company Shares") and cash in lieu of fractions of Company Shares due to a holder of Strongbridge Shares per Strongbridge Share and (ii) one (1) non-tradeable contingent value right, worth up to a maximum of $1.00 per Strongbridge Share settleable in cash, additional Company Shares, or a combination of cash and additional Company Shares, at the Company's sole discretion. On October 5, 2021, pursuant to the Transaction Agreement, we completed the Transactions.

Through the Acquisition, we added Keveyis (dichlorphenamide) to our commercial product portfolio. Keveyis is the first and only treatment approved by FDA for hyperkalemic, hypokalemic, and related variants of primary periodic paralysis ("PPP"), a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis. In addition, we added a clinical-stage product candidate for rare endocrine diseases, Recorlev. Recorlev (levoketoconazole), the pure 2S,4R enantiomer of the enantiomeric pair comprising ketoconazole, is a next-generation steroidogenesis inhibitor which serves as a chronic therapy for adults with endogenous Cushing's syndrome. Levoketoconazole has received orphan designation from the FDA and the European Medicines Agency. Recorlev was acquired as an in-process research and development asset and subsequently approved by the FDA on December 30, 2021 for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative. Recorlev was commercially launched in January 2022.

Patents

We currently own 141 patents issued globally, including a composition of matter patent covering our ready-to-use glucagon formulation that expires in 2036. Upon completion of the Transactions, Xeris Biopharma Holdings, Inc. controls the patents of Xeris Pharma and Strongbridge Dublin Limited, the latter of which has 53 granted patents globally related to proprietary formulations of levoketoconazole (the active pharmaceutical ingredient in Recorlev) and the uses of such formulations in treating certain endocrine-related diseases and syndromes. This includes US Patent No. 11,020,393, which was granted on June 1, 2021, and which provides patent protection through 2040 for the use of Recorlev in the treatment of certain patients with persistent or recurrent Cushing's syndrome.

Financing

We have funded our operations to date primarily with proceeds from the sale of our preferred and common stock and debt financing. We have received gross proceeds of $253.0 million from public equity offerings of our common stock (including our June 2018 initial public offering ("IPO") and our February 2019, February 2020 and June 2020 offerings), $104.9 million from sales of our preferred

stock, $86.3 million from our June 2020 Convertible Notes offering and $63.5 million from the Amended and Restated Loan and Security Agreement (as amended, the "Amended Loan Agreement"), of which $20.0 million was repaid in June 2020.

In February 2020, we completed an equity offering and sold 10,299,769 shares of common stock, including 1,299,769 shares pursuant to the underwriters' option to purchase additional shares of common stock. Net proceeds from the offering were $39.9 million. In June 2020, we completed a public notes offering and sold $86.3 million aggregate principal amount of 5.00% Convertible Senior Notes, including $11.3 million pursuant to the underwriters' option to purchase additional notes which was exercised in full in July 2020. Concurrent with the public notes offering, in June 2020 we completed an equity offering and sold 8,510,000 shares of common stock, including 1,110,000 shares pursuant to the underwriters' option to purchase additional shares of common stock which also was exercised in full in July 2020. Gross proceeds from the equity offering were $23.1 million. Net proceeds from both June 2020 offerings were $102.8 million. During the second half of 2020, $39.1 million in principal amount of Convertible Notes were converted into 13,171,791 shares of our common stock. As of December 31, 2021, the outstanding balance of Convertible Notes was $47.2 million. In October 2020, we entered into a fourth amendment to the Amended Loan Agreement, which provided for an additional $3.5 million term loan which was drawn in November 2020. As of December 31, 2021, the outstanding balance under the Amended Loan Agreement was $43.5 million. As part of the Acquisition, we acquired $38.5 million cash on October 5, 2021. On January 2, 2022, we entered into a securities purchase agreement in connection with a private placement (the "Private Placement") with an affiliate of Armistice Capital, LLC ("Armistice") for aggregate gross proceeds of approximately $30.0 million. The transaction was completed on January 3, 2022.

In March 2022, Xeris Biopharma, Xeris Pharma and certain subsidiary guarantors of the Company entered into a Credit Agreement and Guaranty (the "Hayfin Loan Agreement") with the lenders from time to time parties thereto (the "New Lenders") and Hayfin Services LLP, as administrative agent for the New Lenders, pursuant to which we and our subsidiaries party thereto granted a first priority security interest on substantially all of our assets, including intellectual property, subject to certain exceptions. The Hayfin Loan Agreement provided for the New Lenders to extend $100.0 million in term loans (the "Initial Loan") to us on the closing date and up to an additional $50.0 million in delayed draw term loans during the one year period immediately following the closing date (the "Delayed Draw Term Loans" and, together with the Initial Loan, the "Loans") in no more than three drawings of no less than $10.0 million per drawing subject to us being in pro forma compliance with the financial covenants and other conditions set forth therein. In conjunction with the execution of the Hayfin Loan Agreement, the Amended Loan Agreement balance of $43.5 million was repaid in full and fees of $2.1 million in connection with the loan repayment were paid. In addition to utilizing the proceeds to repay the obligations under the Amended Loan Agreement in full, the proceeds will otherwise be used for general corporate purposes. After repayment, the Loans may not be re-borrowed.

For the years ended December 31, 2021 and 2020, we reported net losses of $122.7 million and $91.1 million, respectively. We have not been profitable since inception, and, as of December 31, 2021, our accumulated deficit was $460.1 million. In the near term, we expect to continue to incur significant expenses, operating losses and net losses as we:

- continue our marketing and selling efforts related to commercialization of Gvoke, Keveyis and Recorlev;
- continue our research and development efforts;
- seek regulatory approval for new product candidates and product enhancements; and
- continue to operate as a public company.

We may continue to seek public equity and debt financing to meet our capital requirements. There can be no assurance that such funding may be available to us on acceptable terms, or at all, or that we will be able to commercialize our product candidates, if approved. In addition, we may not be profitable even if we commercialize any of our product candidates.

Impact of COVID-19

The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and has impacted our business operations, employees, patients and communities as well as the global economy and financial markets. The COVID-19 pandemic continues to evolve and has led to the implementation of various responses, including government-imposed quarantines, stay-at-home orders, travel restrictions, mandated business closures and other public health safety measures.

To date, we and our suppliers and third-party manufacturing partners have been able to continue to supply our products and product candidates to our patients and clinical trials respectively, and currently do not anticipate any interruptions in supply. Our third-party contract manufacturing partners continue to operate at or near normal levels, with enhanced safety measures intended to prevent the spread of the virus. While we currently do not anticipate any interruptions in our manufacturing process, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our third-party suppliers and contract manufacturing partners' ability to supply and/or manufacture our products and product candidates.

We believe that customer demand for our products has been adversely impacted by the COVID-19 pandemic due to the disruption the pandemic has caused in patients' normal access to healthcare as well as our sales and marketing personnel's access to customers. Initially, we suspended in-person interactions by our sales and marketing personnel in healthcare settings. We were engaging with these customers remotely, via webinar programs and virtual meetings, as we sought to continue to support healthcare professionals and patient care. As parts of the country reopened, some of our sales and marketing personnel began to reengage with a limited number of

in-person interactions. However, with the emergence of variants, some areas have implemented or reintroduced restrictions and may again in the future, which may impact our sales and marketing personnel's access to customers. Remote interactions generally are not as effective as in-person interactions. In addition, several conferences and other programs at which we intended to market our products have been postponed, canceled and/or transitioned to virtual meetings. We also have revised our Gvoke patient copay assistance program to offer a copay card with a buy-down to $0 for commercially eligible patients in response to the COVID-19 pandemic.

In addition to our sales and marketing personnel, we moved quickly to transition other employees to a remote work-from-home environment excluding essential services, such as personnel in our laboratory. We have since reopened our offices on a voluntary basis and have implemented safety measures designed to comply with applicable federal, state and local guidelines in response to the COVID-19 pandemic. We may be required to take additional actions that may impact our operations as required by applicable laws or regulations or which we determine to be in the best interests of our employees.

We have incurred operating losses since inception, and we have an accumulated deficit of $460.1 million at December 31, 2021. Although we believe that our cash, cash equivalents, investments, and expected revenue from sales of Gvoke, Keveyis, and Recorlev will enable us to fund our operating and capital expenditure requirements for at least the next 12 months, we cannot predict the impact of the COVID-19 pandemic on our future results of operations and financial condition due to a variety of factors, including the health of our employees, the ability of suppliers to continue to operate and deliver, the ability of Xeris and our customers to maintain operations, continued access to transportation resources, the changing needs and priorities of customers, any further government and/or public actions taken in response to the pandemic, the emergence of variants and acceptance of vaccines, and ultimately the length of the pandemic. As further detailed in "Liquidity and Capital Resources" below, we have relied on equity and debt financing for our funding to date and completed concurrent convertible debt and equity offerings in June/July 2020 under which we raised gross proceeds of $109.4 million and a registered direct offering in March 2021 under which we raised gross proceeds of $27.0 million. Given the impact of COVID-19 on the U.S. and global financial markets, we may be unable to access further equity or debt financing if and when needed.

We are closely monitoring the impact of the COVID-19 pandemic on all aspects of our business, including the impact on our operations and the operations of our customers, suppliers, vendors and business partners. We may take further precautionary and preemptive actions as may be required by federal, state or local authorities. In addition, we have taken and continue to take steps to try and minimize the current environment's impact on our business, including devising contingency plans and backup resources.

We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, our research programs, healthcare systems or the global economy, and we cannot presently predict the scope and severity of any potential business shutdowns or disruptions. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition, including sales, expenses, reserves and allowances, manufacturing, clinical trials, research and development costs and employee-related costs, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain or treat it, as well as the economic impact on local, regional, national and international markets. If we, or any of the third parties with whom we engage, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially or negatively affected, which could have a material adverse impact on our business, results of operations and financial condition.

Components of our Results of Operations

The following discussion sets forth certain components of our statement of operations of Xeris for years ended December 31, 2021 and 2020 as well as factors that impact those items.

Product revenues, net

Product revenues, net, represent gross product sales less estimated allowances for patient copay assistance programs, prompt payment discounts, payor rebates, chargebacks, service fees, and product returns, all of which are recorded at the time of sale to the pharmaceutical wholesaler or other customer. We apply significant judgments and estimates in determining some of these allowances. If actual results differ from our estimates, we make adjustments to these allowances in the period in which the actual results or updates to estimates become known. See "Critical Accounting Policies and Use of Estimates and Assumptions" for further information regarding the significant judgments and estimates involved in the determination of product revenues, net.

Cost of goods sold

Cost of goods sold includes primarily product costs, which include all costs directly related to the purchase of raw materials, charges from our contract manufacturing organizations, and manufacturing overhead costs, as well as shipping and distribution charges. Cost of goods sold also includes losses from excess, slow-moving or obsolete inventory and inventory purchase commitments, if any. Manufacturing costs for Gvoke and Recorlev incurred prior to approval and initial commercialization were expensed as research and development expenses.

Research and development expenses

Research and development expenses consist of expenses incurred in connection with the discovery and development of our product candidates. We recognize research and development expenses as incurred. Research and development expenses that are paid in

advance of performance are capitalized until services are provided or goods are delivered. Research and development expenses include:

- the cost of acquiring and manufacturing preclinical and clinical trial materials and manufacturing costs related to commercial production and scale-up until a product is approved and initially available for commercial sale;
- expenses incurred under agreements with contract research organizations ("CROs") as well as investigative sites and consultants that conduct our preclinical studies and clinical trials;
- personnel-related expenses, which include salaries, benefits and stock-based compensation;
- laboratory materials and supplies used to support our research activities;
- outsourced product development services;
- expenses relating to regulatory activities, including filing fees paid to regulatory agencies; and
- allocated expenses for facility-related costs.

Research and development activities are central to our business model. We expect to continue to incur significant research and development expenses as we advance our pipeline candidates and in particular plan and conduct clinical trials, prepare regulatory filings for our product candidates, and utilize internal resources to support these efforts. Our research and development costs have declined as compared to previous levels as a result of directing significant funding to our commercial activities, with the approval and launch of Gvoke and as we have concluded ongoing clinical programs and not yet initiated any new studies. Based on FDA interactions and expectations for a registrational program to support a mini-dose indication for Glucagon RTU in EIH, we submitted an IND in February 2022. We received FDA clearance in March 2022 and are actively planning to initiate a new phase 2 clinical program by the end of 2022 to further address the management of EIH in people with diabetes who use insulin.

Our research and development expenses may vary significantly over time due to uncertainties relating to the timing and results of our clinical trials, feedback received from interactions with the FDA and the timing of regulatory approvals.

Selling, general and administrative expenses

Selling, general and administrative expenses consist principally of compensation and related personnel costs, marketing and selling expenses, professional fees and facility costs not otherwise included in cost of goods sold or research and development expenses. Our selling and marketing costs have increased significantly as we continue our marketing and selling efforts for Gvoke in the United States. We expect to continue to incur significant marketing and selling expenses in the near term related to the commercialization of Gvoke, Keveyis and Recorlev in the United States.

As a public reporting company, we have incurred greater expenses, including increased payroll, legal and compliance, accounting, insurance and investor relations costs. We expect some of these costs to continue to increase in conjunction with our anticipated growth and complexity as a public reporting company.

Other income (expense)

Other income (expense) consists primarily of interest expense related to our convertible debt and Amended Loan Agreement, interest income earned on deposits and investments, and the change in fair value of our warrants.

Income tax

We have incurred operating losses since inception and therefore do not have any taxable income. As of December 31, 2021, we had $475.7 million in federal net operating loss carryforwards, $309.7 million of various state net operating loss carryforwards, $5.4 million in federal research and orphan drug credits that begin to expire in 2025, and $2.5 million of state research and development credits that will begin to expire in 2022.

Results of Operations

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020 (in thousands):

	Years Ended December 31,		
	2021	2020	$ Change
Product revenues, net	$ 49,280	$ 20,155	$ 29,125
Royalty, contract and other revenue	310	280	30
Total revenue	49,590	20,435	29,155
Cost and expenses:			
Cost of goods sold, excluding amortization of intangible assets	13,318	9,328	3,990
Research and development	25,160	20,921	4,239
Selling, general and administrative	125,718	73,732	51,986
Amortization of intangible assets	550	—	550
Total cost and expenses	164,746	103,981	60,765
Loss from operations	(115,156)	(83,546)	(31,610)
Other income (expense):			
Interest and other income	313	2,965	(2,652)
Interest expense	(7,180)	(10,660)	3,480
Change in fair value of warrants	(702)	(9)	(693)
Total other expense	(7,569)	(7,704)	135
Net loss before benefit from income taxes	(122,725)	(91,250)	(31,475)
Benefit from income taxes	—	110	(110)
Net loss	$ (122,725)	$ (91,140)	$ (31,585)

Product revenues, net

Product revenues, net were $49.3 million and $20.2 million for the years ended December 31, 2021 and 2020, respectively. The $29.1 million increase is primarily due to an increase in demand and the acquisition of a new product, Keveyis.

Cost of goods sold

Cost of goods sold were $13.3 million and $9.3 million for the year ended December 31, 2021 and 2020, respectively. The increase of $4.0 million was primarily made up of product cost on increased unit sales of $6.1 million, primarily offset by lower excess and obsolete expenses.

Research and development expenses

Research and development expenses increased $4.2 million for the year ended December 31, 2021 when compared to the year ended December 31, 2020. The increase was primarily driven by higher pharmaceutical process development and clinical service costs across multiple programs of $4.3 million.

Selling, general and administrative expenses

Selling, general and administrative costs increased $52.0 million for the year ended December 31, 2021 when compared to the year ended December 31, 2020. Approximately $24.4 million of the increase related to the acquisition of Strongbridge, primarily including restructuring and related employee costs of $11.0 million, transaction costs of $8.4 million and insurance costs of $3.5 million. In addition, we incurred $16.8 million of increased commercial-related costs, including an increase to our sales force of $9.4 million and

increased commercial support for Gvoke, Keveyis and Recorlev of $7.4 million. The remaining change due to an increase in general expenses.

Other income (expense)

For the year ended December 31, 2021, interest and other income decreased $2.7 million in comparison to the year ended December 31, 2020, primarily due to lower average balances in cash equivalents and investments and lower interest rates. Additionally, in 2020 other income included a legal settlement of $1.5 million.

For the year ended December 31, 2021, interest expense decreased $3.5 million in comparison to the year ended December 31, 2020. The higher interest expense in 2020 was primarily due to a loss on conversion of convertible debt of $2.6 million and a loss on extinguishment of debt of $0.7 million.

Liquidity and Capital Resources

Our primary uses of cash are to fund costs related to the manufacturing, marketing and selling of products, the research and development of our product candidates, general and administrative expenses and working capital requirements. Historically, we have funded our operations primarily through private placements of convertible preferred stock, public equity offerings of common stock, and issuance of debt. In June 2018, we completed our IPO of 6,555,000 shares of our common stock at a price of $15.00 per share for aggregate net proceeds of $88.9 million after deducting underwriting discounts and commissions as well as other equity offering expenses. In February 2019, we completed an equity offering and sold an aggregate of 5,996,775 shares of common stock at a price of $10.00 per share. Net proceeds from this equity offering were $55.5 million after deducting underwriting discounts and commissions as well as other equity offering expenses. In September 2019, we entered into the Amended Loan Agreement that provided for term loans of up to an aggregate of $85.0 million, of which $60.0 million was drawn in September 2019 and of which $20.0 million was repaid in June 2020. Additional tranches of $15.0 million (the "Term B Loan") and $10.0 million (the “Term C Loan”) were contingent on achievement of certain revenue targets which were not achieved. In August 2019, we filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale by us of up to an aggregate of $250.0 million of our common stock, preferred stock, debt securities, warrants and/or units. We simultaneously entered into a Sales Agreement with Jefferies LLC, as sales agent, to provide for the offering, issuance and sale by us of up to $50.0 million of our common stock from time to time in "at-the-market" offerings under the shelf. As of October 5, 2021, the acquisition closing date, we have sold an aggregate of 204,427 shares of common stock in at-the-market offerings under the shelf for gross proceeds of $1.8 million. The shelf ceased to be accessible upon the consummation of the Transactions. In January 2022, we filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale by us of up to an aggregate of $250.0 million of our common stock, preferred stock, debt securities, warrants and/or units.

In February 2020, we completed an equity offering and sold 10,299,769 shares of common stock. Net proceeds from this equity offering were $39.8 million after deducting underwriting discounts and commissions as well as other equity offering expenses. In June 2020, we completed a public notes offering and sold $86.3 million aggregate principal amount of 5.00% Convertible Senior Notes, including $11.3 million pursuant to the underwriters' option to purchase additional notes which was fully exercised in July 2020. Concurrently with the public notes offering, in June 2020, we completed an equity offering and sold 8,510,000 shares of common stock, including 1,110,000 shares pursuant to the underwriters’ option to purchase additional shares of common stock which was also fully exercised in July 2020. Net proceeds from both June 2020 offerings (including the net proceeds from the exercise of the underwriters' over-allotment options in July 2020) were $102.8 million after deducting underwriting discounts and commissions as well as other offering expenses. During the second half of 2020, $39.1 million in principal amount of Convertible Notes were converted into 13,171,791 shares of our common stock. In March 2021, we completed a registered direct offering of 6,553,398 shares of our common stock, the net proceeds of which were $26.9 million. As of December 31, 2021, the outstanding balance of Convertible Notes was $47.2 million. In October 2020, we entered into a fourth amendment to the Amended Loan Agreement which provided for an additional $3.5 million term loan which was drawn in November 2020. As of December 31, 2021, the outstanding balance under the Amended Loan Agreement was $43.5 million. On May 3, 2021, we entered into a fifth amendment to the Amended Loan Agreement which provides that if we achieve a certain revenue milestone prior to November 30, 2021, then the period for interest-only payments is extended six months to July 2022 and the term loan will be payable in 24 equal monthly installments. If we achieve another revenue milestone prior to May 31, 2022, the period for interest-only payments is further extended three months to October 2022 and the term loan will be payable in 21 equal monthly installments. If we achieve a third revenue milestone by August 31, 2022, the period for interest-only payments is further extended three months, to January 2023 and the term loan will be payable in 18 equal monthly installments. We achieved all revenue milestones and therefore classified the amounts due under the Amended Loan Agreement as non-current on our balance sheet as of December 31, 2021. On January 2, 2022, we entered into a securities purchase agreement in connection with the Private Placement with Armistice for aggregate gross proceeds of approximately $30.0 million and completed the transaction on January 3, 2022.

In March 2022, Xeris Biopharma, Xeris Pharma and certain subsidiary guarantors of the Company entered into a Credit Agreement and Guaranty (the "Hayfin Loan Agreement") with the lenders from time to time parties thereto (the “New Lenders”) and Hayfin Services LLP, as administrative agent for the New Lenders, pursuant to which we and our subsidiaries party thereto granted a first priority security interest on substantially all of our assets, including intellectual property, subject to certain exceptions. The Hayfin Loan Agreement provided for the New Lenders to extend $100.0 million in term loans (the “Initial Loan”) to us on the closing date and up to an additional $50.0 million in delayed draw term loans during the one year period immediately following the closing date (the “Delayed Draw Term Loans” and, together with the Initial Loan, the "Loans") in no more than three drawings of no less than

$10.0 million per drawing subject to us being in pro forma compliance with the financial covenants and other conditions set forth therein. In conjunction with the execution of the Hayfin Loan Agreement, the Amended Loan Agreement balance of $43.5 million was repaid in full and fees of $2.1 million in connection with the loan repayment were paid. In addition to utilizing the proceeds to repay the obligations under the Amended Loan Agreement in full, the proceeds will otherwise be used for general corporate purposes. After repayment, the Loans may not be re-borrowed.

Capital Resources and Funding Requirements

We have incurred operating losses since inception, and we have an accumulated deficit of $460.1 million at December 31, 2021. Based on our current operating plans and existing working capital at December 31, 2021, we believe that our cash resources are sufficient to sustain operations and capital expenditure requirements for at least the next 12 months. We expect to incur substantial additional expenditures in the near term to support the marketing and selling of Gvoke, Keveyis and Recorlev as well as and our ongoing research and development activities. We expect to continue to incur net losses for at least the next 12 months. Our ability to fund marketing and selling of Gvoke, Keveyis and Recorlev, as well as our product development and clinical operations, including completion of future clinical trials, will depend on the amount and timing of cash received from product revenue and potential future financings. Our future capital requirements will depend on many factors, including:

- the successful integration of the Acquisition and achievement of expected revenue and synergies
- the costs of commercialization activities, including product marketing, sales and distribution;
- our degree of success in commercializing Gvoke, Keveyis and Recorlev;
- the costs, timing and outcomes of clinical trials and regulatory reviews associated with our product candidates;
- the effect on our product development activities of actions taken by the FDA or other regulatory authorities;
- the number and types of future products we develop and commercialize;
- the emergence of competing technologies and products and other adverse market developments; and
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims.

We may not be able to successfully integrate and combine the businesses of Xeris and Strongbridge following the completion of the Transactions and we may not realize the anticipated benefits from the Transactions. Also, as we continue the marketing and selling of Gvoke, Keveyis and Recorlev, we may not generate a sufficient amount of product revenues to fund our cash requirements. Accordingly, we may need to obtain additional financing in the future which may include public or private debt and/or equity financings. There can be no assurance that such funding may be available to us on acceptable terms, or at all, or that we will be able to successfully market and sell Gvoke, Keveyis and Recorlev. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. The issuance of equity securities may result in dilution to stockholders. If we raise additional funds through the issuance of additional debt, which may have rights, preferences and privileges senior to those of our common stockholders, the terms of the debt could impose significant restrictions on our operations. The failure to raise funds as and when needed could have a negative impact on our financial condition and ability to pursue our business strategies. If additional funding is not secured when required, we may need to delay or curtail our operations until such funding is received, which would have a material adverse impact on our business prospects and results of operations.

Cash Flows

(**in thousands**)	**Years Ended December 31,**	
	2021	**2020**
Net cash used in operating activities	$ (95,535)	$ (80,558)
Net cash provided by (used in) investing activities	97,964	(27,405)
Net cash provided by financing activities	27,247	126,064

Operating activities

Net cash used in operating activities was $95.5 million for the year ended December 31, 2021, compared to $80.6 million for the year ended December 31, 2020. The increase in net cash used in operating activities was primarily driven by a change in working capital and an increase in net losses due to higher personnel related costs from increased headcount, one-time transaction cost of Strongbridge acquisition and related restructuring costs. For a discussion regarding product revenues, net and increases in spending, refer to "Results of Operations" included in this Item 2, "Management’s Discussion and Analysis of Financial Condition and Results of Operations."

Investing activities

Net cash provided by investing activities was $98.0 million for the year ended December 31, 2021, compared to net cash used in investing activities of $27.4 million for the year ended December 31, 2020. The increase in cash provided by investing activities was

primarily due to a greater number of investments maturing or being sold and invested in cash equivalents to fund operations, as well as $38.5 million of cash acquired from the acquisition of Strongbridge.

Financing activities

Net cash provided by financing activities was $27.2 million for the year ended December 31, 2021, compared to $126.1 million for the year ended December 31, 2020. The decrease was primarily due to the net proceeds of $26.9 million from the March 2021 registered direct offering of our common stock, as compared to the net proceeds of $81.2 million from the convertible debt offering and $3.5 million from the drawdown on the senior loan, $61.5 million from equity offerings of our common stock, partially offset by the $20.0 million pay down of principal on the senior loan.

CRITICAL ACCOUNTING POLICIES AND USE OF ESTIMATES AND ASSUMPTIONS

Our management's discussion and analysis of our financial condition and results of operations on our financial statements have been prepared in accordance with generally accepted accounting principles ("GAAP") in the United States. The preparation of these financial statements requires us to make estimates 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. On an ongoing basis, we evaluate our estimates and judgments, including, among others, those related to revenue recognition and stock-based compensation. We base our estimates on historical experience and on various other factors we believe to be appropriate under the circumstances. Actual results may differ from these estimates under different assumptions or conditions.

We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates. Our significant accounting policies are more fully described in "Note 2 - Summary of Significant Accounting Policies".

Revenue recognition

We apply the guidance in ASC 606, *Revenue Recognition*, to all contracts with customers within the scope of the standard.

We sell product primarily to wholesalers or a specialty pharmacy who subsequently resell to retail pharmacies or patients. We enter into arrangements with payors, group purchasing organizations, and healthcare providers that provide for government-mandated or privately-negotiated rebates, chargebacks and discounts related to our products. We currently sell Gvoke, Keveyis and Recorlev in the United States only and Ogulo (European brand name of Gvoke) in the United Kingdom.

Revenue is recognized when our customer (e.g., a wholesaler or specialty pharmacy) obtains control of promised goods or services, which is when our obligations under the terms of the contract with the customer are satisfied, based on the consideration we expect to receive in exchange for those goods or services.

Revenues are recorded at the net product sales price, which includes estimated allowances for patient copay assistance programs, prompt payment discounts, payor rebates, chargebacks, service fees, and product returns, all of which are recorded at the time of sale to the pharmaceutical wholesaler or other customer. The Company applies significant judgments and estimates in determining some of these allowances. If actual results differ from its estimates, adjustments are made to these allowances in the period in which the actual results or updates to estimates become known.

Patient Copay Assistance Program

We offer savings programs to commercially insured patients under which the cost of a prescription to a patient is discounted. We reimburse pharmacies for this discount through a third-party vendor. We record an accrual to reduce gross sales for the estimated copay on units sold to wholesalers and other customers. The estimate is based on estimated percentages of products that will be prescribed to qualified patients, expected patient utilization of the discount program, average assistance paid based on reporting from the third-party vendor as well as industry data and estimated levels of inventory in the distribution channel. Accrued copay fees are recorded as a reduction of product revenues and included in accrued trade discounts and rebates on the consolidated balance sheets.

Commercial Rebates

We contract with certain private payor organizations, primarily insurance companies and pharmacy benefit managers, to provide rebates with respect to utilization of the products and contracted formulary status. We accrue estimated rebates based on actual average rebate amounts and estimated percent of product that will be prescribed to qualified patients and records the rebate as a reduction of product revenues. Accrued commercial rebates are included in accrued trade discounts and rebates on the consolidated balance sheets.

Government Rebates

We participate in certain federal and state government rebate programs such as the Medicaid Drug Rebate Program, TRICARE Retail Refunds Program, and Medicare Part D Program. We accrue estimated rebates and discounts based on actual average rebate amounts and estimated percent of product that will be prescribed to qualified patients and records the rebates as a reduction of product revenues. Accrued government rebates are included in accrued trade discounts and rebates on the consolidated balance sheets.

Chargebacks

We arrange with certain commercial and government entities allowing them to buy products directly from wholesalers at specific prices. These entities purchase products through wholesalers at the discounted price, and the wholesalers charge the difference between their list price and the discounted price back to us. We accrue estimated chargebacks based on estimated percentages of products sold to these entities, contract prices, and estimated levels of inventory in the distribution channel and records the chargebacks as a reduction of product revenues. Accrued chargebacks are recorded as an allowance against trade receivables on the consolidated balance sheets.

Product Returns

For some products, our customers generally have the right to return product during the period beginning six months prior to the product expiration date and up to one year after the product expiration date. We do not have extensive history of product returns and uses various factors to estimate the provision for returns, including the launch date of products, third-party industry data for comparable products in the market and estimated channel inventory data. In a reporting period, we may decide to constrain revenue for product returns based on information from various sources, including channel inventory levels, inventory dating, prescription data, the expiration dates of product currently being shipped, price changes of competitive products and introductions of generic products. While we believe that our returns reserve is sufficient to avoid a significant reversal of revenue in future periods, if it were to increase or decrease the rate by 1%, it would have a $0.6 million impact on revenue in the year ended December 31, 2021. We record estimated product returns in accrued returns reserve on the consolidated balance sheets and as a reduction of product revenues.

Business combinations

We account for business combinations using the acquisition method of accounting in accordance with ASC 805, *Business Combinations*. Identifiable assets acquired and liabilities assumed are recorded at their acquisition date fair values. The excess of the fair value of purchase consideration over the fair values of the identifiable assets and liabilities is recorded as goodwill. Acquisition related costs are expensed as incurred. Upon acquisition, the accounts and results of operations are consolidated as of and subsequent to the acquisition date.

When determining the fair values of assets acquired and liabilities assumed, we make significant estimates and assumptions, especially with respect to intangible assets. We utilize commonly accepted valuation techniques, such as the income approach in establishing the fair value of intangible assets.

Contingent considerations

The fair value of the CVRs was calculated by using a discounted cash flow method for the Keveyis patent milestone and an option pricing method for the Recorlev and Keveyis sales milestones. In the case of Keveyis milestones, we applied a scenario-based method and weighted them based on the possible achievement of each milestone. This fair value measurement is based on significant inputs not observable in the market and thus represents a Level 3 measurement as defined in ASC 820. This value is then remeasured for future expected payout as well as the increase in fair value due to the time value of money. These gains or losses, if any, are included as a component of operating cash flows.

Warrants

Some of our warrants are classified as liabilities as they represent a financial instrument for a share of common stock. The warrants are revalued each reporting period with the change in fair value recorded in the accompanying statements of operations until the warrants are exercised, expire, or otherwise settled. Upon completion of the Acquisition, each outstanding and unexercised Strongbridge private placement warrant was assumed by the Company such that the applicable holders will have the right to subscribe for the Company's Shares, in accordance with certain terms of the Strongbridge private placement warrants. Pursuant to the terms of the warrant agreement, we could be required to settle the warrants in cash and, as a result, the warrants are required to be measured at fair value and reported as a liability in the consolidated balance sheet. We recorded the fair value of the warrants upon issuance using the Black-Scholes Model and are required to revalue the warrants at each reporting date with any changes in fair value recorded on the statement of operations.

Stock-based compensation expense

The following table summarizes the reporting of total stock-based compensation expense resulting from employee stock options, restricted stock units, and employee stock purchases under the employee stock purchase plan (in thousands):

	Years Ended December 31,	
	2021	2020
Cost of goods sold	$ 106	$ 151
Research and development	1,696	1,229
Selling, general and administrative	9,579	6,893
Total stock-based compensation expense	$ 11,381	$ 8,273

We account for our stock-based compensation awards in accordance with Accounting Standards Codification Topic 718, *Compensation-Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees, including grants of employee stock options, to be recognized in the statements of operations based on their grant date fair values. We estimate the grant date fair value of each option award using the Black-Scholes option-pricing model. We recognize stock-based compensation expense, equal to the grant date fair value of stock options, on a straight-line basis over the requisite service period. We account for forfeitures as they are incurred.

Estimating the fair value of options requires the input of subjective assumptions, including the estimated fair value of our common stock, the expected life of the option, stock price volatility, the risk-free interest rate and expected dividends. The assumptions used in our Black-Scholes option-pricing model represent management's best estimates and involve a number of variables, uncertainties and assumptions and the application of management's judgment, as they are inherently subjective. If any assumptions change, our stock-based compensation expense could be materially different in the future.

The assumptions used in our Black-Scholes option-pricing model are estimated as follows:

- *Expected Term.* We do not believe we are able to rely on our historical exercise and post-vesting termination activity to provide accurate data for estimating the expected term for use in determining the fair value-based measurement of our options. Therefore, we have opted to use the "simplified method" for estimating the expected term of options, which is the average of the weighted-average vesting period and contractual term of the option.
- *Expected Volatility.* As we have limited trading history for our common stock, the expected stock price volatility assumption is determined based on the historical volatilities of a peer group of publicly traded companies for the period of the term prior to our IPO in June 2018 as well as the historical volatility of our own common stock since we began trading subsequent to our IPO. In evaluating similarity, we consider factors such as stage of development, risk profile, enterprise value and position within the industry. We intend to continue to consistently apply this process using the same public companies until a sufficient amount of historical information regarding the volatility of our own common stock share price becomes available.
- *Risk-Free Interest Rate.* The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of the grant for the zero-coupon U.S. Treasury note with a term similar to the expected term of the option.
- *Expected Dividends.* The expected dividend yield is 0% because we have not historically paid, and do not expect for the foreseeable future to pay, a dividend on our common stock.

NEW ACCOUNTING STANDARDS

Refer to "Note 2 - Summary of Significant Accounting Policies", for a description of recent accounting pronouncements applicable to our financial statements.

JOBS ACT ACCOUNTING ELECTION

In April 2012, the Jumpstart Our Business Startups Act of 2012 ("JOBS Act") was enacted. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to take advantage of such extended transition period.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to certain market risks arising from transactions in the normal course of business, principally risk associated with interest rate and foreign currency exchange rate fluctuations.

Interest Rate Risk

Cash and Cash Equivalents and Investments—We are exposed to the risk of interest rate fluctuations on the interest income earned on our cash and cash equivalents and investments. A hypothetical one-percentage point increase or decrease in interest rates applicable to our cash and cash equivalents and investments outstanding at December 31, 2021 would increase or decrease interest income by approximately $1.0 million on an annual basis.

Long-term Debt—Our interest rate risk relates primarily to U.S. dollar LIBOR-indexed borrowings. Based on our outstanding borrowings pursuant to the Amended Loan Agreement at December 31, 2021, interest is incurred at a floating per annum rate in an amount equal to the sum of 6.25% plus the greater of (a) 2.43% and (b) the thirty-day U.S. Dollar LIBOR rate. A one-percentage point increase in interest rates would have no impact on interest expense on an annual basis as the thirty-day U.S. Dollar LIBOR rate at December 31, 2021 was 0.10%, which including a one-percent point increase would remain below 2.43%. Interest on the Convertible Notes is assessed at a fixed rate of 5.0% annually and therefore does not subject us to interest rate risk.

Foreign Exchange Risk

We contract with contract research organizations outside the United States. We may be subject to fluctuations in foreign currency exchange rates in connection with certain of these agreements. Transactions denominated in currencies other than the functional currency are recorded based on exchange rates at the time such transactions arise. As of December 31, 2021, we had immaterial liabilities denominated in the Australian Dollar. Net foreign currency gains and losses did not have a material effect on our results of operations for the year ended December 31, 2021.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Xeris Biopharma Holdings, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Xeris Biopharma Holdings, Inc. and subsidiaries (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2021, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (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 consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2017.

Chicago, Illinois

March 11, 2022

XERIS BIOPHARMA HOLDINGS, INC.

Consolidated Balance Sheets
(in thousands, except share and par value)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 67,271	$ 37,598
Short-term investments	35,162	96,190
Trade accounts receivable, net	17,456	6,875
Inventory	18,118	8,353
Prepaid expenses and other current assets	4,589	3,196
Total current assets	142,596	152,212
Property and equipment, net	6,627	6,707
Goodwill	22,859	—
Intangible assets, net	131,450	—
Other assets	829	232
Total assets	$ 304,361	$ 159,151
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 8,924	$ 3,117
Other accrued liabilities	49,088	15,895
Accrued trade discounts and rebates	15,041	5,984
Accrued returns reserve	4,000	2,889
Other current liabilities	1,987	322
Total current liabilities	79,040	28,207
Long-term debt, net of unamortized debt issuance costs	88,067	87,021
Contingent value rights	22,531	—
Supply agreement liability, less current portion	5,991	—
Deferred rent	6,883	6,629
Deferred tax liabilities	4,942	—
Other liabilities	1,676	3,533
Total liabilities	209,130	125,390
Commitments and contingencies (Note 16)		
Stockholders' Equity:		
Preferred stock—par value $0.0001, 25,000,000 shares and 10,000,000 shares authorized and no shares issued and outstanding as of December 31, 2021 and 2020, respectively	—	—
Common stock—par value $0.0001, 350,000,000 shares and 150,000,000 shares authorized as of December 31, 2021 and 2020, respectively; 124,873,316 and 59,611,202 shares issued and outstanding as of December 31, 2021 and 2020, respectively	13	6
Additional paid in capital	555,359	371,134
Accumulated deficit	(460,110)	(337,385)
Accumulated other comprehensive (loss) income	(31)	6
Total stockholders' equity	95,231	33,761
Total liabilities and stockholders' equity	$ 304,361	$ 159,151

See accompanying notes to consolidated financial statements.

XERIS BIOPHARMA HOLDINGS, INC.

Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Years Ended December 31,	
	2021	**2020**
Product revenues, net	$ 49,280	$ 20,155
Royalty, contract and other revenue	310	280
Total revenue	49,590	20,435
Costs and expenses:		
Cost of goods sold, excluding amortization of intangible assets	13,318	9,328
Research and development	25,160	20,921
Selling, general and administrative	125,718	73,732
Amortization of intangible assets	550	—
Total costs and expenses	164,746	103,981
Loss from operations	(115,156)	(83,546)
Other income (expense):		
Interest and other income	313	2,965
Interest expense	(7,180)	(10,660)
Change in fair value of warrants	(702)	(9)
Total other expense	(7,569)	(7,704)
Net loss before benefit from income taxes	(122,725)	(91,250)
Benefit from income taxes	—	110
Net loss	$ (122,725)	$ (91,140)
Other comprehensive loss, net of tax:		
Unrealized losses on investments	(38)	(10)
Foreign currency translation adjustments	1	(27)
Comprehensive loss	$ (122,762)	$ (91,177)
Net loss per common share - basic and diluted	$ (1.55)	$ (2.14)
Weighted average common shares outstanding - basic and diluted	79,027,062	42,642,901

See accompanying notes to consolidated financial statements.

XERIS BIOPHARMA HOLDINGS, INC.

Consolidated Statements of Stockholders' Equity
(in thousands, except share data)

	Common Stock		Additional Paid In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance, December 31, 2019	27,214,523	$ 3	$ 260,635	$ 43	$ (246,245)	$ 14,436
Net loss	—	—	—	—	(91,140)	(91,140)
Issuance of common stock upon equity offering	18,809,769	2	61,512	—	—	61,514
Issuance of common stock upon conversion of convertible notes	13,171,791	1	39,936	—	—	39,937
Exercise of stock options	100,866	—	172	—	—	172
Vesting of restricted stock units and related repurchases	21,449	—	(63)	—	—	(63)
Stock-based compensation	—	—	8,273	—	—	8,273
Issuance of common stock through employee stock purchase plan	292,804	—	669	—	—	669
Other comprehensive income	—	—	—	(37)	—	(37)
Balance, December 31, 2020	59,611,202	$ 6	$ 371,134	$ 6	$ (337,385)	$ 33,761
Net loss	—	—	—	—	(122,725)	(122,725)
Issuance of common stock upon equity offering	6,553,398	1	26,924	—	—	26,925
Issuance of common stock in connection with the Transactions	58,082,606	6	137,649	—	—	137,655
Issuance of equity awards to Strongbridge equity award holders in connection with the Transactions	—	—	7,964	—	—	7,964
Exercise of stock options	93,399	—	199	—	—	199
Vesting of restricted stock units and related repurchases	316,772	—	(534)	—	—	(534)
Stock-based compensation	—	—	11,381	—	—	11,381
Issuance of common stock through employee stock purchase plan	215,939	—	642	—	—	642
Other comprehensive loss	—	—	—	(37)	—	(37)
Balance, December 31, 2021	124,873,316	$ 13	$ 555,359	$ (31)	$ (460,110)	$ 95,231

See accompanying notes to consolidated financial statements.

XERIS BIOPHARMA HOLDINGS, INC.

Consolidated Statements of Cash Flows

(in thousands)	Years Ended December 31,	
	2021	**2020**
Cash flows from operating activities:		
Net loss	$ (122,725)	$ (91,140)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	1,329	1,467
Amortization of intangible assets	550	—
Amortization of investments	413	84
Amortization of debt issuance costs	961	980
Stock-based compensation	11,381	8,273
Loss on conversion of convertible debt	—	2,124
Loss on extinguishment of debt	—	443
Change in fair value of warrants	702	9
Changes in operating assets and liabilities, net of business acquisition:		
Trade accounts receivable	(6,237)	(2,182)
Prepaid expenses and other current assets	3,290	925
Inventory	(7,418)	(5,143)
Accounts payable	5,527	(2,486)
Other accrued liabilities	12,556	(2,207)
Accrued trade discounts and rebates	4,213	4,609
Accrued returns reserve	1,110	932
Deferred rent	254	(447)
Other	(1,441)	3,201
Net cash used in operating activities	(95,535)	(80,558)
Cash flows from investing activities:		
Capital expenditures	(1,085)	(377)
Purchases of investments	(43,020)	(101,773)
Sales and maturities of investments	103,600	74,745
Cash acquired through acquisition of business	38,469	—
Net cash provided by (used in) investing activities	97,964	(27,405)
Cash flows from financing activities:		
Proceeds from equity offerings	27,000	65,891
Payments of equity offering costs	(54)	(4,315)
Proceeds from issuance of debt	—	94,839
Repayment of debt	—	(25,089)
Payments of debt issuance costs	—	(5,603)
Payments of debt conversion costs	—	(400)
Proceeds from issuance of employee stock purchase plan shares	642	669
Proceeds from exercise of stock awards	193	135
Repurchase of common stock withheld for taxes	(534)	(63)
Net cash provided by financing activities	27,247	126,064
Effect of exchange rate changes on cash and cash equivalents	(3)	(22)
Increase in cash and cash equivalents	29,673	18,079
Cash and cash equivalents, beginning of period	37,598	19,519
Cash and cash equivalents, end of period	$ 67,271	$ 37,598
Supplemental schedule of cash flow information:		
Cash paid for interest	$ 7,294	$ 4,555
Supplemental schedule of non-cash investing and financing activities:		
Issuance of stock for conversion of debt	$ —	$ 37,812
Accrued debt issuance costs	$ —	$ 347
Stock issued in connection with the Acquisition	$ 137,655	$ —
Initial fair value of equity awards and PIPE warrants consideration at acquisition date	$ 8,871	$ —
Initial fair value of contingent consideration at acquisition date	$ 22,531	$ —

See accompanying notes to consolidated financial statements.

Note 1. Organization and nature of the business

Nature of business

Xeris Biopharma Holdings, Inc. ("Xeris Biopharma" or the "Company") is a biopharmaceutical company committed to developing and commercializing innovative solutions to enhance the lives of people with life-threatening diseases. The Company's primary focus is on therapies for patient populations in endocrinology, neurology, and gastroenterology. The Company currently has three commercially available products, Gvoke, a ready-to-use liquid glucagon for the treatment of severe hypoglycemia, Keveyis, the first and only U.S. Food and Drug Administration ("FDA") approved therapy for primary periodic paralysis ("PPP"), and Recorlev, approved by the FDA in December 2021 for the treatment of endogenous hypercortisolemia in adult patients with Cushing's Syndrome. The Company also has a pipeline of development programs to extend the current marketed products into new indications and uses or bring new products forward using the proprietary formulation technology platforms, XeriSol™ and XeriJect™.

On October 5, 2021, Xeris Pharmaceuticals, Inc. ("Xeris Pharma") acquired Strongbridge Biopharma plc ("Strongbridge"), a biopharmaceutical company commercializing therapies for rare diseases with significant unmet needs. Immediately following the acquisition and related transactions, both Xeris Pharma and Strongbridge became wholly owned subsidiaries of Xeris Biopharma. The common stock of Xeris Pharma and the ordinary shares of Strongbridge were de-registered after completion of the Transactions. On October 6, 2021, Xeris Biopharma's common stock, par value $0.0001 per share, commenced trading on the Nasdaq Global Select Market ("Nasdaq") under the ticker symbol "XERS". See "Note 3 – Business combination" for a more detailed description of the acquisition.

As used herein, the "Company" or "Xeris" refers to Xeris Pharma when referring to periods prior to the acquisition of Strongbridge, an Irish public limited company, on October 5, 2021 and to Xeris Biopharma when referring to periods on or subsequent to October 5, 2021. As a result, Xeris Pharma became the predecessor to Xeris Biopharma Holdings, Inc. upon completion of the Merger on October 5, 2021.

Liquidity and capital resources

The Company has incurred operating losses since inception and has an accumulated deficit of $460.1 million as of December 31, 2021. The Company expects to continue to incur net losses for at least the next 12 months beyond the issuance date of these consolidated financials. Based on the Company's current operating plans, existing working capital at December 31, 2021, and capital raised after year-end (refer to Note 19), the Company believes the cash resources are sufficient to sustain operations and capital expenditure requirements for at least the next 12 months from the issuance date of these consolidated financial statements. If needed, the Company may elect to finance the operations through equity or debt financing along with revenues.

There can be no assurance that such funding may be available to the Company on acceptable terms, or at all, or that the Company will be able to successfully market and sell Gvoke, Keveyis and Recorlev. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact the Company's ability to access capital as and when needed. The issuance of equity securities may result in dilution to stockholders. If the Company raises additional funds through the issuance of additional debt, which may have rights, preferences and privileges senior to those of our common stockholders, the terms of the debt could impose significant restrictions on the operations. The failure to raise funds as and when needed could have a negative impact on the Company's financial condition and ability to pursue the business strategies. If additional funding is not secured when required, the Company may need to delay or curtail the operations until such funding is received, which would have a material adverse impact on the business prospects and results of operations.

Significant risks

The Company is subject to a number of risks similar to other specialty pharmaceutical companies, including, but not limited to, successful commercialization and market acceptance of available products and any future products, if and when approved, successful development of the product candidates, the development of new technological innovations by competitors, and protection of intellectual property.

The ongoing global outbreak of the coronavirus disease ("COVID-19") has resulted in significant governmental measures being implemented to control the spread of the virus and has caused the Company to modify the business practices (including remote work for most of the employees from time to time). While the Company cannot predict the scope and severity, these developments and measures could materially and adversely affect the business, results of operations and financial condition. The Company is continuing to closely monitor the impact of the COVID-19 pandemic on all aspects of the business and is taking steps to minimize the impact on the business. However, the extent to which COVID-19 impacts the business, results of operations or financial condition will depend on the extent and severity of the continued spread of COVID-19 globally, the effectiveness of actions taken to contain the pandemic or treat its impact, and the resulting economic consequences, among others. Furthermore, if the Company or any of the third parties with whom the Company engages were to experience shutdowns or other business disruptions, the Company's ability to conduct the

business in the manner and on the timelines presently planned could be materially or negatively affected, which could have a material adverse impact on the business, results of operations and financial condition.

Note 2. Basis of presentation and summary of significant accounting policies and estimates

Basis of presentation

The consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP"). In the opinion of management, the accompanying consolidated financial statements reflect all adjustments, consisting only of normal recurring adjustments, considered necessary for a fair presentation of the Company's financial position, results of operations and cash flows for the periods presented. The results of operations for such periods are not necessarily indicative of the results that may be expected for any future period.

Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") issued by the Financial Accounting Standards Board ("FASB").

Basis of consolidation

These consolidated financial statements include the financial statements of Xeris Biopharma Holdings, Inc. and subsidiaries. All intercompany transactions have been eliminated.

Reclassification

As a result of the acquisition, certain reclassifications of prior period amounts have been made to improve comparability and conform to the current period presentation. Presentation changes were made to the Consolidated Statements of Operations and Comprehensive Loss. In addition, certain reclassifications of prior period data have been made in the Notes to Consolidated Financial Statements to conform to the current period presentation.

Use of estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses included in the financial statements and accompanying notes. Actual results could differ from those estimates.

Revenue recognition

The Company applies the guidance in ASC 606, *Revenue Recognition*, to all contracts with customers within the scope of the standard.

The Company sells product primarily to wholesalers or a specialty pharmacy who subsequently resell to retail pharmacies or patients. The Company enters into arrangements with payors, group purchasing organizations, and healthcare providers that provide for government-mandated or privately-negotiated rebates, chargebacks and discounts related to the Company's products. The Company currently sells Gvoke, Keveyis and Recorlev in the United States only and Ogulo (European brand name of Gvoke) in the United Kingdom.

Revenue is recognized when the Company's customer (e.g., a wholesaler or specialty pharmacy) obtains control of promised goods or services, which is when the Company's obligations under the terms of the contract with the customer are satisfied, based on the consideration the Company expects to receive in exchange for those goods or services.

Revenues are recorded at the net product sales price, which includes estimated allowances for patient copay assistance programs, prompt payment discounts, payor rebates, chargebacks, service fees, and product returns, all of which are recorded at the time of sale to the pharmaceutical wholesaler or other customer. The Company applies significant judgments and estimates in determining some of these allowances. If actual results differ from its estimates, adjustments are made to these allowances in the period in which the actual results or updates to estimates become known.

Patient Copay Assistance Program

The Company offers savings programs to commercially insured patients under which the cost of a prescription to a patient is discounted. The Company reimburses pharmacies for this discount through a third-party vendor. The Company records an accrual to reduce gross sales for the estimated copay on units sold to wholesalers and other customers. The estimate is based on estimated percentages of products that will be prescribed to qualified patients, expected patient utilization of the discount program, average assistance paid based on reporting from the third-party vendor as well as industry data and estimated levels of inventory in the distribution channel. Accrued copay fees are recorded as a reduction of product revenues and included in accrued trade discounts and rebates on the consolidated balance sheets.

Commercial Rebates

The Company contracts with certain private payor organizations, primarily insurance companies and pharmacy benefit managers, to provide rebates with respect to utilization of the products and contracted formulary status. The Company accrues estimated rebates based on actual average rebate amounts and estimated percent of product that will be prescribed to qualified patients and records the rebate as a reduction of product revenues. Accrued commercial rebates are included in accrued trade discounts and rebates on the consolidated balance sheets.

Government Rebates

The Company participates in certain federal and state government rebate programs such as the Medicaid Drug Rebate Program, TRICARE Retail Refunds Program, and Medicare Part D Program. The Company accrues estimated rebates and discounts based on actual average rebate amounts and estimated percent of product that will be prescribed to qualified patients and records the rebates as a reduction of product revenues. Accrued government rebates are included in accrued trade discounts and rebates on the consolidated balance sheets.

Chargebacks

The Company arranges with certain commercial and government entities allowing them to buy products directly from wholesalers at specific prices. These entities purchase products through wholesalers at the discounted price, and the wholesalers charge the difference between their list price and the discounted price back to the Company. The Company accrues estimated chargebacks based on estimated percentages of products sold to these entities, contract prices, and estimated levels of inventory in the distribution channel and records the chargebacks as a reduction of product revenues. Accrued chargebacks are recorded as an allowance against trade receivables on the consolidated balance sheets.

Product Returns

For some products, the Company's customers generally have the right to return product during the period beginning six months prior to the product expiration date and up to one year after the product expiration date. The Company does not have extensive history of product returns and uses various factors to estimate the provision for returns, including the launch date of products, third-party industry data for comparable products in the market and estimated channel inventory data. In a reporting period, the Company may decide to constrain revenue for product returns based on information from various sources, including channel inventory levels, inventory dating, prescription data, the expiration dates of product currently being shipped, price changes of competitive products and introductions of generic products. While the Company believes that the returns reserve is sufficient to avoid a significant reversal of revenue in future periods, if it were to increase or decrease the rate by 1%, it would have a $0.6 million impact on revenue in the year ended December 31, 2021. The Company records estimated product returns in accrued returns reserve on the consolidated balance sheets and as a reduction of product revenues.

Prompt Payment Discounts

As an incentive for prompt payment, the Company offers a discount to most customers. The Company expects that all eligible customers will comply with the contractual terms to earn the discount, and, therefore, the Company accrues the discount on all eligible sales. The Company records the discount as an allowance against trade accounts receivable on the consolidated balance sheets and as a reduction of product revenues.

Service Fees

The Company records service fees paid to the wholesaler and specialty pharmacy customers for distribution and inventory management services as a reduction to product revenues. The Company accrues estimated service fees based on contractually determined amounts. Accrued service fees are included in accrued trade discounts and rebates on the consolidated balance sheets.

Concentration of credit risk

For the years ended December 31, 2021 and 2020, four customers accounted for 95% and 92% of the Company’s gross product revenues, respectively. The same four customers accounted for 99% and 98% of the trade accounts receivable, net at December 31, 2021 and December 31, 2020, respectively.

Cost of goods sold

Cost of goods sold includes primarily product costs, which include all costs directly related to the purchase of raw materials, charges from contract manufacturing organizations, and manufacturing overhead costs, including shipping and distribution charges. Cost of goods sold also includes losses on excess, slow-moving or obsolete inventory and inventory purchase commitments, if any. Manufacturing costs for Gvoke and Recorlev incurred prior to approval and initial commercialization were expensed as research and development expenses.

The Company does not incur material cost of goods sold related to royalty, contract and other revenue.

Research and development expenses

Research and development expenses are expensed as incurred. Research and development expenses include salaries, stock compensation and other personnel-related costs, consulting fees, fees paid for contract research and development services including those for preclinical and clinical trials, laboratory equipment and facilities costs, and other external costs. In addition, manufacturing costs of products prior to approval and initial commercialization are expensed as research and development costs.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are received, the services are performed, or the arrangement is terminated.

Stock-based compensation expense

The Company accounts for stock-based compensation awards in accordance with ASC Topic 718, *Compensation-Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments, including stock options, restricted stock units and employee stock purchases, to be recognized in the statements of operations based on their grant date fair values. The Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model. The use of the Black-Scholes option-pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the common stock consistent with the expected life of the option, the risk-free interest rate and the expected dividend yield of the common stock. Restricted stock units are valued based on the fair market value of the Company’s common stock on the date they were granted. The Company recognizes stock-based compensation expense equal to the grant date fair value of stock options, restricted stock units and employee stock purchases on a straight-line basis over the requisite service period. The Company accounts for forfeitures as they are incurred.

Income taxes

Income taxes are recorded in accordance with ASC 740, *Income Taxes* (“ASC 740”), which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. The Company determines the deferred tax assets and liabilities based on differences between financial reporting and tax bases of assets and liabilities, which are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. The Company's policy is to include interest and penalties related to uncertain tax positions, if any, within the provision for taxes in the statements of operations and comprehensive loss. For the years ended December 31, 2021 and 2020, the Company did not accrue any interest or penalties on uncertain tax positions.

Cash and cash equivalents

The Company considers all demand deposits with financial institutions and highly liquid investments with an original maturity of three months or less when purchased as cash equivalents.

Investments

The Company classifies investments in debt securities as available-for-sale investments. Investments classified as short-term on the balance sheets have original maturities of greater than 90 days but less than one year.

Inventory

Inventory is stated at the lower of cost or net realizable value, using the first-in, first-out convention. Inventory consists of raw materials, work in process and finished goods. The Company has entered into manufacturing and supply agreements for the manufacture or purchase of raw materials and production supplies. The Company's inventory includes the direct purchase cost of materials and supplies, charges from contract manufacturing organizations and manufacturing overhead costs. The Company reviews inventory to assess if there is obsolete or excess inventory and records a charge to cost of goods sold if and when applicable.

Property and equipment

Property and equipment are carried at cost less accumulated depreciation. Depreciation is calculated utilizing the straight-line method over the estimated useful lives of the respective assets:

Lab equipment	5 years
Computer equipment	3 years
Leasehold improvements	Lesser of useful life or lease term
Software	3-5 years
Furniture and fixtures	5 years
Office equipment	5 years

Impairment of long-lived assets

The Company periodically evaluates long-lived assets for potential impairment in accordance with ASC 360, *Property, Plant and Equipment*. Potential impairment is assessed when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recovered. Recoverability of these assets is assessed based on undiscounted expected future cash flows from the assets, considering a number of factors, including past operating results, budgets and economic projections, market trends and product development cycles. If impairments are identified, assets are written down to their estimated fair value.

The Company recognized no impairment charges for the years ended December 31, 2021 and 2020, respectively.

Business combinations

The Company accounts for business combinations using the acquisition method of accounting in accordance with ASC 805, *Business Combinations*. Identifiable assets acquired and liabilities assumed are recorded at their acquisition date fair values. The excess of the fair value of purchase consideration over the fair values of the identifiable assets and liabilities is recorded as goodwill. Acquisition related costs are expensed as incurred. Upon acquisition, the accounts and results of operations are consolidated as of and subsequent to the acquisition date.

When determining the fair values of assets acquired and liabilities assumed, management makes significant estimates and assumptions, especially with respect to intangible assets. The Company utilizes commonly accepted valuation techniques, such as the income approach in establishing the fair value of intangible assets. See "Note 3 – Business combination" for additional detail.

Goodwill

The Company tests goodwill for impairment on an annual basis or whenever events occur that may indicate possible impairment. Goodwill is recorded as the difference, if any, between the aggregate consideration paid for an acquisition and the fair value of the net tangible and identified intangible assets acquired under a business combination. Goodwill is reviewed for impairment at a reporting unit level annually in the fourth quarter, or more frequently if events or circumstances indicate that the goodwill might be impaired. The Company first assesses qualitative factors to determine whether it is necessary to perform the quantitative goodwill impairment test. If, after assessing the totality of events or circumstances, the Company determines that it is not more likely than not that the fair value of the net assets is less than their carrying amount, then the quantitative goodwill impairment test is unnecessary.

If, based on the qualitative assessment, it is determined that it is more likely than not that the fair value of the net assets is less than their carrying amount, then the Company proceeds to perform the quantitative goodwill impairment test. In connection with the annual impairment test conducted in the fourth quarter of 2021, after the acquisition was completed, the Company performed a qualitative assessment in connection with the annual goodwill impairment evaluation and determined that it was more likely than not that the fair value of the net assets exceeded their carrying value.

Intangible assets

Acquired definite life intangible assets are amortized using the straight-line method over their respective estimated useful lives. The Company evaluates the potential impairment of intangible assets if events or changes in circumstances indicate that the carrying amount of the assets may not be fully recoverable or that the useful lives of these assets are no longer appropriate.

For further discussion of identified intangible assets, see “Note 7 – Intangible assets”.

Debt issuance costs

Debt issuance costs incurred in connection with financing arrangements are amortized to interest expense over the life of the respective financing arrangement using the effective interest method. Debt issuance costs, net of related amortization, reduce the carrying value of the related debt.

Contingent considerations

The fair value of the Contingent Value Rights (“CVRs") is calculated by using a discounted cash flow method for the Keveyis patent milestone and an option pricing method for the Recorlev and Keveyis sales milestones. In the case of Keveyis milestones, the Company applies a scenario-based method and weighted them based on the possible achievement of the milestone. This fair value measurement is based on significant inputs not observable in the market and thus represents a Level 3 measurement as defined in ASC 820, *Fair Value Measurement*. The key assumptions used include the discount rate and sales growth. The estimated value of the CVR consideration is preliminary only and is based upon available information and certain assumptions which the Company's management believes are reasonable under the circumstances. The ultimate payout under the CVRs may differ materially from the assumptions used in determining the fair value of the CVR consideration. This value is then remeasured for future expected payout as well as the increase in fair value due to the time value of money. These gains or losses, if any, are recognized in the consolidated statements of operations and comprehensive loss.

Deferred rent

Certain of the Company’s lease agreements provide for scheduled rent increases during the lease term and also for abatement of some or all rental payments for a period of time after the occupancy date. In addition, certain of the Company’s lease agreements provide for tenant improvement allowances whereby the landlord funded the cost to build out the space. The Company records a liability for such lease incentives which is amortized to rent expense on a straight-line basis throughout the lease term.

Warrant liability

Warrants required to be settled in cash are accounted for as liabilities in accordance with ASC 480, *Distinguishing Liabilities from Equity.* The fair value of these warrants are remeasured each reporting period using the Black-Scholes option-pricing model which considers the expected term of the warrants as well as the risk-free interest rate and expected volatility of the Company's common stock. The liability is recorded in other current liabilities on the consolidated balance sheet. Generally, changes in the fair value of the warrant liabilities are recorded in the consolidated statement of operations and comprehensive loss.

Fair value of financial instruments

Fair value is the price that could be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. Fair value determination in accordance with applicable accounting guidance requires that a number of significant judgments be made. Additionally, fair value is used on a non-recurring basis to evaluate assets for impairment or as required for disclosure purposes by applicable accounting guidance on disclosures about fair value of financial instruments. Depending on the nature of the assets and liabilities, various valuation techniques and assumptions are used when estimating fair value. The carrying amounts of certain of the Company’s financial instruments, including cash and cash equivalents, accounts receivable, prepaid expenses and other current assets, and accounts payable, are shown at cost, which approximates fair value due to the short-term nature of these instruments. The debt outstanding under the Amended and Restated Loan and Security Agreement approximates fair value due to the variable interest rate on the debt. Items measured at fair value on a recurring basis include the Company’s investments, warrants and CVRs.

Segment reporting

Operating segments are identified as components of an enterprise for which separate discrete financial information is available and utilized by the chief operating decision maker in making decisions regarding resource allocation and assessing performance. The Company operates in one segment and, other than having conducted certain clinical trials and applied for and received marketing approval for Ogluo outside the United States, all of the Company’s operations are in the United States.

New accounting pronouncements

Recently issued accounting pronouncements

In October 2021, the FASB issued ASU 2021-08, *Business Combinations (Topic 805): Accounting for Contract Assets and Contract Liabilities from Contracts with Customers.* This update requires that an acquirer recognize and measure contract assets and contract liabilities acquired in a business combination in accordance with Topic 606, *Revenue from Contracts with Customers.* This standard requires that an acquirer recognize and measure such contract assets and contract liabilities under Topic 606, Revenue from Contracts with Customers, as if it had originated the contracts. This standard also allows for election of certain practical expedients, which are applied on an acquisition-by-acquisition basis. This standard is effective for the Company for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years. Early adoption is permitted, including for any interim period, and if elected, this standard is applied retrospectively for any acquisitions that occurred in the fiscal year of interim adoption. Since the Company already adopted ASC 2014-09, *Revenue from Contracts with Customers (Topic 606)*, which provides a single comprehensive accounting model on revenue recognition for contracts with customers, the Company elected to early adopt ASU 2021-08 in the fourth quarter 2021 as the Company completed the acquisition of Strongbridge. Therefore, the Company has accounted for the acquisition of all contracts with customers from the Strongbridge acquisition in accordance with ASC 606. Under previous U.S. GAAP, the Company would have discounted the acquired contracts with customers to present value as of the acquisition closing date.

In May 2021, the FASB issued ASU No. 2021-04, *Earnings Per Share (Topic 260), Debt-Modifications and Extinguishments (Subtopic 470-50), Compensation-Stock Compensation (Topic 718), and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40)*. This standard addresses issuer's accounting for certain modifications or exchanges of freestanding equity-classified written call options. This standard is effective for all entities, for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. Early adoption is permitted. The Company does not currently expect the adoption of this new standard to have a material impact on the financial statements.

In August 2020, the FASB issued ASU 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*. This standard eliminates certain accounting models to simplify the accounting for convertible instruments, expands the disclosure requirements related to the terms and features of convertible instruments, and amends the guidance for the derivatives scope exception for contracts settled in an entity's own equity. This standard enhances the consistency of earnings-per-share ("EPS") calculations by requiring that an entity use the if-converted method and that the effect of potential share settlement be included in diluted EPS calculations and disclosures. This standard is effective for the Company for fiscal years beginning after December 15, 2023. Early adoption is permitted but not earlier than periods beginning after December 15, 2020. The Company is currently evaluating the impact the adoption of this new standard will have on the financial statements and disclosures.

In March 2020, the FASB issued ASU 2020-04, *Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting*. This standard provides optional expedients for application of GAAP, if certain criteria are met, to contracts and other transactions that reference London Inter-bank Offered Rate ("LIBOR") or other reference rates that are expected to be discontinued because of reference rate reform. This standard is effective for all entities as of March 12, 2020 through December 31, 2022. The Company does not currently expect the adoption of this new standard to have a material impact on the financial statements.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*. This standard eliminates certain exceptions in the current guidance related to the approach for intra-period tax allocation and the methodology for calculating income taxes in an interim period and amends other aspects of the guidance to help clarify and simplify U.S. GAAP. This standard will be effective for the Company for annual periods beginning after December 15, 2021 and interim periods within fiscal years beginning after December 15, 2022. Early adoption of this standard is permitted. The Company does not currently expect the adoption of this new standard to have a material impact on the financial statements.

In January 2017, the FASB issued ASU 2017-04, *Intangibles – Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment.* The standard simplifies the subsequent measurement of goodwill by eliminating Step 2 from the goodwill impairment test. Under the new standard, the Company is required to perform its annual or interim goodwill impairment test by comparing the fair value of the reporting unit with its carrying amount, and recognize an impairment charge for the amount by which the carrying amount exceeds the reporting unit's fair value. The guidance is effective for the Company for fiscal years beginning after December 15, 2022, including interim periods within that annual period, with early adoption permitted. Since the Company started to have goodwill after the business combination in the fourth quarter 2021, the Company early adopted this guidance prospectively on January 1, 2021, and it did not have any impact on the Company's consolidated financial statements.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. This standard requires entities to estimate an expected lifetime credit loss on financial assets ranging from

short-term trade accounts receivable to long-term financings and report credit losses using an expected losses model rather than the incurred losses model that was previously used and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, the standard will require allowances to be recorded instead of reducing the amortized cost of the investment. This standard limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and requires the reversal of previously recognized credit losses if fair value increases. This standard is effective for the Company for fiscal years beginning after December 15, 2020, and interim periods within fiscal years beginning after December 15, 2021. On November 15, 2019, the FASB delayed the effective date of FASB ASC Topic 326 for certain small public companies and other private companies. As amended, the effective date of ASC Topic 326 was delayed until fiscal years beginning after December 15, 2022 for SEC filers that are eligible to be smaller reporting companies under the SEC's definition, as well as private companies and not-for-profit entities. The Company is currently evaluating the impact the adoption of this new standard will have on the financial statements.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842).* The new standard requires lessees to record a right-of-use asset and a lease liability for all leases with a term of greater than twelve months regardless of their classification. Leases will be classified as either operating or finance leases under the new guidance. Operating leases will result in straight-line expense in the income statement, similar to current operating leases, and finance leases will result in more expense being recognized in the earlier years of the lease term, similar to current capital leases. This standard is effective for the Company for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. The FASB has recently extended the effective date of this standard for certain companies. As amended in ASU 2020-05, this standard will be effective for the Company for fiscal years beginning after December 15, 2021 and interim periods within fiscal years beginning after December 15, 2022. The Company is currently evaluating the impact the adoption of this new standard will have on the financial statements and related disclosures; however, since the Company is a lessee to certain leases for property whose terms exceed twelve months, it expects, once adopted, to report assets and liabilities related to these leases on the balance sheet.

Note 3. Business combination

On May 24, 2021, Xeris Pharma issued an announcement pursuant to Rule 2.5 of the Irish Takeover Panel Act 1997 (as amended), Takeover Rules, 2013, disclosing that the boards of directors of Xeris Pharma and Strongbridge (with the exception of Jeffrey W. Sherman, M.D., a director in common to both companies, who abstained from the voting), had reached agreement on the terms of a recommended acquisition of Strongbridge by Xeris Pharma (the "Acquisition"). Xeris Pharma, Strongbridge, Xeris Biopharma and Wells MergerSub, Inc., a Delaware corporation ("MergerSub"), entered into a Transaction Agreement, dated as of May 24, 2021 (the "Transaction Agreement").

On October 5, 2021 (the "acquisition closing date"), pursuant to the Transaction Agreement, Xeris Pharma completed the acquisition of Strongbridge. Upon completion of the Acquisition, (a) the Company acquired Strongbridge by means of a scheme of arrangement (the "Scheme") under Irish law pursuant to which the Company acquired all of the outstanding ordinary shares of Strongbridge ("Strongbridge Shares") in exchange for (i) 0.7840 of a share of the Company's common stock ("Company Shares") and cash in lieu of fractions of Company Shares in exchange for each Strongbridge Share held by such Strongbridge Shareholders and (ii) one (1) non-tradeable CVR, worth up to a maximum of $1.00 per Strongbridge Share settleable in cash, additional Company Shares, or a combination of cash and additional Company Shares, at the Company's sole election and (b) MergerSub merged with and into Xeris Pharma, with Xeris Pharma, as the surviving corporation in the merger (the "Merger," and the Merger together with the Acquisition, the "Transactions").

Upon completion of the Merger, (a) each share of Xeris Pharma common stock was assumed by the Company and converted into the right to receive one Company Share and any cash in lieu of fractional entitlements due to a Xeris Pharma shareholder and (b) each Xeris Pharma option, stock appreciation right, restricted share award and other Xeris Pharma share based award that was outstanding was assumed by the Company and converted into an equivalent equity award of the Company, which award was subject to the same number of shares and the same terms and conditions as were applicable to the Xeris Pharma award in respect of which it was issued. On October 6, 2021, the Company's common stock, par value $0.0001 per share, commenced trading on the Nasdaq Global Select Market ("Nasdaq") under the ticker symbol "XERS".

At the effective time of the Scheme, Strongbridge's outstanding equity awards were treated as set forth in the Transaction Agreement, such that (i) each Strongbridge Share Award was vested and settled for Strongbridge Shares immediately prior to the effective time of the Scheme, (ii) each Strongbridge Option became fully vested and exercisable immediately prior to the effective time of the Scheme, (iii) each unexercised Strongbridge Option was assumed by the Company and converted into an option to purchase Company Shares (each, a "Strongbridge Rollover Option"), with the exercise price per Company Share and the number of Company Shares underlying the Strongbridge Rollover Option adjusted to reflect the conversion from Strongbridge Shares into Company Shares, provided that each Strongbridge Rollover Option will continue to have, and be subject to, the same terms and conditions that applied to the corresponding Strongbridge Rollover Option (except for terms rendered inoperative by reason of the Acquisition or for immaterial

administrative or ministerial changes that are not adverse to any holder other than in any de minimis respect), provided that the terms of each Strongbridge Rollover Option with an exercise price of $4.50 or less (prior to the adjustment described above) were amended to provide that it shall remain exercisable for a period of time following the effective time of the Scheme equal to the lesser of (A) the maximum remaining term of such corresponding Strongbridge Option and (B) the fourth anniversary of the effective date of the Merger, in each case regardless of whether the holder of such Strongbridge Rollover Option experiences a termination of employment or service on or following the effective time of the Scheme and (iv) the Company issued to each holder of a Strongbridge Rollover Option one CVR with respect to each Strongbridge Share subject to the applicable Strongbridge Option, provided that in no event shall such holder be entitled to any payments with respect to such CVR unless the corresponding Strongbridge Option has been exercised on or prior to any such payment.

Additionally, on completion of the Acquisition, (a) each outstanding and unexercised Strongbridge warrant (except private placement warrants) was assumed by the Company such that, upon exercise, the applicable holders will have the right to have delivered to them the reference property (as such term is defined in the Strongbridge assumed warrants) and (b) each outstanding and unexercised Strongbridge private placement warrant was assumed by the Company such that the applicable holders will have the right to subscribe for Company Shares, in accordance with certain terms of the Strongbridge private placement warrants.

The Acquisition was accounted for as a business combination using the acquisition method of accounting under the provisions of ASC 805, *Business Combinations*.

The Acquisition will diversify and increase the Company’s revenue base into the specialized commercial platforms and expand the development pipeline. Additionally, the Company expects to achieve significant synergies by eliminating redundant processes and headcount, most notably within the commercial, executive and general and administrative functions.

Acquisition consideration

The acquisition-date fair value of the consideration transferred totaled $169.1 million, which consisted of the following:

Fair value of consideration transferred (in thousands, except share number)		
Xeris Biopharma Holdings, Inc. common shares (58,082,606 shares)	$	137,655
Unexercised Strongbridge options assumed by Xeris Pharma and converted into options to purchase Company Shares		6,404
Strongbridge warrants		2,467
Contingent consideration (Contingent value rights)		22,531
Total consideration	$	169,057

The Company’s acquisition accounting is primarily pending final valuation and potential CVR fair value adjustments to the consideration. The fair value of the common stock issued was determined based on the closing market price of shares of the Company’s common stock on the acquisition date.

The fair value of the private placement warrants was determined using the Black-Scholes valuation model which considers the expected terms of the private placement warrants from the acquisition closing date as well as the risk-free interest rate, current exercise price of $2.50 multiplied by (the average of Xeris Pharma closing prices for the 20-day period ending three trading days prior to acquisition closing date/the average of Strongbridge closing prices for the 20-day period ending three trading days prior to acquisition closing date) and a volatility of 50%.

The CVRs represent contingent additional consideration of up to $1.00 for each CVR, payable to CVR holders, to satisfy future performance milestones, settleable in cash, common stock, or a combination of cash and common stock, at the Company's sole election. The CVRs are conditioned upon the achievement of the following:

- Keveyis Milestone: $0.25 per CVR, upon the earlier of the first listing of any patent in the FDA's Orange Book for Keveyis by the end of 2023 or the first achievement of at least $40 million in net sales of Keveyis in 2023;
- 2023 Recorlev Milestone: $0.25 per CVR, upon the first achievement of at least $40 million in net sales of Recorlev in 2023; and
- 2024 Recorlev Milestone: $0.50 per CVR, upon the first achievement of at least $80 million in net sales of Recorlev in 2024.

Refer to "Note 12 - Fair Value Measurements", for information related to the fair value measurements on CVRs and valuation methods utilized.

As of the acquisition closing date, there were approximately 74.1 million CVRs. There will be additional issuance of up to 10.5 million. CVRs to holders of Strongbridge rollover options and assumed warrants upon exercise.

Preliminary purchase price allocation

In accordance with ASC 805, Xeris Pharma was determined to be the accounting acquirer in the Acquisition. The Company has applied the acquisition method of accounting that requires, among other things, that identifiable assets acquired and liabilities assumed generally be recognized on the balance sheet at fair value as of the acquisition date. In determining the fair value, the Company utilized various forms of the income, cost and market approaches depending on the asset or liability being fair valued. The estimation of fair value required significant judgment related to future net cash flows (including revenue, operating expenses, and working capital), discount rates reflecting the risk inherent in each cash flow stream, competitive trends, market comparables and other factors. Inputs were generally determined by taking into account historical data (supplemented by current and anticipated market conditions), trends and growth rates.

The initial allocation of the purchase price was based on preliminary valuations and assumptions. During the fourth quarter of 2021, the Company did record $4.9 million of net deferred tax liabilities based on jurisdictional outcomes. Otherwise, there were no material measurement period adjustments.

The table below presents the estimated fair value that was allocated to Strongbridge's assets and liabilities based upon fair values as determined by the Company (in thousands):

		Fair Value
Cash and cash equivalents	$	38,469
Trade accounts receivable		4,344
Inventory		1,862
Prepaid expenses and other current assets		4,683
Property and equipment		161
IPR&D		121,000
Other intangible asset		11,000
Other assets		860
Total identifiable assets acquired		182,379
Accounts payable		(279)
Other accrued liabilities		(13,703)
Accrued trade discounts and rebates		(4,844)
Supply agreement liability		(12,000)
Deferred tax liabilities		(4,942)
Other liabilities		(413)
Total liabilities assumed		(36,181)
Net identifiable assets acquired		146,198
Goodwill		22,859
Net assets acquired	$	169,057

The above allocation of the purchase price is provisional and is still subject to change within the measurement period (up to one year from the acquisition date) as a result of additional information obtained with regards to facts and circumstances that existed as of the acquisition date. The final allocation of the purchase price is expected to be completed as soon as practicable, but no later than one year from the date of the Transactions.

The following is a description of the methods used to determine the fair values of significant assets and liabilities.

In-process research and development ("IPR&D") and other intangible asset

The IPR&D intangible asset represents the recording of the acquired IPR&D indefinite-lived intangible asset related to Recorlev. The other intangible asset represents the commercial product in the form of Keveyis. The fair value for the IPR&D and other intangible assets were based on assumptions developed by management and other information compiled by management including, but not limited to, discounted future expected cash flows. The fair value of intangibles relies heavily on projected future net cash flows including, but not limited to, key assumptions for revenue and operating expenses. The discount rates used for intangible assets are

based on current market rates and reflect the risk inherent in each cash flow stream. The estimated useful life of the intangible asset of Keveyis is five years which reflects the time period in which the Company expects to receive the benefits of the related cash flows.

Goodwill

The excess of the consideration transferred over the fair value of assets acquired and liabilities assumed was recognized as goodwill. The goodwill is generated from operational synergies and cost savings the Company expects to achieve from the combined operations and Strongbridge's knowledgeable and experienced workforce. The majority of the goodwill is not expected to be deductible for tax purposes.

Transaction costs

In connection with the Transactions, the Company incurred significant expenses in the second through fourth quarter of 2021 such as transaction costs (e.g., bankers' fees, legal fees, consultant fees, etc.). Total transaction costs recorded in the selling, general and administrative expenses totaled $8.4 million for the year ended December 31, 2021.

Supplemental pro forma information

The following unaudited supplemental pro forma financial information assumes the companies were combined as of January 1, 2020. The pro forma financial information as presented below is for informational purposes only and is based on estimates and assumptions that have been made solely for purposes of developing such pro forma information. This is not necessarily indicative of the results of operations that would have been achieved if the Acquisition had taken place on January 1, 2020, nor is it necessarily indicative of future results. Consequently, actual results could differ materially from the unaudited pro forma financial information presented below. The following table presents the pro forma operating results as if Strongbridge had been included in the Company's Condensed Consolidated Statements of Operations as of January 1, 2020 (unaudited, in thousands):

	Years Ended December 31,	
	2021	2020
Revenue	$ 79,509	$ 51,166
Net loss	$ (160,342)	$ (132,367)

These amounts have been calculated after applying the Company's accounting policies and adjusting the results of Xeris to reflect the additional depreciation and amortization that would have been charged assuming the fair value adjustments to intangible assets had been applied on January 1, 2020.

The unaudited supplemental pro forma information above does not include any cost saving synergies from operating efficiencies. There is a tax impact on the pro forma adjustments due to deferred tax liabilities being greater than the deferred tax assets in Ireland. For the other non-Irish entities, there is no tax impact of the pro forma adjustments reflected as both companies are, and have been for some time, in net operating loss positions and have full valuation allowances against their net deferred tax assets on both a historical and pro forma basis.

Note 4. Short-term investments

The Company classifies investments in debt securities as available-for-sale. Debt securities are comprised of highly liquid investments with minimum "A" rated securities and, as of December 31, 2021, consist of U.S. Treasury and agency bonds and corporate entity commercial paper and securities, all with maturities of more than three months but less than one year at the date of purchase. Debt securities as of December 31, 2021 had an average remaining maturity of 0.5 years. The debt securities are reported at fair value with unrealized gains or losses recorded in accumulated other comprehensive income (loss) in the consolidated balance sheet. Refer to "Note 12 - Fair Value Measurements", for information related to the fair value measurements and valuation methods utilized.

The following table represents the Company's available-for-sale investments by major security type as of December 31, 2021 and 2020 (in thousands):

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Total Fair Value
Investments:				
Commercial paper	$ 21,773	$ —	$ —	$ 21,773
Corporate securities	12,072	2	(7)	12,067
Foreign government securities	1,324	—	(2)	1,322
Total available-for-sale investments	$ 35,169	$ 2	$ (9)	$ 35,162

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Total Fair Value
Investments:				
Commercial paper	$ 18,179	$ —	$ —	$ 18,179
Corporate securities	13,597	29	(1)	13,625
U.S. government securities	64,383	7	(4)	64,386
Total available-for-sale investments	$ 96,159	$ 36	$ (5)	$ 96,190

The Company reviews available-for-sale investments for other-than-temporary impairment loss periodically. The Company considers factors such as the duration, severity of and reason for the decline in value, the potential recovery period and our intent to sell. For debt securities, the Company also consider whether (i) it is more likely than not that the Company will be required to sell the debt securities before recovery of their amortized cost basis and (ii) the amortized cost basis cannot be recovered as a result of credit losses. During the years ended December 31, 2021 and 2020, the Company did not recognize any other-than-temporary impairment losses. All marketable securities with unrealized losses have been in a loss position for less than twelve months.

Note 5. Inventory

The components of inventories consisted of the following (in thousands):

	December 31, 2021	December 31, 2020
Raw materials	$ 5,181	$ 2,874
Work in process	7,442	4,247
Finished goods	5,495	1,232
Inventory	$ 18,118	$ 8,353

Inventory reserves were $1.0 million and $2.2 million at December 31, 2021 and December 31, 2020, respectively.

Note 6. Property and equipment

Property and equipment consisted of the following (in thousands):

	December 31, 2021	December 31, 2020
Lab equipment	$ 3,739	$ 2,684
Furniture and fixtures	1,355	1,355
Computer equipment	307	277
Office equipment	28	8
Software	307	307
Leasehold improvements	5,026	4,627
	10,762	9,258
Less: accumulated depreciation and amortization	(4,135)	(2,551)
Property and equipment, net	$ 6,627	$ 6,707

Depreciation and amortization expense relating to property and equipment was $1.3 million and $1.5 million for the years ended December 31, 2021 and 2020, respectively.

Note 7. Intangible assets

Identified intangible assets consisted of the following (in thousands):

		December 31, 2021		
	Life (Years)	Gross assets	Accumulated amortization	Net
Definite-lived intangible asset - Keveyis	5	$ 11,000	$ (550)	$ 10,450
Definite-lived intangible asset - Recorlev	14	121,000	—	121,000
Total intangible assets		$ 132,000	$ (550)	$ 131,450

Keveyis is the developed product rights obtained from Strongbridge's acquisition of U.S. marketing rights to Keveyis (dichlorphenamide) from Taro Pharmaceuticals U.S.A., Inc. ("Taro").

The IPR&D product Recorlev acquired from the Acquisition was approved by FDA on December 30, 2021. The IPR&D asset has been reclassified as a definite-lived intangible asset to be amortized on a straight-line basis over an estimated useful life of 14 years assigned based on the economic life and remaining patent life.

As of December 31, 2021, expected amortization expense for intangible assets subject to amortization for the next five years is as follows (in thousands):

2022	$ 10,843
2023	10,843
2024	10,843
2025	10,843
2026	10,293
Thereafter	77,785
Total minimum lease payments	$ 131,450

Note 8. Other accrued liabilities

Other accrued liabilities consisted of the following (in thousands):

	December 31, 2021	December 31, 2020
Accrued employee costs	$ 19,638	$ 7,989
Supply agreement - current portion	6,009	—
Accrued supply chain costs	595	1,702
Accrued marketing and selling costs	3,237	1,114
Accrued research and development costs	1,998	678
Accrued restructuring charges	6,715	811
Accrued interest expense	1,413	1,527
Accrued Strongbridge transaction costs	1,839	—
Accrued other costs	7,644	2,074
Other accrued liabilities	$ 49,088	$ 15,895

Note 9. Restructuring costs

In the third quarter of 2020, the Company commenced a plan to relocate the research and development laboratory from San Diego to Chicago. The costs associated with the plan include employee termination and relocation costs and other facility exit costs. The Company incurred total restructuring costs of approximately $2.0 million related to this plan. Costs of $0.3 million were incurred in the year ended December 31, 2021, all of which is included in research and development expenses in the consolidated statements of operations and comprehensive loss. The restructuring was materially completed in the fourth quarter of 2021.

After the completion of the Acquisition on October 5, 2021, the Company undertook a strategic restructuring to streamline the organization and utilize the operating expense synergy. The costs associated with the restructuring include employee termination. The Company expects to incur total restructuring cost of approximately $11.1 million related to this plan. Costs of $9.7 million were incurred in the year ended December 31, 2021, of which $0.1 million is included in research and development expenses, $9.4 million is included in selling, general and administrative expenses, and $0.2 million is included in costs of goods sold in the consolidated statements of operations and comprehensive loss. The Company anticipates the restructuring related to the Strongbridge acquisition to be substantially complete by the end of the first quarter of 2022. The restructuring reserve is included in other accrued liabilities in the consolidated balance sheet.

The following table summarizes the initial restructuring reserve in connection with the Strongbridge acquisition and the payments made during the year ended December 31, 2021 (in thousands):

	Employee Termination and Relocation Costs
Restructuring costs	$ 9,657
Payments	(2,944)
Balance accrued at December 31, 2021	$ 6,713

Note 10. Long-term debt

Convertible Senior Notes

In June 2020, Xeris Pharma completed a public offering of $86.3 million aggregate principal amount of Xeris Pharma's 5.00% Convertible Senior Notes due 2025 (the "Convertible Notes"), including $11.3 million pursuant to the underwriters' option to purchase additional notes which was exercised in full in July 2020. Xeris Pharma incurred debt issuance costs of $5.1 million in connection with the issuance of the Convertible Notes. Xeris Pharma used $20.0 million and $4.2 million of the net proceeds from the sale to prepay a portion of the principal amount on the Term A Loan (as defined below) and the remaining amount of borrowings outstanding under the PPP Loan (as defined below), respectively.

The Convertible Notes are governed by the terms of a base indenture for senior debt securities dated June 30, 2020 (the “Base Indenture”), between Xeris Pharma and U.S. Bank National Association, as trustee, as supplemented by the first supplemental indenture thereto dated June 30, 2020, between U.S. Bank National Association, as trustee, and the second supplemental indenture

thereto dated October 5, 2021 ("the Supplemental Indentures" and together with the Base Indenture, the "Indenture"), among the Company, Xeris Pharma and U.S. Bank National Association, as trustee. The Convertible Notes bear cash interest at the rate of 5.00% per annum, payable semi-annually in arrears on January 15 and July 15 of each year, beginning on January 15, 2021, to holders of record at the close of business on the preceding January 1 and July 1, respectively. The Convertible Notes will mature on July 15, 2025, unless earlier converted or redeemed or repurchased by the Company.

At any time before the close of business on the second scheduled trading day immediately before the maturity date, holders of Convertible Notes may convert their Convertible Notes at their option into shares of the Company's common stock, together, if applicable, with cash in lieu of any fractional share, at the then-applicable conversion rate. The conversion rate for the Convertible Notes will initially be 326.7974 shares of the Company's common stock per $1,000 principal amount of Convertible Notes, which represents an initial conversion price of approximately $3.06 per share of common stock, and is subject to adjustment under the terms of the Convertible Notes. In the event of certain circumstances, the Company will increase the conversion rate, provided that the conversion rate will not exceed 367.6470 shares of the Company's common stock per $1,000 principal amount of Convertible Notes.

In the second half of 2020, $8.4 million in principal amount of Convertible Notes were converted into 2,736,591 shares of Xeris Pharma's common stock at the conversion rate of 326.7974 shares per $1,000 principal amount of Convertible Notes. Additionally, in the fourth quarter of 2020, Xeris Pharma entered into separate, privately negotiated exchange agreements with certain holders of Convertible Notes to exchange $30.7 million in principal amount of Convertible Notes for 10,435,200 shares of Xeris Pharma's common stock. Xeris Pharma recognized a $2.6 million loss related to the convertible note exchange transactions.

The Convertible Notes are senior, unsecured obligations and are equal in right of payment with Xeris Pharma's existing and future senior, unsecured indebtedness, senior in right of payment to its future indebtedness, if any, that is expressly subordinated to the Convertible Notes, and effectively subordinated to its existing and future secured indebtedness to the extent of the value of the collateral securing that indebtedness. The Convertible Notes are structurally subordinated to all existing and future indebtedness and other liabilities, including trade payables, and (to the extent Xeris Pharma is not a holder thereof) preferred equity, if any, of the Company's other direct and indirect subsidiaries.

As a result of the Transactions, and pursuant to the Second Supplemental Indenture, the Convertible Notes are no longer convertible into shares of common stock of Xeris Pharma common stock. Instead, subject to the terms and conditions of the Indenture, the Convertible Notes will be exchangeable into cash and shares of common stock of the Company in proportion to the transaction consideration payable pursuant to the Transaction Agreement, and the "Reference Property" provisions in the Indenture.

Pursuant to the Second Supplemental Indenture, the Company agreed to guarantee (a) the full and punctual payment when due of all monetary obligations of Xeris Pharma under the Indenture and (b) the full and punctual performance within applicable grace periods of all other obligations of Xeris Pharma under the Indenture.

Senior Secured Loan Facility

In February 2018, Xeris Pharma entered into the Loan and Security Agreement, dated as of February 28, 2018 (as amended, the "Original Loan Agreement"), with Oxford Finance LLC ("Oxford"), as the collateral agent (in such capacity, the "Collateral Agent") and a lender, and Silicon Valley Bank, as a lender ("SVB", and together with Oxford, the "Lenders"), which provided for a senior secured loan facility of up to an aggregate principal amount of $45.0 million. The first tranche of $20.0 million was drawn down in February 2018 (the "2018 Term A Loan"). The second tranche of $15.0 million was drawn down in September 2018 (the "2018 Term B Loan"). Xeris Pharma also issued warrants to the Lenders to purchase common stock, which is further discussed in "Note 11 - Warrants".

In September 2019, Xeris Pharma entered into an Amended and Restated Loan and Security Agreement (the "Loan Agreement") with the Lenders which amended and restated the Original Loan Agreement in its entirety. The Loan Agreement provided for the Lenders to extend up to $85.0 million in term loans to Xeris Pharma in three tranches. The initial tranche of $60.0 million (the "Term A Loan") was drawn down in September 2019. Additional tranches of $15.0 million (the "Term B Loan") and $10.0 million (the "Term C Loan") were contingent on achievement of certain revenue targets which were not achieved. In conjunction with the execution of the Loan Agreement, the 2018 Term A Loan and 2018 Term B Loan were repaid and the final payment fee of $2.3 million was paid.

Effective April 21, 2020, Xeris Pharma entered into that certain First Amendment to Amended and Restated Loan and Security Agreement with the Lenders (the "First Amendment") to amend the Loan Agreement to allow Xeris Pharma to incur indebtedness under the U.S. Small Business Administration (the "SBA") the Paycheck Protection Program enabled by the Coronavirus Aid, Relief and Economic Security Act of 2020 (the "CARES Act") in the amount of $5.1 million (the "PPP Loan").

On June 30, 2020, Xeris Pharma entered into that certain Second Amendment to Amended and Restated Loan and Security Agreement with the Lenders (the "Second Amendment") to amend the Loan Agreement to provide for the Lenders' consent to and allow for Xeris Pharma's underwritten public offering of Xeris Pharma's 5.00% Convertible Senior Notes due 2025 and permit the Company to prepay the PPP Loan in full. The Second Amendment also provided for the extension of the interest-only payment period through December

31, 2021, after which the term loans would be payable in 30 equal monthly installments. However, if Xeris Pharma achieved a certain revenue milestone prior to January 1, 2022, then the period for interest-only payments would be extended through September 30, 2022, after which the term loans would be payable in 21 equal monthly installments. In addition the Second Amendment further provided for an extension of the maturity date from June 1, 2023 to June 1, 2024. After repayment, no loans may be re-borrowed.

Pursuant to the Second Amendment, Xeris Pharma prepaid a portion of the Term A Loan equal to the sum of (i) $20.0 million, plus all accrued and unpaid interest as of the date of the Second Amendment, (ii) the applicable final payment fee of $0.6 million, (iii) the applicable prepayment fee of $0.3 million and (iv) all outstanding Lenders' expenses as of the date of the Second Amendment.

Additionally, Xeris Pharma is required to maintain a minimum balance of $5.0 million in unrestricted cash at SVB at all times and to pay an amendment fee of up to $0.1 million at the earliest to occur of the maturity date, acceleration of any term loan, or prepayment of any term loan amount.

On August 5, 2020, Xeris Pharma entered into that certain Third Amendment to Amended and Restated Loan and Security Agreement with the Lenders (the "Third Amendment") to amend the Loan Agreement to (i) amend the definition of "Permitted Indebtedness" to include a new standby letter of credit in an amount not to exceed $0.4 million issued to the landlord for Xeris Pharma's new leased laboratory space and (ii) permit the sale of certain equipment related to the relocation of Xeris Pharma's research and development laboratory from San Diego to Chicago.

On October 23, 2020, Xeris Pharma entered into that certain Fourth Amendment to Amended and Restated Loan and Security Agreement with the Lenders (the "Fourth Amendment") to amend the Loan Agreement to provide an additional tranche of $3.5 million (the "Term D Loan", and, together with the Term A Loan, Term B Loan, and Term C Loan, the "Term Loan"), available upon execution. The Term D Loan of $3.5 million was drawn in November 2020 and will be payable under the same payment terms as the term loans. After repayment, the loan may not be re-borrowed.

On May 3, 2021, Xeris Pharma entered into that certain Fifth Amendment to Amended and Restated Loan and Security Agreement with the Lenders (the "Fifth Amendment") to amend the Loan Agreement. The Fifth Amendment provides that if Xeris Pharma achieves a certain revenue milestone prior to November 30, 2021, then the period for interest-only payments is extended six months to July 2022 and the Term Loan will be payable in 24 equal monthly installments. If Xeris Pharma achieves another revenue milestone prior to May 31, 2022, the period for interest-only payments is further extended three months, to October 2022 and the Term Loan will be payable in 21 equal monthly installments. If Xeris Pharma achieves a third revenue milestone by August 31, 2022, the period for interest-only payments is further extended three months, to January 2023 and the Term Loan will be payable in 18 equal monthly installments. The Company achieved all revenue milestones and therefore classified the amounts due under the Amended Loan Agreement as non-current on the balance sheet as of December 31, 2021.

On May 24, 2021, Xeris Pharma entered into that certain Consent Under Amended and Restated Loan and Security Agreement (the "Consent") with the Lenders to permit the Company to execute, deliver and perform (a) the Transaction Agreement with Strongbridge and (b) that certain Expenses Reimbursement Agreement dated as of May 24, 2021 by and between Xeris Pharma and Strongbridge pursuant to which Xeris Pharma and Strongbridge agreed to certain reimbursement obligations related to the transactions contemplated by the Transaction Agreement.

In connection with the completion of the Transactions, on October 5, 2021, the Company entered into that certain Joinder and Sixth Amendment to Amended and Restated Loan and Security Agreement (the "Sixth Amendment") with Xeris Pharma, the Lenders and Strongbridge US, Inc. ("Strongbridge US") (each of Strongbridge US and the Company, a "New Borrower") to amend the Loan Agreement. The Sixth Amendment adds the New Borrowers as borrowers under the Loan Agreement and provides for the grant by the New Borrowers to the Collateral Agent, for the ratable benefits of the Lenders, a first priority security interest on substantially all of their assets, including intellectual property, subject to certain exceptions. The Sixth Amendment also updates certain negative covenants and definitions to among, other things, permit certain intercompany arrangements and restructuring activities, as well as modifies the revenue milestones to address both Gvoke and non-Gvoke revenues. The Company achieved each revenue milestone and has therefore classified the amounts due under the Loan Agreement (as amended by that certain First Amendment, Second Amendment, Third Amendment, Fourth Amendment, Fifth Amendment, Consent and Sixth Amendment, the "Amended Loan Agreement") as non-current on the balance sheet as of December 31, 2021.

All of the loans incur interest at a floating per annum rate in an amount equal to the sum of 6.25% plus the greater of (a) 2.43% and (b) the thirty-day U.S. Dollar LIBOR rate (or, the LIBOR replacement rate as applicable). For the period from the funding date of the Term A Loan through and including December 31, 2021, the interest rate was 8.68%. The Company has incurred total debt issuance costs of $2.0 million related to the Original Loan Agreement and the Amended Loan Agreement, which are being amortized to interest expense over the life of the loan using the effective interest method. The remaining balance of unamortized debt issuance costs have been reflected as a direct reduction to the loan balance.

The Amended Loan Agreement allows the Company to voluntarily prepay the outstanding amounts thereunder, but not less than $2.0 million of the outstanding principal at any time. The Company is subject to a prepayment fee equal to 1.50% of the principal amount being prepaid. Also, a final payment fee of 3.0% multiplied by the amount to be repaid is due upon the earliest to occur of the maturity date of the Amended Loan Agreement, the acceleration of the amounts outstanding under the Amended Loan Agreement or prepayment of such borrowings and is recorded in other liabilities on the consolidated balance sheets.

The Amended Loan Agreement contains customary representations and warranties, events of default (including an event of default upon a material adverse change of the Company) and affirmative and negative covenants, including, among others, covenants that limit or restrict the Company's ability to incur additional indebtedness, grant liens, merge or consolidate, make acquisitions, pay dividends or other distributions or repurchase equity, make investments, dispose of assets and enter into certain transactions with affiliates, in each case subject to certain exceptions.

Refer to "Note 19 - Subsequent events" for discussion over the Hayfin Loan Agreement executed after December 31, 2021.

The components of debt are as follows (in thousands):

	December 31, 2021	December 31, 2020
Convertible Notes	$ 47,175	$ 47,175
Senior secured loan facility	43,500	43,500
Less: unamortized debt issuance costs	(2,608)	(3,654)
Long-term debt, net of unamortized debt issuance costs	$ 88,067	$ 87,021

The following table sets forth the Company's future minimum principal payments on the senior secured loan facility (which reflect the Fifth Amendment) and the Convertible Notes (in thousands):

2022	$ —
2023	29,000
2024	14,500
2025	47,175
	$ 90,675

For the year ended December 31, 2021, the Company recognized interest expense of $7.2 million, of which $1.0 million related to the amortization of debt issuance costs. For the year ended December 31, 2020, the Company recognized interest expense of $10.7 million, of which $1.0 million related to the amortization of debt issuance costs. Included in the 2020 interest expense are a loss on conversion of convertible debt and a loss on extinguishment of debt of $2.6 million and $0.7 million, respectively.

Note 11. Warrants

As of December 31, 2021, the following warrants were outstanding:

Warrants classified as liabilities:	Outstanding Warrants	Exercise Price per Warrant	Expiration Date
2018 Term A Warrants	53,720	$11.169	February 2025
2018 Term B Warrants	40,292	$11.169	September 2025
Assumed Strongbridge private placement warrants	4,446,425	$3.005	June 2022
	4,540,437		
Warrants classified as equities (Strongbridge assumed warrants):			
Warrants in connection with Horizon and Oxford loan agreement	125,999	$3.130	December 2026
Warrants in connection with CRG loan agreement	309,122	$9.410	July 2024
Warrants in connection with CRG loan amendment in January 2018	978,628	$12.760	January 2025
Warrants in connection with Avenue Capital loan agreement	209,633	$2.390	May 2025
Warrants in connection with Avenue Capital loan agreement	209,633	$2.390	December 2025
	1,833,015		

The Company recognized gains (losses) of $(768,000), $39,000 and $27,000 upon the change in fair value of the warrants during the year ended December 31, 2021 related to the assumed Strongbridge private placement warrants, the 2018 Term A Warrants and the

2018 Term B Warrants, respectively. The Company recognized gains (losses) of $4,000, $(8,000) and $(5,000) upon the change in fair value of the warrants during the year ended December 31, 2020 related to the 2014 Warrants, the 2018 Term A Warrants and the 2018 Term B Warrants, respectively.

Refer to "Note 19 - Subsequent events" for discussion over the Hayfin Loan Agreement executed after December 31, 2021.

Note 12. Fair value measurements

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Fair value measurements are classified and disclosed in one of the following categories:

Level 1: Measured using unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities;

Level 2: Measured using quoted prices in active markets for similar assets or liabilities, quoted prices for identical or similar assets or liabilities in markets that are not active, or inputs, other than quoted prices in active markets, that are observable either directly or indirectly; and

Level 3: Measured based on prices or valuation models that require inputs that are both significant to the fair value measurement and less observable from objective sources (i.e., supported by little or no market activity).

Fair value measurements are classified based on the lowest level of input that is significant to the measurement. The Company’s assessment of the significance of a particular input to the fair value measurement requires judgment, which may affect the valuation of the assets and liabilities and their placement within the fair value hierarchy levels. The determination of the fair values stated below takes into account the market for the financial assets and liabilities, the associated credit risk and other factors as required. The Company considers active markets as those in which transactions for the assets or liabilities occur in sufficient frequency and volume to provide pricing information on an ongoing basis.

The following tables present the Company's fair value hierarchy for those assets and liabilities measured at fair value as of December 31, 2021 and 2020 (in thousands):

	Total as of December 31, 2021	Level 1	Level 2	Level 3
Assets				
Cash and cash equivalents:				
Cash and money market funds	$ 67,271	$ 67,271	$ —	$ —
Investments:				
Corporate securities	12,067	—	12,067	—
Commercial paper	21,773	—	21,773	—
Foreign government	1,322	—	1,322	—
Total investments	$ 35,162	$ —	$ 35,162	$ —
Liabilities				
Contingent value rights	$ 22,531	$ —	$ —	$ 22,531
Warrant liabilities	$ 1,769	$ —	$ —	$ 1,769

	Total as of December 31, 2020	Level 1	Level 2	Level 3
Assets				
Cash and cash equivalents:				
Cash and money market funds	$ 37,598	$ 37,598	$ —	$ —
Investments:				
U.S. government securities	64,386	64,386	—	—
Corporate securities	13,625	—	13,625	—
Commercial paper	18,179	—	18,179	—
Total investments	$ 96,190	$ 64,386	$ 31,804	$ —
Liabilities				
Warrant liabilities	$ 159	$ —	$ —	$ 159

Warrant liability

The fair value of the Company's warrant liabilities is based on a Black-Scholes valuation which considers the expected term of the warrants as well as the risk-free interest rate and expected volatility of the Company's common stock. The uncertainty of the fair value measurement due to the use of unobservable inputs and interrelationships between these unobservable inputs could have resulted in higher or lower fair value measurement.

The Company has determined that the warrant liabilities' fair values are Level 3 items within the fair value hierarchy. The following table presents the change in the warrant liabilities (in thousands):

Balance at December 31, 2020	$	159
Assumption of Strongbridge private placement warrants		908
Change in fair value of warrants		702
Balance at December 31, 2021	$	1,769

Contingent Value Rights

The fair value of the CVRs is calculated by using a discounted cash flow method for the Keveyis patent milestone and an option pricing method for the Recorlev and Keveyis sales milestones. In the case of Keveyis milestones, the Company applies a scenario-based method and weighted them based on the possible achievement of the milestone. This fair value measurement is based on significant inputs not observable in the market and thus represents a Level 3 measurement as defined in ASC 820, *Fair Value Measurement*. The key assumptions used include the discount rate and sales growth. The estimated value of the CVR consideration is preliminary only and is based upon available information and certain assumptions which the Company's management believes are reasonable under the circumstances. The ultimate payout under the CVRs may differ materially from the assumptions used in determining the fair value of the CVR consideration.

Contingent consideration obligations are recorded at their estimated fair values and these obligations are revalued each reporting period until the related contingencies are resolved. The contingent value rights are adjusted to fair value using the methods described above at the end of each reporting period. Significant changes which increase or decrease the probabilities of achieving the related milestones or shorten or lengthen the time required to achieve such events would result in corresponding increases or decreases in the fair values of these obligations.

As of December 31, 2021, the CVRs were revalued at $22.5 million using the same methods described above. During the period from October 5, 2021 to December 31, 2021, no gains or losses were recognized in the consolidated statements of operations from changes in the fair values of the CVRs. See "Note 16 – Commitments and contingencies" for a discussion of the CVRs.

There were no transfers between any of the levels of the fair value hierarchy during the years ended December 31, 2021 and 2020.

Note 13. Stockholders' equity

The Company’s 375.0 million authorized shares of stock are divided into 350.0 million shares of common stock, par value $0.0001 per share, and 25.0 million shares of undesignated preferred stock, par value $0.0001 per share. At December 31, 2021 none of the 25.0 million shares of preferred stock were outstanding, and the Company has no present plans to issue any shares of preferred stock. The Company’s board of directors has the authority, without action by the Company’s stockholders, to designate and issue the preferred stock in one or more series and to designate the rights, preferences, limitations and privileges of each series of preferred stock, which may be greater than the rights of the Company’s common stock.

The Company has not paid any cash dividends on the common stock during the periods presented.

In February 2020, the Company completed an equity offering of the common stock pursuant to the Shelf. The Company sold an aggregate of 10,299,769 shares of common stock at a price of $4.15 per share, including 1,299,769 shares pursuant to the underwriters’ option to purchase additional shares of common stock. Net proceeds from the equity offering were approximately $39.9 million after deducting underwriting discounts and commissions as well as other public offering expenses.

In June 2020, the Company completed an equity offering of the common stock pursuant to the Shelf. The Company sold an aggregate of 8,510,000 shares of common stock at a price of $2.72 per share, including 1,110,000 shares pursuant to the underwriters' option to purchase additional shares which was fully exercised in July 2020. Net proceeds from the equity offering were approximately $21.6 million after deducting underwriting discounts and commissions as well as other public offering expenses.

In the second half of 2020, $8.4 million in principal amount of Convertible Notes were converted into 2,736,591 shares of the Company’s common stock at the conversion rate of 326.7974 shares per $1,000 principal amount of Convertible Notes. Additionally, in the fourth quarter of 2020, the Company entered into separate, privately negotiated exchange agreements with certain holders of Convertible Notes to exchange $30.7 million in principal amount of Convertible Notes for 10,435,200 shares of the Company’s common stock.

In March 2021, the Company completed a registered direct offering of 6,553,398 shares of the common stock at a price of $4.12 per share. Net proceeds from the equity offering were approximately $26.9 million after deducting offering expenses.

On October 5, 2021, the Company completed the acquisition of Strongbridge. Upon completion of the Merger, (a) each share of Xeris Pharma common stock was assumed by the Company and converted into the right to receive one Company Share and any cash in lieu of fractional entitlements due to a Xeris Pharma shareholder and (b) each Xeris Pharma option, stock appreciation right, restricted share award and other Xeris Pharma share based award that was outstanding was assumed by the Company and converted into an equivalent equity award of the Company, which award was subject to the same number of shares and the same terms and conditions as were applicable to the Xeris Pharma award in respect of which it was issued.

Upon completion of the Merger, the Company acquired all of the outstanding Strongbridge Shares in exchange for (i) 0.7840 of a share of the Company Shares and cash in lieu of fractions of Company Shares in exchange for each Strongbridge Share held by such Strongbridge Shareholders and (ii) one CVR. Strongbridge's outstanding equity awards were treated as set forth in the Transaction Agreement, such that (i) each Strongbridge Share Award was vested and settled for Strongbridge Shares immediately prior to the effective time of the Scheme, (ii) each Strongbridge Option became fully vested and exercisable immediately prior to the effective time of the Scheme, (iii) each unexercised Strongbridge Option was assumed by the Company and converted into an option to purchase Company Shares.

Upon vesting and settlement of RSUs or exercise of stock options, at the election of the grantee, the Company does not collect withholding taxes in cash from employees. Instead, the Company withholds upon settlement as RSUs vest, or as stock options are exercised, the portion of those shares with a fair market value equal to the amount of the minimum statutory withholding taxes due. The withheld shares are accounted for as repurchases of common stock. The Company then pays the minimum statutory withholding taxes in cash. During the year ended December 31, 2021, 458,416 RSUs vested for which 141,644 shares were withheld to cover the minimum statutory withholding taxes of $0.5 million. During the year ended December 31, 2020, 31,250 RSUs vested for which 9,801 shares were withheld to cover the minimum statutory withholding taxes of $0.1 million.

Note 14. Stock compensation plan

In 2011, the Company adopted the 2011 Stock Option Issuance Plan (the "2011 Plan") and subsequently amended it to authorize the Board of Directors to issue up to 4,714,982 incentive stock option and non-qualified stock option awards.

The 2018 Stock Option and Incentive Plan (the "2018 Plan") was adopted by the Board of Directors in April 2018 and approved by the Company's stockholders in June 2018 to award up to 1,822,000 shares of common stock. This plan became effective on the date immediately prior to the effectiveness of the Company's IPO registration statement. The 2018 Plan replaced the 2011 Plan as the Board of Directors decided not to make additional awards under the 2011 Plan following the closing of the IPO, which occurred in June 2018. The 2018 Plan allows the compensation committee to make equity-based and cash-based incentive awards to the Company's officers, employees, directors and other key persons (including consultants). No grants of stock options or other awards may be made under the 2018 Plan after the tenth anniversary of the effective date.

The 2018 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2019, and each January 1 thereafter, by 4% of the outstanding number of shares of our common stock on the immediately preceding December 31, or such lesser number of shares as determined by the compensation committee. This number is subject to adjustment in the event of a stock split, stock dividend or other change affecting the Company's common stock. On January 1, 2021 and 2020, the number of shares of common stock available for issuance under the 2018 Plan was automatically increased by 2,384,448 shares and 1,088,580 shares, respectively. As of December 31, 2021, there were 1,569,336 shares of common stock available for future issuance under the 2018 Plan.

The 2018 Employee Stock Purchase Plan (the "ESPP") was adopted by the Board of Directors in April 2018 and approved by the Company's stockholders in June 2018 to issue up to 193,000 shares of common stock to participating employees. Through the ESPP, eligible employees may authorize payroll deductions of up to 15% of their compensation to purchase up to the number of shares of common stock determined by dividing $25,000 by the closing market price of Xeris common stock on the offering date. The purchase price per share at each purchase date is equal to 85% of the lower of (i) the closing market price per share of Xeris common stock on the employee's offering date or (ii) the closing market price per share of Xeris common stock on the purchase date. Each offering period has a six-month duration and purchase interval with a purchase date of the last business day of June and December each year. This plan became effective on the date immediately prior to the effectiveness of the Company's IPO registration statement. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2019 and each January 1 thereafter through January 1, 2028, by the least of (i) 1% of the outstanding number of shares of our common stock on the immediately preceding December 31; (ii) 386,000 shares or (iii) such lesser number of shares as determined by the ESPP administrator. On January 1, 2021 and 2020, the number of shares of common stock available for issuance under the ESPP increased by 386,000 shares and 272,145 shares, respectively. The number of shares reserved under the ESPP is subject to adjustment in the event of a stock split, stock dividend or other change affecting the Company's common stock. The Company issued 215,939 shares at a weighted average price of $2.98 per share during the year ended December 31, 2021. As of December 31, 2021, there were 477,727 shares available for issuance under the ESPP.

The Equity Inducement Plan (the "Inducement Plan") was adopted by the Board of Directors in February 2019. The Inducement Plan was adopted without stockholder approval pursuant to Rule 5635(c)(4) of the Nasdaq Listing Rules. The Inducement Plan allows the Company to make stock option or restricted stock unit awards to prospective employees of the Company as an inducement to such individuals to commence employment with the Company. The Company uses this Inducement Plan to help it attract and retain prospective employees who are necessary to support the commercial launch of Gvoke and the expansion of the Company generally. The Company initially reserved 750,000 shares of common stock for the issuance of awards under the Inducement Plan. This number is subject to adjustment in the event of a stock split, stock dividend or other change affecting the Company's common stock. As of December 31, 2021, there were 197,621 shares of common stock available for future issuance under the Inducement Plan.

On October 8, 2020, the Company's stockholders, upon recommendation of the Board of Directors, approved an amendment to the Company's 2011 Plan and 2018 Plan to allow the Company to permit certain employee option holders, subject to specified conditions, to exchange some or all of their outstanding options to purchase shares of the Company's common stock for a lesser number of new options to purchase shares of the Company's common stock (the "Option Exchange").

On November 10, 2020, the Company filed with the SEC a Tender Offer Statement on Schedule TO defining the terms and conditions of the Option Exchange. The total number of shares of common stock underlying a new option with respect to an exchanged eligible option was determined by dividing the number of shares of common stock underlying the exchanged eligible option by the applicable exchange ratio and rounding to the nearest whole number, subject to the terms and conditions described in the Exchange Offer. On December 10, 2020, the completion date of the Option Exchange, the Company canceled the options accepted for exchange and granted 832,907 new options to purchase shares of common stock in exchange for 1,127,906 options issued under the 2011 Plan and 2018 Plan. The exercise price per share of the options granted pursuant to the Exchange Offer was $4.09 per share, which was the closing price per share of common stock on The Nasdaq Global Select Market on the grant date of such new options. The new options will vest and become exercisable in two equal installments following the grant date, subject to an option holder's continuous service, and expire seven years from the grant date. On the grant date, the fair values of the options exchanged were similar to the fair values of the new options granted and, as such, the incremental compensation cost related to the Option Exchange was not material.

Assumed Plans

At the effective time of the Scheme, Strongbridge's outstanding equity awards were treated as set forth in the Transaction Agreement, such that (i) each Strongbridge Share Award was vested and settled for Strongbridge Shares immediately prior to the effective time of the Scheme, (ii) each Strongbridge Option became fully vested and exercisable immediately prior to the effective time of the Scheme, (iii) each unexercised Strongbridge Option was assumed by the Company and converted into an option to purchase Company Shares (each, a "Strongbridge Rollover Option"), with the exercise price per Company Share and the number of Company Shares underlying the Strongbridge Rollover Option adjusted to reflect the conversion from Strongbridge Shares into Company Shares, provided that each Strongbridge Rollover Option will continue to have, and be subject to, the same terms and conditions that applied to the corresponding Strongbridge Rollover Option (except for terms rendered inoperative by reason of the Acquisition or for immaterial administrative or ministerial changes that are not adverse to any holder other than in any de minimis respect), provided that the terms of each Strongbridge Rollover Option with an exercise price of $4.50 or less (prior to the adjustment described above) were amended to provide that it shall remain exercisable for a period of time following the effective time of the Scheme equal to the lesser of (A) the maximum remaining term of such corresponding Strongbridge Option and (B) the fourth anniversary of the effective date of the Merger, in each case regardless of whether the holder of such Strongbridge Rollover Option experiences a termination of employment or service on or following the effective time of the Scheme.

On the acquisition closing date, the Company assumed all then-outstanding stock options and shares available and reserved for issuance under some legacy equity incentive plans of Strongbridge, including the Strongbridge 2015 equity compensation plan and Strongbridge 2017 inducement plan (collectively, the "Assumed Plans"). Shares reserved under the Assumed Plans will be available for future grants. The Company also assumed all then-outstanding stock options from the rest of the legacy equity incentive plans of Strongbridge without assuming the shares available and reserved for issuance under these plans. The number of shares subject to stock options outstanding under all Strongbridge legacy equity incentive plans are included in the tables below. As of December 31, 2021, there were 2.9 million shares reserved for future grants under the Assumed Plans.

CVRs were also issued to the holders of Strongbridge vested and unexercised options that were outstanding and assumed by the Company at the acquisition date.

Stock options

Stock options are granted with an exercise price equal to the market price of the Company's stock at the date of grant. Stock option awards typically vest over either two, three or four years after the grant date and expire seven to ten years from the grant date.

The fair value of each option is estimated on the date of grant using a Black-Scholes option valuation model that uses the assumptions noted in the following table. The expected term of options represents the period of time that options granted are expected to be outstanding. The risk-free interest rate for periods during the contractual life of the option is based on the U.S. Treasury yield curve in effect at the time of grant. The expected stock price volatility assumption is based on the historical volatilities of a peer group of publicly traded companies as well as the historical volatility of the Company's common stock since the Company began trading subsequent to the IPO in June 2018 over the period corresponding to the expected life as of the grant date. The expected dividend yield is based on the expected annual dividend as a percentage of the market value of the Company's ordinary shares as of the grant date.

The fair value of stock options granted was estimated with the following weighted average assumptions:

	Years Ended December 31,	
	2021	2020
Expected term (years)	6.0	5.9
Risk-free interest rate	1.15 %	0.42 %
Expected volatility	76.34 %	70.19 %
Expected dividends	—	—

Stock option activity under the 2011 Plan, 2018 Plan, Inducement Plan and Assumed Plans for the year ended December 31, 2021 was as follows:

	Number of Options	Weighted Average Exercise Price Per Share	Weighted Average Contractual Life (Years)
Outstanding - January 1, 2021	4,953,906	$ 5.84	7.46
Granted	741,613	4.86	
Assumed	6,400,246	6.17	
Exercised	(93,399)	2.14	
Forfeited	(411,080)	6.31	
Expired	(228,950)	11.42	
Outstanding - December 31, 2021	11,362,336	$ 5.86	5.62
Exercisable - December 31, 2021	9,645,482	$ 5.94	5.18
Vested and expected to vest at December 31, 2021	11,362,336	$ 5.86	5.62

The weighted average fair value of awards granted during the year ended December 31, 2021 was $3.22 per share. The total intrinsic value of options exercised during the year ended December 31, 2021 was $0.1 million. As of December 31, 2021, the aggregate intrinsic value of awards vested and expected to vest was $1.8 million.

At December 31, 2021, there was a total of $6.0 million of unrecognized stock-based compensation expense related to stock options that is expected to be recognized over a weighted average period of 1.9 years.

Restricted Share Units

The Company grants RSUs to employees. RSUs that are granted vest over either three or four years in equal annual installments beginning on the one-year anniversary of the date of grant, provided that the employee is employed by the Company on such vesting date. If and when the RSUs vest, the Company will issue one share of common stock for each whole RSU that has vested, subject to satisfaction of the employee's tax withholding obligations. Stock-based compensation expense related to RSUs is recognized on a straight-line basis over the employee's requisite service period.

A summary of outstanding RSU awards and the activity for the year ended December 31, 2021 was as follows:

	Number of Units	Weighted Average Grant Date Fair Value Per Share
Unvested balance - January 1, 2021	766,550	$ 7.07
Granted	1,817,594	4.62
Vested	(458,416)	6.29
Forfeited	(120,687)	4.94
Unvested balance - December 31, 2021	2,005,041	$ 5.15

As of December 31, 2021, there was $7.1 million of unrecognized stock-based compensation expense related to RSUs, which is expected to be recognized over the weighted-average remaining vesting period of 2.2 years.

Employee Stock Purchase Plan

The fair value of the ESPP Plan shares was estimated using the Black-Scholes option-pricing model with the following weighted average assumptions:

	Years Ended December 31,	
	2021	2020
Expected term (years)	0.5	0.5
Risk-free interest rate	0.08 %	1.01 %
Expected volatility	77.40 %	108.70 %
Expected dividends	—	—

The following table summarizes the reporting of total stock-based compensation expense resulting from stock options, RSUs and the ESPP (in thousands):

	Years Ended December 31,	
	2021	2020
Cost of goods sold	$ 106	$ 151
Research and development	1,696	1,229
Selling, general and administrative	9,579	6,893
Total stock-based compensation expense	$ 11,381	$ 8,273

Note 15. Other employee benefit plans

Defined Contribution Plan

The Company sponsors an employee retirement plan qualifying under Section 401(k) of the Internal Revenue Code for all eligible employees in the United States. Employees become eligible to contribute to the plan upon meeting certain age requirements and 30 days of service. Commencing in 2019, the Company began discretionary matching employee contributions up to certain limits. For the years ended December 31, 2021 and 2020, the Company made $0.7 million and $0.6 million of matching contributions to the plan, respectively.

Deferred Compensation Plan

The Compensation Committee of the Board of Directors adopted a deferred compensation plan ("Deferred Compensation Plan") in April 2020. The Deferred Compensation Plan allows a select group of executive management and non-employee directors to defer payment of certain of their cash compensation. Participants in the Deferred Compensation Plan who are employees may defer all or a portion of their annual base salaries and all or a portion of their annual cash performance-based compensation. Participants who are non-employee directors may defer all or a portion of their annual cash retainers. The participants' elective deferrals are 100% vested immediately and accrue interest at a rate of two percent per annum. The Deferred Compensation Plan is unfunded and unsecured. As of December 31, 2021, the total deferred compensation liability under the Deferred Compensation Plan was approximately $1.6 million and was recorded in other current liabilities in the consolidated balance sheets.

Note 16. Commitments and contingencies

Commitments

Commitments to Taro Pharmaceuticals U.S.A., Inc. ("Taro")

Upon the completion of Strongbridge acquisition, the Company also acquired the supply agreement Strongbridge had with Taro to produce Keveyis. Strongbridge was obligated to purchase annual minimum amounts of product totaling approximately $29.1 million over a six-year period from Taro. As of December 31, 2021, the remaining obligation under the Supply Agreement was $14.1 million. The agreement with Taro may extend beyond the orphan exclusivity period unless terminated by either party pursuant to the terms of the agreement. If terminated by Taro at the conclusion of the orphan exclusivity period, the Company has the right to manufacture the product on its own or has the product manufactured by a third party on its behalf. The Company is also required to reimburse Taro for royalty obligation resulting from its sale of Keveyis to the Company.

Indemnifications

In the ordinary course of business and in connection with the sale of assets and businesses and other transactions, the Company often agrees to indemnify our counterparties against certain liabilities that may arise in connection with a transaction or that are related to events and activities prior to or following a transaction, such as breaches of contracts, unfavorable tax consequences and employee liabilities. If a counterparty were to make a successful indemnification claim against us, the Company may be required to reimburse the loss and such amount could be material to our consolidated financial statements. Where appropriate, the obligation for such indemnifications is recorded as a liability. Because these agreements generally do not specify the maximum amount of indemnification a counterparty may be entitled to, the overall maximum amount of our potential indemnification liability under these agreements cannot be reasonably estimated. However, the Company believes that the likelihood of a material liability being triggered under these indemnification obligations is not probable at this time.

Leases

The Company has non-cancellable operating leases for office and laboratory space, which expire at various times in 2031 and 2033. The non-cancellable lease agreements provide for monthly lease payments which increase during the term of each lease agreement.

Future minimum lease payments under operating leases at December 31, 2021 are as follows (in thousands):

2022	$	1,813
2023		2,031
2024		1,981
2025		1,931
2026		1,982
Thereafter		11,741
Total minimum lease payments	$	21,479

Total rent expense under these operating leases was approximately $2.4 million and $2.3 million for the years ended December 31, 2021 and 2020, respectively.

As of December 31, 2021, the Company had unused letters of credit of $1.4 million which were issued primarily to secure leases.

Contingencies

CVR liability

Upon closing the Transactions, the Company entered into a CVR Agreement. Each CVR entitles its holder to receive additional consideration of up to $1.00, to satisfy future performance milestones, settleable in cash, common stock, or a combination of cash and common stock, at the Company's sole election. As of the acquisition closing date, there were approximately 74.1 million CVRs. There will be additional issuance of up to 10.5 million CVRs to holders of Strongbridge rollover options and assumed warrants upon exercise.

Litigation

From time to time, the Company may become involved in various legal actions arising in the ordinary course of business. As of December 31, 2021, management was not aware of any existing, pending or threatened legal actions that would have a material impact on the financial position or results of operations of the Company.

Note 17. Net loss per common share

Basic and diluted net loss per common share are determined by dividing net loss applicable to common stockholders by the weighted average common shares outstanding during the period. For all periods presented, the shares issuable upon conversion, exercise or vesting of Convertible Notes, warrants, stock option awards and RSUs have been excluded from the calculation because their effects would be anti-dilutive. Therefore, the weighted average common shares outstanding used to calculate both basic and diluted net loss per common share are the same.

The following potentially dilutive securities were excluded from the computation of diluted weighted average common shares outstanding due to their anti-dilutive effect:

	As of December 31,	
	2021	**2020**
Shares to be issued upon conversion of Convertible Notes	15,416,667	15,416,667
Vested and unvested stock options	11,362,336	4,953,906
Restricted stock units	2,005,041	766,550
Warrants	6,373,452	94,012
Total anti-dilutive securities excluded from EPS computation[1]	35,157,496	21,231,135

[1] Total anti-dilutive securities exclude CVRs which are settleable in cash, additional Xeris Biopharma shares, or a combination, at the election of the Company.

Note 18. Income taxes

A reconciliation of the expected income tax benefit computed using the federal statutory income tax rate of 21% to the Company's effective income tax rate is as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Federal tax benefit at statutory rate	$ (25,772)	$ (19,162)
State tax benefit, net of federal benefit	(4,422)	(4,375)
Research and development and orphan drug credits	(350)	(480)
Uncertain tax positions	(302)	(16)
Permanent adjustments to expenses	1,779	710
Stock-based compensation	901	1,014
Return to provision adjustment	(2,450)	(1,203)
Statutory tax rate differential	663	—
Changes in valuation allowance	29,642	23,543
Other	311	(141)
Total income tax benefit	$ —	$ (110)

The benefit for income taxes for 2020 is attributable to an Australian research and development tax incentive that was refunded to the Company based on the 2020 income tax filing.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of the assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. A valuation allowance is required to be established or maintained when, based on currently available information, it is more likely than not that all or a portion of a deferred tax asset will not be realized. The guidance on accounting for income taxes provides important factors in determining whether a deferred tax asset will be realized, including whether there has been sufficient taxable income in recent years and whether sufficient income can reasonably be expected in future years in order to utilize the deferred tax asset. For the years ended December 31, 2021 and 2020, the Company evaluated the need to maintain a valuation allowance for deferred tax assets based on our assessment of whether it is more likely than not that deferred tax benefits will be realized through the generation of future taxable income. Appropriate consideration is given to all available evidence, both positive and negative, in assessing the need for a valuation allowance.

Significant components of the Company's deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating losses	$ 100,790	$ 74,894
Federal research and orphan drug credits	7,184	8,362
Stock-based compensation	3,177	1,894
Other temporary differences	27,094	7,785
Valuation allowance	(137,881)	(92,493)
Total assets	364	442
Deferred tax liabilities:		
Fixed and intangible assets	(197)	(404)
Other deferred tax liabilities	(5,109)	(38)
Total liabilities	(5,306)	(442)
Net deferred tax liabilities	$ (4,942)	$ —

As of December 31, 2021, the Company had federal net operating loss carryforwards of $475.7 million and various state net operating loss carryforwards of $309.7 million. As of December 31, 2020, the Company had federal net operating loss carryforwards of $284.8

million and various state net operating loss carryforwards of $220.6 million. Net operating loss carryforwards for U.S. federal income tax purposes that were generated prior to January 1, 2018 have a twenty-year carryforward life, and the earliest layers will begin to expire in 2025. Under the Tax Cuts and Jobs Act of 2017, federal net operating losses incurred in 2018 and later years may be carried forward indefinitely, but the deductibility of such net operating losses is limited to 80% of the current year's taxable income. U.S. state net operating loss carryforwards will start to expire in 2029 for the earliest net operating loss layers to the extent there is not sufficient state taxable income to utilize those net operating loss carryforwards.

At December 31, 2021, the Company had $5.4 million and $2.5 million of federal and state income tax credits, respectively, to reduce future tax liabilities. At December 31, 2020, the Company had $8.0 million and $1.7 million of federal and state income tax credits, respectively, to reduce future tax liabilities. The federal income tax credits consist primarily of orphan drug credits and research and development credits. The U.S. state income tax credits consist primarily of California and Illinois research and development credits. Both the U.S. federal orphan drug credits and research and development credits have a twenty-year carryforward life. The U.S. federal orphan drug credits and research and development credits will both begin to expire in 2025.

A reconciliation of the beginning and ending amounts of valuation allowances for the years ended December 31, 2021 and 2020 is as follows (in thousands):

Valuation allowance at December 31, 2019	$	(68,950)
Increase for 2020 activity		(23,543)
Valuation allowance at December 31, 2020		(92,493)
Increase for 2021 activity		(45,388)
Valuation allowance at December 31, 2021	$	(137,881)

The Company is required to recognize the financial statement effects of a tax position when it is more likely than not, based on the technical merits, that the position will be sustained upon examination. The Company accounts for the uncertainty in income taxes by utilizing a comprehensive model for the recognition, measurement, presentation and disclosure in financial statements of any uncertain tax positions that have been taken, or are expected to be taken, on an income tax return. The changes in the Company's uncertain income tax positions for the years ended December 31, 2021 and 2020, excluding interest and penalties, consisted of the following (in thousands):

	December 31,	
	2021	**2020**
Beginning balance - uncertain tax positions	$ 929	$ 945
Increases related to tax positions taken during the current year	17	48
Decreases related to tax positions taken during the prior year	(319)	(64)
Ending balance - uncertain tax positions	$ 627	$ 929

For the year ended December 31, 2021, the increase in current year uncertain tax positions was attributable primarily to U.S. federal orphan drug credits and research and development credits and the decrease related to tax positions taken during the prior year was a result of return to provision adjustments. In the Company's balance sheet, uncertain tax positions of $0.6 million were offset against deferred tax assets. Tax years prior to 2018 generally are not subject to examination by the Internal Revenue Service or state or local taxing authorities.

The Company policy is to include interest and penalties related to uncertain tax penalties, if any, within the provision for taxes in the statements of operations. During the years ended December 31, 2021 and 2020, the Company incurred no interest and penalties related to income taxes.

19. Subsequent events

Private placement

On January 3, 2022, the Company entered into a securities purchase agreement in connection with a private placement with an affiliate of Armistice Capital, LLC ("Armistice") for aggregate gross proceeds of approximately $30.0 million. In accordance with the purchase agreement, the Company issued to Armistice an aggregate of (i) 10,238,908 shares of the Company's common stock, par value $0.0001 per share at a purchase price of $2.93 per share, and (ii) warrants to purchase an aggregate of 5,119,454 shares of the Company's common stock at an exercise price of $3.223 per share. The warrants became exercisable immediately upon the closing of

the transaction and have a term of five years from the earliest of the date (a) of effectiveness of the resale registration statement, which was February 7, 2022, (b) all of the shares and the Company's common stock issuable upon exercise of the warrants (the “Warrant Shares”) have been sold pursuant to Rule 144 or may be sold pursuant to Rule 144 without the requirement for the Company to be in compliance with the current public information required under Rule 144 and without volume or manner-of-sale restrictions, (c) following the one-year anniversary of the date of closing provided that the holder of Shares or Warrant Shares is not an affiliate of the Company, or (d) all of the shares and Warrant Shares may be sold pursuant to an exemption from registration under Section 4(a)(1) of the Securities Act without volume or manner-of-sale restrictions.

Loan facility

In March 2022, the Company, Xeris Pharma and certain subsidiary guarantors of the Company entered into a Credit Agreement and Guaranty (the "Hayfin Loan Agreement") with the lenders from time to time parties thereto (the “New Lenders”) and Hayfin Services LLP, as administrative agent for the New Lenders, pursuant to which the Company and its subsidiaries party thereto granted a first priority security interest on substantially all of their assets, including intellectual property, subject to certain exceptions. The Hayfin Loan Agreement provided for the New Lenders to extend $100.0 million in term loans (the “Initial Loan”) to the Company on the closing date and up to an additional $50.0 million in delayed draw term loans during the one year period immediately following the closing date (the “Delayed Draw Term Loans” and, together with the Initial Loan, the “Loans”) in no more than three drawings of no less than $10.0 million per drawing, subject to the Company being in pro forma compliance with the financial covenants and other conditions set forth therein. In conjunction with the execution of the Hayfin Loan Agreement, the Amended Loan Agreement balance of $43.5 million was repaid in full and fees of $2.1 million in connection with the loan repayment were paid. In addition to utilizing the proceeds to repay the obligations under the Amended Loan Agreement in full, the proceeds will otherwise be used for general corporate purposes. After repayment, the Loans may not be re-borrowed.

The New Lenders also received warrants to purchase 1,315,789 shares of the common stock of the Company at a price of $2.28 per share (the “Warrants"). The Warrants are (i) exercisable until the seventh (7th) anniversary of the closing date; (ii) freely transferable and detachable from the Loans; and (iii) subject to customary warrant holder rights and protections, including structural-based anti-dilution protection and adjustments for stock dividends, splits, combinations, reclassifications and the like.

All of the Loans incur interest at a floating per annum rate in an amount equal to the sum of (i) 9.0% (or 8.0% per annum if the replacement rate in effect is the Wall Street Journal Prime Rate) plus (ii) the greater of (x) (1) CME Group Benchmark Administration Limited (CBA) Term SOFR (or the replacement rate, if applicable) if CBA Term SOFR is greater than 1.00% plus 0.26161% or (2) 1.00% if CME Term SOFR is less than 1.00% and (y) one percent (1.00%) per annum (or 2.0% per annum if the replacement rate in effect is the Wall Street Journal Prime Rate). The Company has incurred total debt issuance costs of approximately $6.1 million related to the Hayfin Loan Agreement, which are being amortized to interest expense over the life of the loan using the effective interest method. The remaining balance of unamortized debt issuance costs have been reflected as a direct reduction to the loan balance.

The Hayfin Loan Agreement allows the Company to voluntarily prepay the outstanding amounts thereunder. The Company is subject to an early prepayment fee equal to (i) for any prepayment that occurs prior to the second anniversary of the closing date, the applicable make-whole amount, (ii) for any prepayment that occurs after the second anniversary of the closing date but on or prior to the fourth anniversary of the closing date: (x) the amount of any principal so prepaid, multiplied by (y) for any prepayment that occurs (A) after the second anniversary of the closing date and on or prior to the third anniversary of the closing date, five percent (5.0%), (B) after the third anniversary of the closing date and on or prior to the fourth anniversary of the closing date, three percent (3.0%), and (C) after the fourth anniversary of the closing date, zero percent (0.0%).

The Hayfin Loan Agreement contains customary representations and warranties, events of default and affirmative and negative covenants, including, among others, covenants that limit or restrict the Company’s ability to incur additional indebtedness, grant liens, merge or consolidate, make acquisitions, pay dividends or other distributions or repurchase equity, make investments, dispose of assets and enter into certain transactions with affiliates, in each case subject to certain exceptions.

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 principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) promulgated under the Securities Exchange Act of 1934, as amended ("Exchange Act"). Based on such evaluation, our principal executive officer and principal financial officer have concluded that the disclosure controls and procedures were effective as of December 31, 2021 to ensure that information required to be disclosed by the Company in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time period specified in the U.S. Securities and Exchange Commission's ("SEC") rules and forms, and to ensure that information required to be disclosed by the Company in the reports 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 disclosure.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Under the supervision and with the participation of our management, including the Chief Executive Officer and the Chief Financial Officer, we conducted an evaluation of the effectiveness of the Company's internal control over financial reporting as of December 31, 2021 based on the 2013 framework established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's internal control over financial reporting includes policies and procedures that provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with GAAP. Based on our evaluation under this framework, our management concluded that the Company's internal control over financial reporting was effective as of December 31, 2021.

In addition, we are an "emerging growth company," as defined under the JOBS Act, and are subject to reduced public company reporting requirements. The JOBS Act provides that an "emerging growth company" is not required to have the effectiveness of the Company's internal control over financial reporting audited by its external auditor for as long as the Company is deemed to be an "emerging growth company."

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the three months ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not Applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item will be contained in our Definitive Proxy Statement to be filed with the SEC in connection with the Annual Meeting of Stockholders within 120 days after the conclusion of our fiscal year ended December 31, 2021 and is incorporated in this Annual Report on Form 10-K by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be contained in our Definitive Proxy Statement to be filed with the SEC in connection with the Annual Meeting of Stockholders within 120 days after the conclusion of our fiscal year ended December 31, 2021 and 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 will be contained in our Definitive Proxy Statement to be filed with the SEC in connection with the Annual Meeting of Stockholders within 120 days after the conclusion of our fiscal year ended December 31, 2021 and 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 will be contained in our Definitive Proxy Statement to be filed with the SEC in connection with the Annual Meeting of Stockholders within 120 days after the conclusion of our fiscal year ended December 31, 2021 and is incorporated in this Annual Report on Form 10-K by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Our independent public accounting firm is KPMG LLP, Chicago, Illinois, PCAOB Auditor ID: 185.

The information required by this item will be contained in our Definitive Proxy Statement to be filed with the SEC in connection with the Annual Meeting of Stockholders within 120 days after the conclusion of our fiscal year ended December 31, 2021 and is incorporated in this Annual Report on Form 10-K by reference.

PART IV

ITEM 15. EXHIBIT AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this Form 10-K:

1. Financial Statements

   See Index to Financial Statements at Item 8 herein.

2. Financial Statement Schedules

   All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

ITEM 16. FORM 10-K SUMMARY

None.

XERIS PHARMACEUTICALS, INC.

FORM 10-K

INDEX TO EXHIBITS

Exhibit No.	Description
2.1	Transaction Agreement, dated as of May 24, 2021, by and among the Registrant, Strongbridge Biopharma plc, Xeris Pharmaceuticals, Inc. and Wells MergerSub, Inc. (incorporated by reference to Annex A of the Registrant's Registration Statement on Form S-4 (File No. 333-257642) filed with the Securities and Exchange Commission on on July 2, 2021)
2.2	Expenses Reimbursement Agreement, dated May 24, 2021, by and between the Xeris Pharmaceuticals, Inc. and Strongbridge Biopharma plc (Incorporated by reference to Exhibit 2.3 to Xeris Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-38536) filed with the Securities and Exchange Commission on May 24, 2021)
2.3	Contingent Value Rights Agreement, dated as of October 5, 2021, by and between the Registrant, Computershare, Inc. and Computershare Trust Company, N.A. (Incorporated by reference to Exhibit 2.2 to our Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
3.1	Amended and Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
3.2	Amended and Restated By-laws of the Registrant (Incorporated by reference to Exhibit 3.2 to our Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
4.1	Specimen Stock Certificate Evidencing Shares of Common Stock (Incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-3 (File No. 333-262404) filed with the Securities and Exchange Commission on January 28, 2022)
4.2	Second Amended and Restated Investors' Rights Agreement by and among Xeris Pharmaceuticals, Inc. and certain of its stockholders, dated December 31, 2015 (Incorporated by reference to Exhibit 4.1 to the Xeris Pharmaceuticals, Inc. Registration Statement on Form S-1 (File No. 333-225191) filed with the Securities and Exchange Commission on May 24, 2018)
4.3*	Description of Registrant's Securities
4.4	Base Indenture, dated as of June 30, 2020, by and between Xeris Pharmaceuticals, Inc. and U.S. Bank National Association (Incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
4.5	First Supplemental Indenture, dated as of June 30, 2020, by and between Xeris Pharmaceuticals, Inc.and U.S. Bank National Association (Incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
4.6	Form of 5.00% Convertible Senior Note due 2025 (included in Exhibit 4.5)
4.7	Second Supplemental Indenture, by and among the Registrant, Xeris Pharmaceuticals, Inc. and U.S. Bank National Association, dated October 5, 2021 (Incorporated by reference to Exhibit 4.3 to our Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
4.8	Form of Registration Rights Agreement between the Registrant and Armistice Capital Master Fund Ltd. dated as of January 2, 2022 (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-40880) filed with the Securities and Exchange Commission on January 3, 2022)
10.1#	2011 Stock Option and Incentive Plan and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.1 to Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1 (File No. 333-225191) filed with the Securities and Exchange Commission on May 24, 2018)

Exhibit No.	Description
10.2#	2018 Stock Option and Incentive Plan and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.2 to Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1/A (File No. 333-225191) filed with the Securities and Exchange Commission on June 11, 2018)
10.3#	Senior Executive Cash Incentive Bonus Plan (Incorporated by reference to Exhibit 10.3 to Xeris Pharmaceutical, Inc.'s Registration Statement on Form S-1 (File No. 333-225191) filed with the Securities and Exchange Commission on May 24, 2018)
10.4#	Form of Director Indemnification Agreement (Incorporated by reference to Exhibit 10.2 to our Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
10.5#	Form of Officer Indemnification Agreement (Incorporated by reference to Exhibit 10.3 to our Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
10.6#	Amended and Restated Employment Agreement by and among the Registrant, Xeris Pharmaceuticals, Inc. and Paul Edick, dated as of October 5, 2021 (Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
10.7#	Amended and Restated Employment Agreement by and among the Registrant, Xeris Pharmaceuticals, Inc. and John Shannon, dated as of October 5, 2021 (Incorporated by reference to Exhibit 10.2 to our Current Report on Form 8-K (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
10.8#	Amended and Restated Employment Agreement by and among the Registrant, Xeris Pharmaceuticals, Inc. and Steven Pieper, dated as of October 5, 2021 (Incorporated by reference to Exhibit 10.3 to our Current Report on Form 8-K (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
10.9+	API Supply Agreement, dated as of January 1, 2018, by and between Xeris Pharmaceuticals, Inc. and Bachem Americas, Inc. (Incorporated by reference to Exhibit 10.12 to Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1 (File No. 333-225191) filed with the Securities and Exchange Commission on May 24, 2018)
10.10+	First Amendment to API Supply Agreement, dated as of February 26, 2021, by and between Xeris Pharmaceuticals, Inc. and Bachem Americas, Inc. (Incorporated by reference to Exhibit 10.1 to Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on May 13, 2021)
10.11+	Quality Assurance Agreement, dated as of November 20, 2015, by and between Bachem AG and Xeris Pharmaceuticals, Inc., as amended by (i) Amendment 1 to the Quality Assurance Agreement, dated as of October 31, 2016, by and between Bachem AG and Xeris Pharmaceuticals, Inc. and (ii) Amendment 2 to the Quality Assurance Agreement, dated as of January 26, 2017, by and between Bachem AG and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.13 to Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1 (File No. 333-225191) filed with the Securities and Exchange Commission on May 24, 2018)
10.12+	Commercial Supply Agreement, dated as of May 14, 2018, by and between Pyramid Laboratories Inc. and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.14 to Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1/A (File No. 333-225191) filed with the Securities and Exchange Commission on June 14, 2018)
10.13+	Amendment 2 to the Commercial Supply Agreement, dated as of May 13, 2021, by and between Pyramid Laboratories Inc. and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.2 to Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on August 5, 2021)
10.14+	Joint Development Agreement, dated as of January 29, 2016, by and between Xeris Pharmaceuticals, Inc. and Scandinavian Health Limited (Incorporated by reference to Exhibit 10.15 to Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1 (File No. 333-225191) filed with the Securities and Exchange Commission on May 24, 2018)

Exhibit No.	Description
10.15	Loan and Security Agreement, dated as of February 28, 2018, by and between Oxford Finance LLC, Silicon Valley Bank and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.16 to Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1 (File No. 333-225191) filed with the Securities and Exchange Commission on May 24, 2018)
10.16+	Quality Agreement, dated as of November 16, 2016, by and between Pyramid Laboratories Inc. and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.17 to Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1 (File No. 333-225191) filed with the Securities and Exchange Commission on May 24, 2018)
10.17+	Amendment 1 to the Quality Agreement, dated as of May 11, 2021, by and between Pyramid Laboratories Inc. and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.3 to Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on August 5, 2021)
10.18#	2018 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.18 to Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1/A (File No. 333-225191) filed with the Securities and Exchange Commission on June 11, 2018)
10.19+	Product Supply Agreement by and between SHL Pharma, LLC and Xeris Pharmaceuticals, Inc., dated August 1, 2018 (Incorporated by reference to Exhibit 10.1 to Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on November 8, 2018)
10.20#	Inducement Equity Plan (Incorporated by reference to Exhibit 99.1 of Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-8 (File No. 333-229587) filed with the Securities and Exchange Commission on February 8, 2019)
10.21	First Amendment to Office Lease Agreement, dated as of November 20, 2018, by and between 180 N LaSalle Property Owner LLC and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.22 of Xeris Pharmaceuticals, Inc.'s Registration Statement on Form S-1 (File No. 333-229600) filed with the Securities and Exchange Commission on February 11, 2019)
10.22	Amended and Restated Loan and Security Agreement, dated as of September 10, 2019, by and between Oxford Finance LLC, Silicon Valley Bank and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.1 to Xeris Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-38536) filed with the Securities and Exchange Commission on September 10, 2019)
10.23	Second Amendment to Loan and Security Agreement, dated as of May 15, 2019, by and among Oxford Finance LLC, Silicon Valley Bank and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.1 to Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on August 6, 2019)
10.24#	Deferred Compensation Plan (Incorporated by reference to Exhibit 10.1 to Xeris Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-38536) filed with the Securities and Exchange Commission on April 10, 2020)
10.25+	Amendment 3 to the Quality Assurance Agreement, dated as of February 26, 2020, by and between Xeris Pharmaceuticals, Inc. and Bachem AG (Incorporated by reference to Exhibit 10.3 of Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on May 7, 2020)
10.26+	Amendment 4 to the Quality Assurance Agreement, dated as of May 5, 2021, by and between Bachem AG and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.4 to Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on August 5, 2021)
10.27	First Amendment to Amended and Restated Loan and Security Agreement, dated as of April 21, 2020, by and among Oxford Finance LLC, Silicon Valley Bank and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.4 of Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on May 7, 2020)

Exhibit No.	Description
10.28+	Second Amendment to Amended and Restated Loan and Security Agreement, dated as of June 30, 2020, by and among Oxford Finance LLC, Silicon Valley Bank and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.1 of Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on August 10, 2020)
10.29+	First Amendment to the Product Supply Agreement, dated as of June 24, 2020, by and between Xeris Pharmaceuticals, Inc. and SHL Pharma LLC (Incorporated by reference to Exhibit 10.2 of Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on August 10, 2020)
10.30+	Third Amendment to Amended and Restated Loan and Security Agreement, dated as of August 5, 2020, by and among Oxford Finance LLC, Silicon Valley Bank and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.2 of Xeris Pharmaceuticals, Inc.' s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on November 9, 2020)
10.31+	Fourth Amendment to Amended and Restated Loan and Security Agreement, dated as of October 23, 2020, by and among Oxford Finance LLC, Silicon Valley Bank and the Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.34 to Xeris Pharmaceuticals, Inc.' s Annual Report on Form 10-K (File No. 001-38536) filed with the Securities and Exchange Commission on March 9, 2021)
10.32	Consent Under Amended and Restated Loan and Security Agreement, dated as of May 24, 2021, by and among Xeris Pharmaceuticals, Inc., Oxford Finance LLC, and Silicon Valley Bank (Incorporated by reference to Exhibit 10.4 to Xeris Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-38536) filed with the Securities and Exchange Commission on May 24, 2021)
10.33	Fifth Amendment to Amended and Restated Loan and Security Agreement, dated May 3,2021, by and among Xeris Pharmaceuticals, Inc., Oxford Finance LLC, and Silicon Valley Bank (Incorporated by reference to Exhibit 10.5 to Xeris Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-38536) filed with the Securities and Exchange Commission on August 5, 2021)
10.34	Joinder and Sixth Amendment to Amended and Restated Loan and Security Agreement, dated October 5, 2021, by and among the Registrant, Xeris Pharmaceuticals, Inc., Oxford Finance LLC and Silicon Valley Bank (Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
10.35	Form of Exchange Agreement (Incorporated by reference to Exhibit 10.1 to Xeris Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-38536) filed with the Securities and Exchange Commission on November 16, 2020)
10.36	Amended and Restated Quality Agreement, dated as of November 16, 2020, by and between Pyramid Laboratories Inc. and Xeris Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 10.36 to Xeris Pharmaceuticals, Inc.' s Annual Report on Form 10-K (File No. 001-38536) filed with the Securities and Exchange Commission on March 9, 2021)
10.37#	Separation Agreement, dated as of July 28, 2021, by and between Xeris Pharmaceuticals, Inc. and Barry Deutsch (Incorporated by reference to Exhibit 10.1 to Xeris Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-38536) filed with the Securities and Exchange Commission on July 29, 2021)
10.38+	Asset Purchase Agreement, dated December 12, 2016, between Taro Pharmaceutical North America, Inc. and Strongbridge plc (Incorporated by reference to Exhibit 10.3 to Strongbridge Biopharma plc's Form F-3 (File No. 333-215531) filed with the Securities and Exchange Commission on January 12, 2017)
10.39+	Supply Agreement, dated December 12, 2016, between Taro Pharmaceutical North America, Inc. and Strongbridge plc (Incorporated by reference to Exhibit 10.4 to Strongbridge Biopharma plc's Form F-3 (File No. 333-215531) filed with the Securities and Exchange Commission on January 12, 2017)
10.40	Investors' Rights Agreement, dated as of February 10, 2015, by and among Cortendo AB and the Investors listed therein (incorporated by reference to Exhibit 10.11 to Strongbridge Biopharma plc's Form F-1 (File No. 333-206654) filed with the Securities and Exchange Commission on August 28, 2015)

Exhibit No.	Description
10.41#	Strongbridge Biopharma plc 2015 Equity Compensation Plan (incorporated by reference to Exhibit 10.13 of Strongbridge Biopharma plc's Annual Report on Form 10-K (File No. 001-37569) filed with the Securities and Exchange Commission on February 27, 2019)
10.42#	Strongbridge Biopharma plc Non-Employee Director Equity Compensation Plan (incorporated by reference to Exhibit 10.14 of Strongbridge Biopharma plc's Annual Report on Form 10-K (File No. 001-37569) filed with the Securities and Exchange Commission on February 27, 2019)
10.43#	Strongbridge Biopharma plc 2017 Inducement Plan (incorporated by reference to Exhibit 10.15 of Strongbridge Biopharma plc's Annual Report on Form 10-K (File No. 001-37569) filed with the Securities and Exchange Commission on February 27, 2019)
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Independent Registered Public Accounting Firm
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended
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
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith

# Indicates a management contract or any compensatory plan, contract or arrangement

+ Portions of this exhibit (indicated by asterisks) have been omitted pursuant to confidential treatment order, and this exhibit has been submitted separately to the U.S. Securities and Exchange Commission.

SIGNATURES

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

Xeris Biopharma Holdings, Inc.

By /s/ Paul R. Edick
Paul R. Edick
Chief Executive Officer and Chairman

Date March 11, 2022

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below as of March 11, 2022, by the following persons on behalf of the registrant and in the capacities indicated.

SIGNATURE	**TITLE**
/s/ Paul R. Edick Paul R. Edick	Chief Executive Officer and Chairman (Principal Executive Officer)
/s/ Steven M. Pieper Steven M. Pieper	Chief Financial Officer (Principal Financial Officer and Principal Accounting officer)
/s/ B.J. Bormann B.J. Bormann	Director
/s/ Dawn Halkuff Dawn Halkuff	Director
/s/ Garheng Kong Garheng Kong	Director
/s/ Jeffrey Sherman Jeffrey Sherman	Director
/s/ John H. Johnson John H. Johnson	Director
/s/ John Schmid John Schmid	Director
/s/ Marla Persky Marla Persky	Director

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES AND EXCHANGE ACT OF 1934, AS AMENDED

The common stock, par value $0.0001 per share ("Common Stock") of Xeris Biopharma Holdings, Inc. (the "Company," "we," "us," and "our") is registered under Section 12 of the Securities Exchange Act of 1934, as amended. The following description sets forth certain general terms and provisions of our Common Stock. These descriptions are in all respects subject to and qualified in their entirety by, and should be read in conjunction with the applicable provisions of, our Amended and Restated Certificate of Incorporation ("Certificate of Incorporation") and our Amended and Restated Bylaws ("Bylaws"), each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, and by applicable law. We encourage you to read our Certificate of Incorporation, our Bylaws and the applicable provisions of the Delaware General Corporation Law for additional information.

Authorized Capital Stock

Our authorized capital stock consists of 350,000,000 shares of Common Stock and 25,000,000 shares of preferred stock, par value $0.0001 per share ("Preferred Stock"), all of which shares of Preferred Stock are undesignated.

Common Stock

Only our Common Stock is registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

Holders of our Common Stock are entitled to one vote for each share of Common Stock held of record for the election of directors and on all matters submitted to a vote of the stockholders. Holders of our Common Stock are entitled to receive dividends as may be declared from time to time by our board of directors out of funds legally available therefor. The holders of our Common Stock do not have any cumulative voting rights. Holders of our Common Stock have no preemptive, subscription, redemption or conversion rights, and no sinking fund provisions are applicable to our Common Stock.

In the event of our dissolution, liquidation or winding up, holders of our Common Stock are entitled to share pro rata in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any Preferred Stock then outstanding. The rights, preferences and privileges of holders of Common Stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of Preferred Stock that we may designate and issue in the future.

Preferred Stock

Our board of directors is authorized, without further action by the stockholders, to designate and issue up to an aggregate of 25,000,000 shares of Preferred Stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of Common Stock. Our board of directors may authorize the issuance of Preferred Stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of Common Stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation.

The purpose of authorizing our board of directors to issue Preferred Stock in one or more series and determine the number of shares in the series and its rights, preferences, privileges and restrictions is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of Preferred Stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes, could, under certain circumstances, have the effect of delaying, deferring or preventing a change in control of our company, as further discussed below under "—Anti-Takeover Effects of Delaware Law and Provisions of our Charter and our Bylaws—Provisions of our Charter and our Bylaws—Undesignated Preferred Stock."

No shares of Preferred Stock are outstanding as of the date of our Annual Report on Form 10-K with which this Exhibit 4.3 is filed as an exhibit.

Registration Rights

Pursuant to the terms of Xeris Pharma's investors' rights agreement, dated as of December 31, 2015, certain of our stockholders are entitled to rights with respect to the registration of their shares under the Securities Act until the earliest of the fifth (5th) anniversary of our initial public offering, or such holder's registrable securities could be sold without any restriction on volume or manner of sale on any 90-day period under Rule 144 or any successor rule, as described below. We refer to these shares collectively as registrable securities.

Demand Registration Rights

The holders of 1,387,985 shares of our Common Stock are entitled to demand registration rights. Under the terms of the investors' rights agreement, we will be required, upon the written request of holders of at least 20% of the securities eligible for registration then outstanding or such lesser percentage that would result in an aggregate offering price of at least $10.0 million, to file a registration statement and use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale. We are required to effect only two registrations pursuant to this provision of the investors' rights agreement.

Short-Form Registration Rights

Pursuant to Xeris Pharma's investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of majority in interest of these holders to sell registrable securities at an aggregate price of at least $1.0 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are not required to effect more than two registrations that have been declared or ordered effective by the SEC pursuant to this provision of the investors' rights agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to Xeris Pharma's investors' rights agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of 1,387,985 shares of our Common Stock are entitled to include their shares in the registration. Subject to certain exceptions contained in the investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Xeris Pharma's investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short form registration rights granted under Xeris Pharma's investors' rights agreement will terminate on the fifth anniversary of the completion of Xeris Pharma's initial public offering or at such time after such offering when the holders' shares may be sold without restriction pursuant to Rule 144 within a 90-day period.

Anti-Takeover Effects of Delaware Law and Provisions of our Certificate of Incorporation and our Bylaws

Our Certificate of Incorporation and Bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or

- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;

- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and

- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Choice of Forum

Our bylaws provide that unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on behalf of the company, (ii) any action asserting a claim of, or a claim based on, a breach of a fiduciary duty owed by any company director, officer or other employee to the company or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, or (iv) any action asserting a claim governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein (the "Delaware Forum Provision"). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Securities Exchange Act of 1934. In addition, our bylaws further provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision").

Our bylaws also provide that any person or entity purchasing or otherwise acquiring any interest in shares of our Common Stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision.

We recognize that the Delaware Forum Provision and the Federal Forum Provision in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware. Additionally, the Delaware Forum Provision and/or the Federal Forum Provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The Court of Chancery of the State

of Delaware or the federal district courts of the United States, as applicable, may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders.

Provisions of our Charter and our Bylaws

Our Certificate of Incorporation and Bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our Certificate of Incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our Certificate of Incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

Meetings of Stockholders

Our Certificate of Incorporation and Bylaws provide that special meetings of stockholders may be called at any time by the board of directors, or by a majority of the members of the board of directors, or by a committee of the board of directors which has been duly designated by the board of directors and whose powers and authority, as provided in a resolution of the board of directors or in these Bylaws, include the power to call such meetings, but such special meetings may not be called by any other person or persons.

Advance Notice Requirements

Our Bylaws provide that stockholders must give timely written notice to bring business before an annual meeting of stockholders or to nominate candidates for election as directors at an annual meeting of stockholders. Generally, to be timely, a stockholder's notice will be required to be delivered to our principal executive offices not later than the 90th day nor earlier than the 120th day prior to the one (1)-year anniversary of the preceding year's annual meeting; provided, however, that if the date of the annual meeting is more than thirty (30) days before or more than sixty (60) days after such anniversary date, notice by the stockholder to be timely must be so delivered, or mailed and received, not later than the 90th day prior to such annual meeting or, if later, the tenth day following the day on which public disclosure of the date of such annual meeting was first made. Our Bylaws also specify the form and content of a stockholder's notice.

Amendment to Bylaws

Our board of directors is authorized to amend, alter, change, adopt and repeal our Bylaws by a majority vote. Our stockholders also have the power to amend, alter, change, adopt and repeal our Bylaws by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote on such an amendment or repeal, voting as a single class; provided, however, that if our board of directors recommends that stockholders approve such amendment or repeal at such meeting of stockholders, such amendment or repeal shall only require the affirmative vote of the majority of outstanding shares entitled to vote on such amendment or repeal, voting together as a single class.

Undesignated Preferred Stock

Our Certificate of Incorporation provides for 25,000,000 authorized shares of Preferred Stock. The existence of authorized but unissued shares of Preferred Stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of Preferred Stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of

incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of Preferred Stock. The issuance of shares of Preferred Stock could decrease the amount of earnings and assets available for distribution to holders of shares of Common Stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Nasdaq Global Select Market Listing

Our Common Stock is listed on The Nasdaq Global Select Market under the symbol "XERS."

Transfer Agent and Registrar

The transfer agent and registrar for our Common Stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 250 Royall Street, Canton, Massachusetts 02021, and its telephone number is (800) 962-4284.

Exhibit 21.1

XERIS BIOPHARMA HOLDINGS, INC.

LIST OF SUBSIDIARIES

Name	Jurisdiction of Incorporation
Xeris Pharmaceuticals, Inc.	Delaware
Xeris Pharmaceuticals Australia Pty Ltd	Australia
Strongbridge Biopharma Limited	Ireland
Strongbridge Dublin Limited	Ireland
Cortendo AB	Sweden

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statements (Nos. 333-262403 and 333-262404) on Form S-3 and (No. 333-260068) on Form S-8 of our report dated March 11, 2022, with respect to the consolidated financial statements of Xeris Biopharma Holdings, Inc.

/s/ KPMG LLP

Chicago, Illinois

March 11, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO RULE 13a-14(a) OR 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Paul R. Edick, certify that:

1. I have reviewed this annual report on Form 10-K of Xeris Biopharma Holdings, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2022

/s/ Paul R. Edick
By: Paul R. Edick
Chief Executive Officer and Chairman
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO RULE 13a-14(a) OR 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Steven M. Pieper, certify that:

1. I have reviewed this annual report on Form 10-K of Xeris Biopharma Holdings, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2022

By: /s/ Steven M. Pieper
Steven M. Pieper
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Xeris Biopharma Holdings, Inc. (the "Company") on Form 10-K for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Paul R. Edick, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, to the best of my knowledge, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material aspects, the financial condition and results of operations of the Company.

Date: March 11, 2022

By: /s/ Paul R. Edick
Paul R. Edick
Chief Executive Officer and Chairman
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Xeris Biopharma Holdings, Inc. (the "Company") on Form 10-K for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Steven M. Pieper, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, to the best of my knowledge, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material aspects, the financial condition and results of operations of the Company.

Date: March 11, 2022

By: /s/ Steven M. Pieper
Steven M. Pieper
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)