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, 2020

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: 001-38536

XERIS PHARMACEUTICALS, INC.

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

Delaware	**20-3352427**
(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, 2020, the aggregate market value of the Registrant's common stock held by non-affiliates of the Registrant was approximately $118.4 million based on the closing sales price as reported on the Nasdaq Exchange.

As of February 28, 2021, 59,764,999 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 2021 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, 2020.

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 several years and may not be able to achieve or sustain revenues or profitability in the future.
- Although we generate revenue from our first products, Gvoke®, which is available in a pre-filled syringe ("Gvoke PFS") and an auto-injector ("Gvoke HypoPen®"), 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 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.
- The market opportunity for Gvoke and our product candidates may be smaller than we estimate.
- Our reliance on third-party suppliers, including single-source suppliers, and a limited number of options for alternate sources for Gvoke or our product candidates could harm our ability to develop our product candidates or to commercialize Gvoke or any product candidates that are approved.
- Reimbursement decisions by third-party payors 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.
- If our third-party manufacturers of Gvoke or our product candidates are unable to increase the scale of their production of our products or our product candidates, or increase the product yield of manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed or interrupted.
- We expect to seek to establish collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.
- 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 U.S. Food & Drug Administration 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.
- Delays in conducting clinical trials could result in increased costs to us and delay our ability to obtain regulatory approval for our product candidates.
- Gvoke 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.
- 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.
- It is difficult and costly to protect our intellectual property and our proprietary technologies, and we may not be able to ensure their protection.
- 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 PHARMACEUTICALS, INC.

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Year Ended December 31, 2020

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;
- the pricing and reimbursement of Gvoke 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 and our product candidates;
- the commercialization, marketing and manufacturing of Gvoke 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 or any of our product candidates, if approved;
- our expectations related to the anticipated launch of our ready-to-use glucagon 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 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 specialty pharmaceutical company delivering innovative solutions to simplify the experience of administering important therapies that people rely on every day around the world. With novel technology platforms, XeriSol™ and XeriJect™, that enable ready-to-use, room-temperature stable formulations of injectable and infusible therapies, we are advancing a portfolio of solutions in various therapeutic categories. Our first product, Gvoke®, delivers ready-to-use glucagon via a pre-filled syringe ("Gvoke PFS") or auto-injector ("Gvoke HypoPen®") for the treatment of severe hypoglycemia, a potentially life-threatening condition, in people with diabetes. Gvoke was approved in September 2019 by the U.S. Food & Drug Administration ("FDA") for the treatment of severe hypoglycemia 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, and each is 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 February 11, 2021 the European Commission ("EC") granted a marketing authorization for Ogluo® (glucagon) for the treatment of severe hypoglycemia in adults, adolescents, and children aged two years and over with diabetes mellitus. We currently plan to commercially launch Ogluo in select European countries beginning in the fourth quarter of 2021. We are also continuing to evaluate additional applications of our ready-to-use glucagon formulation to address needs in hypoglycemia and related conditions. In addition, we are applying our technology platforms to other commercially available drugs to enable more convenient and patient-friendly subcutaneous ("SC") and intramuscular ("IM") routes of administration, including the development of products to address unmet needs in both diabetes and epilepsy. We own the rights to our proprietary formulation technology platforms, Gvoke, and our product candidates domestically and internationally, with 117 patents issued globally, including a composition of matter patent covering our ready-to-use glucagon formulation that expires in 2036. Throughout this document, unless otherwise noted, references to Gvoke include Gvoke PFS, Gvoke HypoPen and Ogluo.

Our proprietary XeriSol and XeriJect non-aqueous formulation technologies have the potential to offer distinct advantages over conventional product formulations, including eliminating the need for reconstitution and refrigeration, enabling long-term, room-temperature stability, significantly reducing injection volume, and eliminating the requirement for intravenous ("IV") infusion by enabling patient-convenient SC or IM administration. With our technology, our new product formulations are designed to be easier to use by patients, caregivers, and health practitioners and help reduce costs for payers and the healthcare system. The target molecules are peptides and small molecules for XeriSol and monoclonal antibodies and biologics for XeriJect. The formulations produced using these technologies can be delivered through commercially available syringes, auto-injectors, multi-dose pens and infusion pumps. Current aqueous formulations of certain drugs present numerous challenges for patients and caregivers, including multi-step reconstitution, refrigerated storage, reduced shelf life, large injection volumes, and IV administration over long periods of time. Our formulation technologies have broad applicability across many therapeutic areas, which we believe could provide more opportunities. There is increasing interest in our technology platforms by other drug development companies that seek higher drug concentrations and drug combinations in subcutaneous forms. In addition to use of these technologies for development of our own product candidates, we are currently conducting three technology platform collaboration projects with large pharmaceutical companies. Additional projects are under discussion with both large pharmaceutical and specialized biotech companies.

Our key priority is continuing the successful commercialization of our first product, Gvoke, for the treatment of severe hypoglycemia and increasing the adoption and penetration of emergency glucagon therapy, by offering a glucagon product that better meets the needs of patients and caregivers. Diabetes is a widespread condition that affects an estimated 463 million people worldwide. In the United States, an estimated 34 million children and adults have diabetes, of which 6.8 million are treated with insulin. In the United States, all of the approximately 1.4 million people with Type 1 Diabetes ("T1D") and 5.4 million people with Type 2 Diabetes ("T2D") require insulin therapy to lower their blood glucose levels to achieve normal blood sugar levels and avoid hyperglycemia. Conversely, insulin treatment in people with both T1D and T2D 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. However, relative to the number of people on insulin treatment, few prescriptions for glucagon are written. Only approximately 641,000 prescriptions for glucagon are filled annually. In American Diabetes Association's ("ADA") 2021 Standards of Care guidelines, it is recommended 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. Level 2 hypoglycemia is defined as blood glucose <54 mg/dl. Level 3 is defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery.

The current standard of care for severe hypoglycemia in the ambulatory setting is the emergency administration of glucagon, a hormone that raises the concentration of glucose in the bloodstream. Traditional glucagon kits consist of a glucagon powder that must be reconstituted with a liquid diluent and drawn into a syringe using a multi-step procedure that can be difficult to successfully administer, particularly in an emergency. In published comparative human factors studies with traditional glucagon 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. The under use or unsuccessful use of these traditional glucagon kits leaves

people at risk of experiencing prolonged severe hypoglycemic events, which, if left untreated, can lead to serious health consequences and death. Due to the limitations of traditional glucagon kits and other factors, only approximately 465,000 total prescriptions for traditional glucagon kits were written in 2020 in the United States. Annually, hypoglycemic and severe hypoglycemic events in the United States result in approximately $1.8 billion in costs related to emergency, inpatient and ambulatory care.

Our ready-to-use Gvoke does not require reconstitution or refrigeration and is stable at room temperature for two years. Gvoke is available in either a pre-filled syringe or an auto-injector with no visible needle. In our human factors studies, 99% of users were able to successfully administer the full dose with our ready-to-use Gvoke. In addition to Gvoke, Eli Lilly's Baqsimi®, a nasally administered glucagon powder, was approved by the FDA and launched in 2019. These two new, ready-to-use products, Gvoke and Baqsimi, together represented approximately 35% of the total emergency glucagon units dispensed in the year ended 2020.

Our commercial strategy is to drive awareness with clinicians by targeting high prescribers of mealtime insulin and glucagon to activate demand through targeted direct-to-patient promotion and patient advocacy groups. Our market access team has secured broad unrestricted access to Gvoke across all payor types. The combination of our promotional efforts in this category and Eli Lilly’s in support of its Baqsimi are driving a significant increase in prescription activity for glucagon in general. In fact, since the field launch of Gvoke PFS in January 2020, total glucagon prescriptions across all types and formulations were higher by 13.1% compared to 2019. According to IQVIA, total prescriptions written in 2020 for Baqsimi and Gvoke were approximately 137,900 and 38,800, respectively. Total units reported in 2020 were approximately 941,000, representing total U.S. sales of $264 million. These include 616,000 traditional glucagon kits, 251,000 units of Baqsimi, and 74,000 Gvoke units (as adjusted for a consistent unit of measure). We believe that increasing penetration, including by new entrants such as Gvoke that address unmet patient and caregiver needs, may result in a potential market opportunity of up to $3.8 billion.

Outside the United States, we estimate there are an additional 3.5 million people with diabetes in Europe and an additional 12.5 million people with diabetes in Japan and China that are clinically appropriate for emergency glucagon treatment. On February 11, 2021 the EC granted a marketing authorization for Ogluo for the treatment of severe hypoglycemia in adults, adolescents, and children aged two years and over with diabetes mellitus. The EC decision follows the positive opinion received from the Committee for Medicinal Products for Human Use ("CHMP") of the European Medicines Agency ("EMA") in December 2020. We currently plan to commercially launch Ogluo in select European countries beginning in the fourth quarter of 2021. In addition, we expect Gvoke to be available in Israel and the Palestinian Authority in 2022 through our distribution agreement with Megapharm Ltd. We plan to pursue development and commercialization collaborations for most, if not all, of the non-U.S. markets we seek to enter.

We are also applying our glucagon formulation to other hypoglycemic conditions with significant unmet medical need. In 2020, the following development programs produced positive clinical trial results:

- Post-Bariatric Hypoglycemia ("PBH"), a serious complication of bariatric surgery that can arise from excessive insulin, or hyperinsulinism, due to the change in gastric anatomy resulting from bariatric surgery.
- Exercise-Induced Hypoglycemia ("EIH") in people with diabetes. Exercise, particularly aerobic exercise, often results in a significant drop in blood glucose levels for people on insulin.

We plan to advance at least one of these programs forward. By applying our ready-to-use glucagon to treat multiple conditions, we expect to leverage operating efficiencies across our supply chain, research and development, and commercial and medical organizations.

We are also applying our technology platforms to develop additional product candidates, such as a fixed ratio co-formulation of pramlintide and insulin ("Pram-Insulin") for the management of diabetes and a ready-to-use, liquid-stable diazepam delivered via an injectable rescue pen for the emergency treatment of epileptic seizures. Additionally, we believe we have the potential to advance a number of programs in other indications based on the promising data we have seen from formulations in our laboratory as well as from an early clinical trial. We also believe that our strong product candidate portfolio, complemented by external expansion opportunities, will support our vision to effectively and efficiently meet the needs of our target markets. Both the Pram-Insulin and diazepam programs produced positive clinical trial results in 2020, and in October 2020 we were granted Fast Track designation by the FDA for our diazepam formulation. We have identified these two programs as candidates for out-licensing.

The nature of our product candidates and target conditions provides us with a potentially faster and capital-efficient development and regulatory pathway to approval. The FDA has granted orphan drug status to several indications for our product candidates, including our ready-to-use glucagon for PBH and Congenital Hyperinsulinism ("CHI") and our ready-to-use, liquid-stable formulation of diazepam for the treatment of Dravet syndrome and acute repetitive seizures ("ARS") in patients with epilepsy. Additionally, we have received orphan drug designation from the EMA for CHI Noninsulinoma Pancreatogenous Hypoglycemia Syndrome ("NIPHS"), which includes patients with PBH.

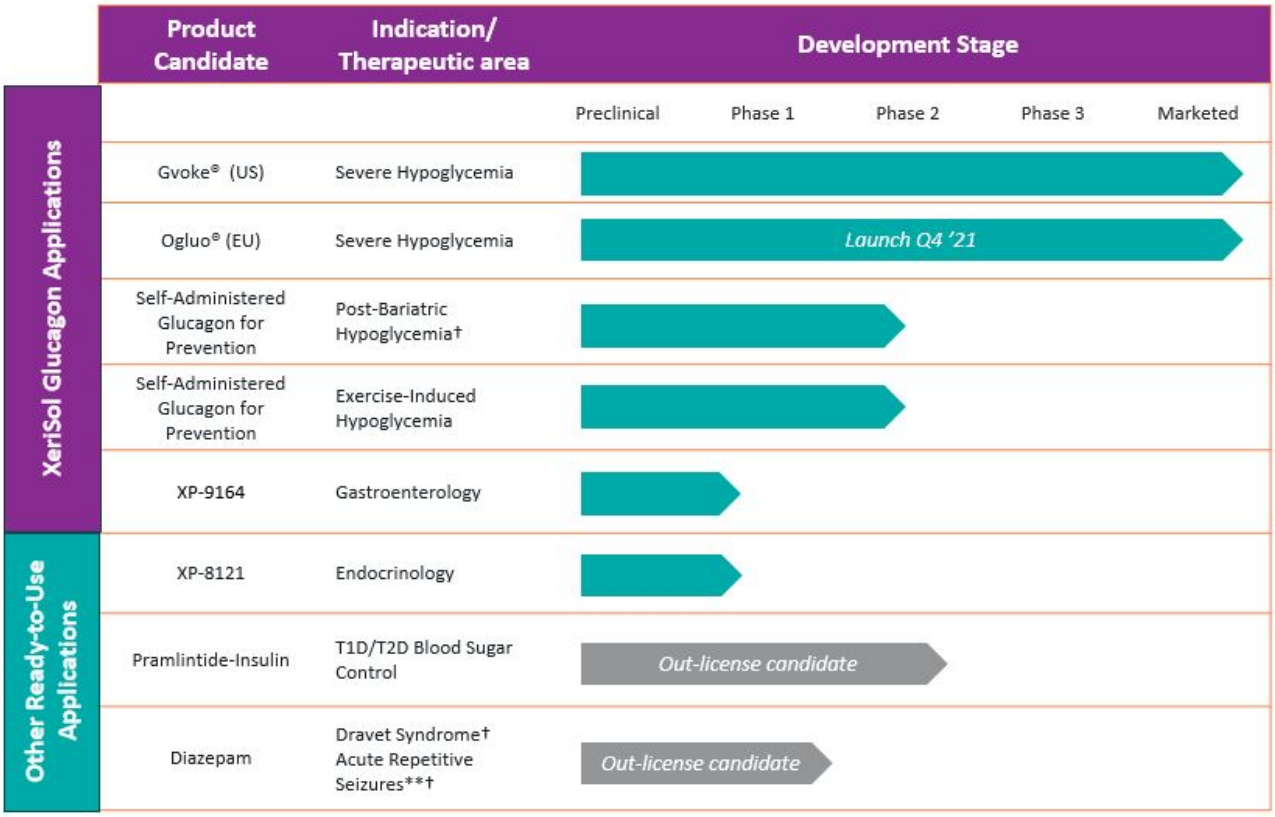
In the United States, this designation provides us with research and development tax credits and exemption from FDA user fees, as well as seven years of orphan drug exclusivity upon product approval. In the European Union ("EU"), this designation provides us with ten years of market exclusivity upon product approval and a single MAA application to the EMA through centralized review and

the potential for reduced regulatory review fees. In addition, because certain conditions that we intend to target are rare conditions, we believe our clinical trials may be of smaller size than studies for conditions that are not rare conditions. Furthermore, because the product candidates developed using our technology platforms are designed to be reformulations of currently approved products, in the United States, for most of our products, we expect to utilize the FDA's pathway under Section 505(b)(2) of the U.S. Federal Food, Drug and Cosmetic Act ("FDCA") which permits submissions to rely, in part, on the safety and effectiveness of a previously approved product, which may potentially result in a more expeditious pathway to FDA approval.

Our management team includes veterans in drug development, discovery and commercialization, with executive experience in leading global pharmaceutical and healthcare companies, including Durata Therapeutics, Baxter Healthcare, Merck, Searle, Takeda, Warner Chilcott, MedPointe Healthcare, Amgen, Amylin Pharmaceuticals, PowderJect Technologies and Alpharma.

Our Pipeline

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



† Orphan Drug Designation

** Fast Track Designation

Our Strategy

Our strategy is to utilize our proprietary non-aqueous formulation technology platforms to convert marketed and development-stage products that have poor solubility and stability into ready-to-use, user-friendly injectable and infusible drugs for multiple therapeutic areas and conditions, including hypoglycemia, diabetes, epilepsy, gastroenterology and endocrinology. We also seek to apply our formulation technology platforms to enhance the formulations of proprietary products and candidates of other pharmaceutical and biotechnology companies. The key elements of our strategy include:

- ***Maximize the commercial potential of Gvoke***. We began the field launch of Gvoke PFS and Gvoke HypoPen in the United States in January 2020 and July 2020, respectively. We are targeting healthcare professionals who are high prescribers of glucagon and/or mealtime insulin products, using both field and inside sales teams, engaging with professional associations, and activating demand through targeted direct-to-patient promotion and patient advocacy groups.
- ***Launch our ready-to-use liquid stable glucagon in Europe.*** On February 11, 2021 the EC granted a marketing authorization for Ogluo for the treatment of severe hypoglycemia in adults, adolescents, and children aged two years and over with diabetes mellitus. The EC decision follows the positive opinion received from the CHMP of the EMA in December 2020. We currently plan to commercially launch our liquid glucagon formulation as Ogluo in select European countries beginning in the fourth quarter of 2021. In addition, we expect Gvoke to be available in Israel and the Palestinian Authority in 2022 through our distribution agreement with Megapharm Ltd. We plan to pursue development and commercialization collaborations for most, if not all, of the non-U.S. markets we seek to enter.
- ***Continue to advance our ready-to-use glucagon portfolio to address hypoglycemia associated with other conditions***. We are applying our ready-to-use, room-temperature stable liquid glucagon formulation to other hypoglycemic conditions for non-rescue indications, such as PBH and EIH. The product presentation for these two indications is a vial of our liquid glucagon for self-administration via a syringe or transfer to a pump reservoir for continuous infusion. Additionally, we have completed preclinical studies for a gastroenterology indication. We plan to leverage efficiencies across our portfolio, such as our supply chain, research and development, and our commercial and medical organizations, and to use commercially available drug delivery devices for our liquid glucagon formulation programs.
- ***Continue to leverage our technology and expertise to develop a portfolio of non-glucagon product candidates***. We are also applying our formulation technology platforms to other commercially available drugs for multiple conditions. We completed a Phase 2 clinical trial of our fixed-ratio pramlintide-insulin co-formulation combination product for the treatment of diabetes, from which we announced positive topline results. In addition, we are developing an improved formulation of diazepam to be administered through a ready-to-use injectable rescue pen for which we are evaluating indications such as the treatment of patients with Dravet syndrome and ARS. In 2019, we completed a clinical study evaluating the preclinical pharmacokinetic ("PK") and pharmacodynamics ("PD") of our ready-to-use, room-temperature stable liquid diazepam formulation in normal volunteers and announced positive results. Based on these results, we initiated and completed an additional Phase 1b weight-based study, in which we announced positive topline results in July 2020. In October 2020, we were granted Fast Track designation by the FDA for our novel formulation of diazepam, which could advance directly into a Phase 3 registration study in both pediatric and adult patients with epilepsy. Finally, we have completed preclinical development for an additional product candidate in endocrinology.
- ***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 enhance the formulation, delivery and clinical profile of other companies' proprietary drugs and biologics. We currently are working with some major pharmaceutical companies on feasibility programs to evaluate the formulation of their proprietary therapeutics with XeriSol or XeriJect. We plan to continue to explore the application of our formulation technology platforms to proprietary drugs and biologics from additional pharmaceutical and biotechnology companies. Our strategic goal is to enter into broader development agreements with these partners upon successful completion of the feasibility programs. Such agreements may provide the potential for milestone payments and royalty streams.

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.

Ready-to-Use Glucagon

Our novel, room-temperature stable liquid glucagon formulation represents a significant advancement over freeze-dried, or lyophilized, glucagon, enabling a ready-to-use solution that can be quickly and easily injected or infused subcutaneously. This formulation is designed to provide the flexibility to dose different volumes of liquid glucagon using a range of delivery devices to suit the needs of people with hypoglycemic conditions. We believe our ready-to-use glucagon has the potential to change the paradigm for the treatment of hypoglycemic conditions and improve the lives of people who experience hypoglycemia.

Our Products

Gvoke

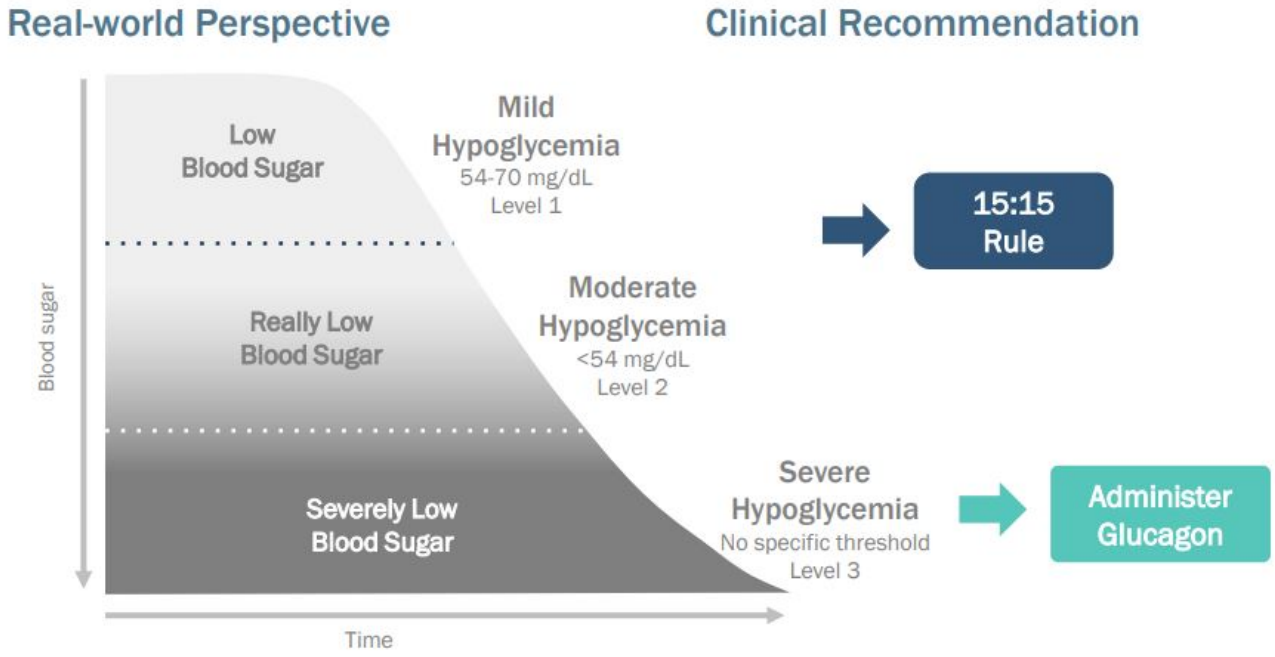
Gvoke offers ready-to-use, room-temperature stable glucagon that is designed to be administered subcutaneously in a simple two-step process via a commercially available pre-filled syringe or auto-injector. In our human factors studies, 99% of users were able to successfully administer the full dose with 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 the 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 February 11, 2021 the EC granted a marketing authorization for Ogluo for the treatment of severe hypoglycemia in adults, adolescents, and children aged two years and over with diabetes mellitus. The EC decision follows the positive opinion received from the CHMP of the EMA in December 2020. We currently plan to commercially launch Ogluo in select European countries beginning in the fourth quarter of 2021. We plan to pursue development and commercialization collaborations for most, if not all, of the non-U.S. markets we seek to enter.

Hypoglycemia Background

Diabetes is a widespread condition that affects an estimated 463 million people worldwide with an estimated 22 million drug-treated people in the United States. Among people with diabetes in the United States, all of the approximately 1.4 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. Conversely, 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, moderate or severe hypoglycemic events. Definitions, symptoms and treatment recommendations for hypoglycemia per the ADA and the American Association of Clinical Endocrinologists ("AACE") are summarized in the figure below:



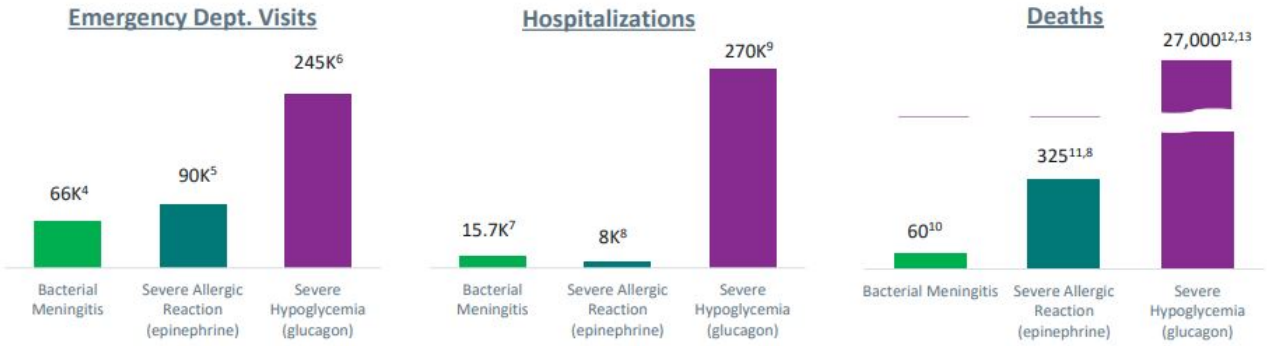
Hypoglycemic events of any severity are a daily concern for people with diabetes. Severe hypoglycemic events are extremely frightening for patients and caregivers and can result in cardiovascular disease, seizure, coma, and, if left untreated, death. Fear of hypoglycemia and the morbidity and mortality 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.

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. 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.

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.

Risks associated with severe hypoglycemia are greater than other highly treated medical conditions in the U.S., as summarized in the figure below:

	Bacterial Meningitis	Severe Allergic Reaction (epinephrine)	Severe Hypoglycemia (glucagon)
Clinically Appropriate Patient Population	~3.9M teenagers[3]	5.2M patients[1,2,8]	6.8M patients



1. Wood, et al, Anaphylaxis in America: The prevalence and characteristics of anaphylaxis in the United States. Journal of Allergy and Clinical Immunology. February, 2014.
2. "Clinically appropriate patient population" in the allergy market is based on those patients who were deemed to have a very likely history of anaphylaxis. This definition required involvement of at least 2 organ systems, including respiratory systems, cardiovascular systems, or both, as well as seeking treatment in the emergency department and feeling their life was in danger.
3. Based on 2018 CDC Recommended Immunizations for Children 7-18 Years Old (**https://www.cdc.gov/vaccines/schedules/downloads/teen/parent-version-schedule-7-18yrs.pdf**) and the CDC National Vital Statistics Report, Births: Final Data for 2016 (**https://www.cdc.gov/nchs/data/nvsr/nvsr67/nvsr67_01.pdf**).
4. Takhar, et al, U.S. emergency department visits for meningitis, 1993-2008, June 2012.
5. Motosue, et al, Increasing Emergency Department Visits for Anaphylaxis 2005-2014, Journal of Allergy and Clinical Immunology. January-February, 2017, Volume 5, Issue 1, Pages 171–175.e3, 2017.
6. Centers for Disease Control and Prevention (CDC), National Diabetes Statistics Report, 2017 Estimates of Diabetes and Its Burden in the United States.
7. AHRQ, Healthcare Cost and Utilization Project, July 2008 (**https://www.hcup-us.ahrq.gov/reports/statbriefs/sb57.pdf**).
8. Ma et al., The Journal of Allergy & Clinical Immunology (JACI), April 2014 Volume 133, Issue 4, Pages 1075–1083, and the United States Census Bureau, World Bank (2016).
9. T1D - Singh et al., ADA 2013 (279-OR); T2D - Singh et al., EASD 2012 (#628).
10. CDC, Active Bacterial Core surveillance (ABCs), Estimated number of cases and deaths of invasive Neisseria meningitides infections in the United States, 2015 (**https://wwwn.cdc.gov/BactFacts/index.html**).
11. M Tejedor-Alonso, et al., Epidemiology of Anaphylaxis: Contributions From the Last 10 Years. J Investig Allergol Clin Immunol 2015; Vol. 25(3): 163-175.
12. Lee, et al. The Association of Severe Hypoglycemia With Incident Cardiovascular Events and Mortality in Adults With Type 2 Diabetes. Diabetes Care 2018;41:104–111 10. Datamonitor, Epidemiology: Type 1 and Type 2 Diabetes Forecast 2015-2035.
13. Datamonitor, Epidemiology: Type 1 and Type 2 Diabetes Forecast 2015-2035.

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 in July 2019, a nasally administered glucagon powder, 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 U.S. in 2020, Eli Lilly's GEK and Baqsimi represented approximately 50% and 27%, respectively, Novo Nordisk's GlucaGen HypoKit represented approximately 14%, Gvoke represented approximately 8% and Fresenius Kabi's Glucagon Emergency Kit represented approximately 1%.

Xeris 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) or auto-injector (Gvoke HypoPen). Gvoke PFS and Gvoke HypoPen are 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.
- *Two-year 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 contrast to traditional glucagon kits, Gvoke features the following benefits:

	GEK 	Xeris Gvoke PFS 	Xeris Gvoke HypoPen 
No Reconstitution in Emergency	X	✓	✓
Auto-Injection	X	X	✓
Needle Auto-Retraction and Needle Guard	X	X	✓
Dose Volume Pre-measured for Pediatrics	X	✓	✓
Room-Temperature Stable as a Liquid	X	✓	✓
Rate of Successful Full Dose Delivery in Human Factors Studies	6 – 31%[1]	99%[2,3]	99%[2,3]

1. Biodel (Diabetes Tech Meeting, October 2015) – GEM; Locemia/Lilly (EASD 2015 Poster) – Intranasal; and Xeris Comparative Human Factors (ATTD Meeting, February 2016); 2. Brett Newswanger, Steven Prestrelski & Anthony D. Andre (2019) Human factors studies of a prefilled syringe with stable liquid glucagon in a simulated severe hypoglycemia rescue situation, Expert Opinion on Drug Delivery, 16:9, 1015-1025, DOI: 10.1080/17425247.2019.1653278; 3. Valentine V, Newswanger B, Prestrelski S, Andre AD, Garibaldi M. Human factors usability and validation studies of a glucagon autoinjector in a simulated severe hypoglycemia rescue situation. Diabetes Technol Ther. 2019;21(9):522-530.

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.

Xeris 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 compound annual growth rate in incidence of diagnosed and treated people with diabetes is approximately 4% per year. An additional 88 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 1.4 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 6.8 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 U.S. potential market opportunity may be up to $3.8 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. According to a 2015 study published in the journal *Endocrine Practice*, approximately 50% of people with T1D and approximately 3% of people with T2D with a new insulin prescription had a filled glucagon prescription. We believe that the drawbacks of traditional kits and the lack of conversations regarding glucagon limit their adoption. Two of the top reasons given by people with diabetes for non-renewal of glucagon prescriptions were that they were not confident that a caregiver or other person would be able to correctly administer the kit, and their healthcare professional did not discuss the need for a new one with them. In the United States, approximately 465,000 total prescriptions for emergency glucagon kits were written in 2020 in the United States, resulting in the purchase of approximately 616,000 single-dose kits. In 2020, a total of 941,000 units of emergency glucagon products were dispensed in the U.S., representing total sales of approximately $264 million.

In our Healthcare Professional Perceptions Study, results indicated that glucagon would be prescribed to more people across all clinically appropriate patient segments if our Gvoke HypoPen were available. Similarly, in our Caregiver and Patient Perceptions Study, almost two-thirds of people with T1D and T2D who use insulin said they would proactively ask for a prescription for Gvoke HypoPen if available. Importantly, over half of those same people did not currently have a filled glucagon prescription. During an emergency hypoglycemic event, these individuals would often be required to seek treatment through ambulance calls, hospital admissions or office visits. We believe that these studies show that more people would want to have emergency glucagon on-hand if there was a product that better met their needs. We believe this represents an opportunity for Gvoke to shift the site of care from the emergency room or hospital to less costly settings such as the home.

Outside the United States, we estimate that an additional 3.5 million people with diabetes in Europe and an additional 12.5 million people with diabetes in Japan and China are clinically appropriate for glucagon treatment. However, in 2018, only approximately 733,000 emergency glucagon products were sold in the United Kingdom, Germany, France, Italy and Spain combined, and only approximately 4,000 were sold in Japan and China combined, which we believe indicates that the market for emergency glucagon products is significantly underpenetrated in those regions.

Commercial Strategy

Our commercial strategy is to increase the number of people on insulin therapy who have emergency glucagon products available. 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 and Gvoke HypoPen in July 2020. 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, current 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.** Approximately 80% of all patients currently have unrestricted access to Gvoke. 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 have engaged with payors to more fully understand their drivers and barriers and convey the health and pharmacoeconomic value of Gvoke.

- **Impact of 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. As parts of the United States reopened, 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 in many areas, our ability to connect with our customers in person became much more limited and we are currently back to almost exclusively remote interactions. In addition, several conferences and other programs at which we intended to market Gvoke have been postponed, canceled and/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. Outside the United States, we plan to collaborate with local companies.

Our Product Candidates

Ready-to-Use Glucagon for Other Hypoglycemia Conditions

We are applying our ready-to-use liquid-stable glucagon formulation to treat other hypoglycemic conditions with significant unmet medical need. In particular, our formulation may be applied to conditions requiring continuous doses or smaller "mini-doses" of glucagon over a longer administration period. We intend to leverage work across our programs to substantially reduce development costs for each indication and enable expanded uses for our ready-to-use glucagon to follow Gvoke. Development aspects that can be leveraged include:

- Chemistry, manufacturing and controls ("CMC")
- Nonclinical toxicology program
- Clinical supplies manufacturing

For other hypoglycemic conditions, we intend to leverage our completed preclinical studies across our glucagon portfolio, which demonstrated the safety of the ready-to-use glucagon and supported further clinical development. We have been awarded a $1.0 million grant from the Leona M. and Harry B. Helmsley Charitable Trust for preclinical studies of glucagon product candidates for sub-chronic/chronic conditions.

For commercialization of ready-to-use glucagon for certain other hypoglycemic conditions, we expect to target endocrinologists, diabetologists and primary care providers that are currently prescribing glucagon and rapid acting insulin. Many of these physicians, particularly endocrinologists, are also currently treating PBH patients and we believe there is significant overlap between these physicians and those who would prescribe ready-to-use glucagon for diabetes.

In December 2013, we filed an IND application for the use of ready-to-use glucagon delivered via a wearable patch pump. This IND has supported our clinical development efforts in PBH and an assessment in a bi-hormonal artificial pancreas closed-loop system. We are the sponsor of this IND, which is active as of the date of this Annual Report on Form 10-K.

Ready-to-Use Glucagon for Post-Bariatric Hypoglycemia

We are developing a ready-to-use glucagon formulation for chronic self-administration in PBH, a challenging complication of bariatric surgery that may significantly impair quality of life, but for which there are currently no approved treatments. In January 2018, we received orphan drug designation from the FDA for our ready-to-use glucagon for the treatment of patients with hyperinsulinemic hypoglycemia, of which PBH is a category. In November 2018, we received EU orphan product designation for the treatment of NIPHS which includes patients with PBH.

Post-Bariatric Hypoglycemia Market

Obesity and related comorbidities such as T2D and cardiovascular disease are increasingly recognized as a major threat to individual and public health, with sustained weight loss difficult to achieve. Clinicians and patients alike have embraced the results of recent controlled clinical trials demonstrating the efficacy of surgical procedures performed on the stomach or intestines, known as bariatric surgery, to not only induce sustained weight loss but also to improve or normalize obesity-related comorbidities, including T2D. The number of bariatric surgeries performed in the United States has increased substantially from an estimated 158,000 procedures per year in 2011 to 252,000 in 2018. While benefits of bariatric surgery are now achieved with a lower risk of surgical complications, longer-term intestinal and nutritional complications can still occur.

One challenging and sometimes severe complication of bariatric surgery is hyperinsulinemic hypoglycemia. Hyperinsulinemic hypoglycemia, and more specifically PBH, is most commonly associated with Roux-en-Y gastric bypass ("RYGB"), a procedure in which the small intestine is re-routed to a small resected stomach pouch. However, PBH also has been observed following sleeve gastrectomy, a procedure that reduces the size of the stomach. In the U.S., approximately 17% of bariatric procedures performed are RYGB, while approximately 61% are sleeve gastrectomy. PBH is defined as documented plasma glucose levels below 70 mg/dL in conjunction with hypoglycemic symptoms and the relief of such symptoms with the normalization of glucose levels. Symptoms include palpitations, lightheadedness and sweating. A subset of post-bariatric surgery patients develops very severe hypoglycemia involving a shortage of glucose in the brain, known as neuroglycopenic symptoms, typically occurring one to three years following bariatric surgery and associated with confusion, decreased attentiveness, seizure and loss of consciousness. For these patients, quality of life can be severely affected as many cannot care for themselves or even be left alone and may ultimately lose their employment due to this disability.

Hypoglycemia typically occurs after meals, particularly those rich in simple carbohydrates. Due to the change in gastric anatomy resulting from bariatric surgery, plasma insulin concentrations are inappropriately high after meals, which can lead to severe hypoglycemia in these patients. Treatment of hypoglycemia requires rapid-acting carbohydrates such as glucose tablets, which in PBH patients can contribute to rebound hyperglycemia that triggers further insulin secretion and recurrent hypoglycemia.

There are currently no approved treatments for PBH. Current strategies to manage PBH include dietary modification aimed at reducing intake of high glycemic index carbohydrates. Both diet and off-label administration of pre-meal acarbose, an anti-diabetic drug used to treat T2D, aim to minimize rapid post-meal surges in glucose that trigger insulin secretion. Additional off-label therapies include those aimed at reducing insulin secretion. In severe cases, gastric restriction or banding has been required to slow gastric emptying, and gastrostomy tubes have been used to provide the sole source of nutrition. Despite strict adherence to medical nutrition therapy and clinical use of multiple medical options, patients continue to have frequent hypoglycemia. While hypoglycemia most commonly occurs following meals, it can also occur in response to increased activity and emotional stress. Importantly, patient safety is additionally compromised when hypoglycemia unawareness develops with recurrent hypoglycemia. We believe there is an urgent need for therapeutic options to allow optimal nutrition, maintain health and quality of life and improve safety in patients with PBH.

Because episodes of hypoglycemia normally occur in the ambulatory setting, the reported prevalence of PBH varies, but we estimate that roughly 1% to 2% of bariatric surgery patients experience PBH. As bariatric procedures have been performed for over ten years, based on our analysis of market research, we estimate a standing population of approximately 85,000 patients who fail mealtime nutritional therapy and experience PBH in the United States and require additional treatment options. A similar size patient population is estimated to exist in Europe. Depending on the severity of their condition, these patients may require chronic episodic administration of glucagon ranging from multiple times a month to multiple times a day.

Xeris Offering–Ready-to-Use Glucagon for PBH

We have developed a ready-to-use glucagon formulation that can be easily and quickly injected or infused subcutaneously from a syringe, pen or pump. Injection of small doses of our liquid-stable glucagon after meals may offer a novel mechanism for PBH patients to treat or prevent hypoglycemia. Importantly, these smaller and more physiologic doses are designed to prevent rebound hyperglycemia associated with glucose tablets, carbohydrate intake and rescue doses of glucagon. Further, small doses of glucagon may offer a direct treatment mechanism for PBH, as opposed to indirect methods aimed at preventing hypoglycemia that are currently employed using various off-label therapeutic options.

Primary market research has shown endocrinologists are comfortable with glucagon’s mechanism of action and current safety profile and view ready-to-use glucagon as a welcome treatment option for PBH patients. Physicians surveyed reported ready-to-use glucagon utilization of 35% to 59% if the product can prevent half of severe hypoglycemic events in PBH patients.

As there are currently no therapeutic options indicated for treatment of PBH and the condition has been designated a rare disease, we believe that payors will include our ready-to-use glucagon on their formularies, if approved. We intend to conduct additional payor research as product development progresses.

Clinical Experience in PBH

We have completed a proof-of-concept clinical trial and a randomized controlled Phase 2 clinical trial for our ready-to-use glucagon for the treatment of PBH. A new IND application for self-administration of our ready-to-use glucagon with a vial/syringe went into effect on October 19, 2018. This IND authorized us to initiate an additional Phase 2 trial evaluating our ready-to-use, room-temperature stable liquid glucagon formulation for patients who experience hyperinsulinemic hypoglycemia after bariatric surgery. We received positive top-line results from the in-clinic and outpatient phases of this Phase 2 clinical trial.

Phase 2 Clinical Trials

XSGO-PB01: A Phase 2 Proof-Of-Concept Study of Sensor Guided, Clinician-Administered Delivery of Glucagon Infusion from a Patch Pump to Prevent Post-Prandial Hypoglycemia in Post-Bariatric Surgery Patients

We conducted an iterative design-and-evaluation Phase 2 clinical trial to assess the performance of a novel event-based hypoglycemia prediction algorithm that triggered delivery of mini-doses of ready-to-use glucagon from a patch pump. For the trial, which was conducted from the first quarter of 2016 through the second quarter of 2017, we recruited seven patients 18 to 65 years of age with a history of RYGB surgery and PBH with neuroglycopenia who were uncontrolled on medical nutrition therapy and medications. In an inpatient setting, subjects received a mixed-meal tolerance test ("MMTT"), which is known to cause hypoglycemia in these patients. Upon receipt of an alarm based on continuous glucose monitor data, subjects were given small, subcutaneous infusions of ready-to-use glucagon from a pump, with the aim of preventing hypoglycemia. The primary endpoint of this study was to investigate the ability of the patch pump to detect and direct timing of glucose administration. The secondary endpoint of this study was to investigate the safety profile of ready-to-use glucagon administered from a pump.

Ready-to-use glucagon bolus through the infusion pump was observed to rapidly raise serum glucagon levels, and the doses employed were not associated with increased insulin or C-peptide concentrations. Nadir glucose and time spent under 75 mg/dL in the period after the glucagon bolus were reduced progressively with each new stage of protocol development, which involved implementing either earlier hypoglycemia alarms or larger glucagon doses. All seven patients successfully completed nine treatment visits in this trial. Results showed the treatment to be well-tolerated, with discomfort at the infusion site and erythema the most frequent adverse events, and no severe adverse events.

Since this was the first implementation of the ready-to-use glucagon formulation in mini-doses for PBH, the dose was chosen with caution to prevent rebound hyperglycemia that has been observed with use of rescue doses of glucagon. Using these results, we determined the dose required to effectively prevent hypoglycemic events in the postprandial setting. The results of this trial were published in the peer-reviewed journal *Diabetes Technology & Therapeutics*.

XSGO-PB02: Closed-Loop Glucagon Pump for Treatment of Post-Bariatric Hypoglycemia

Following the positive proof-of-concept outcome of XSGO-PB01, in the fourth quarter of 2017, we initiated a randomized, placebo-controlled, double-blind Phase 2 clinical trial to assess the efficacy of ready-to-use glucagon to prevent and treat hypoglycemia occurring in patients with PBH in response to meals. The primary objective of this trial was to investigate the efficacy of a closed-loop glucagon pump for PBH measured by real-time continuous glucose monitoring ("CGM"). Secondary objectives included safety and tolerability. Following an MMTT, subjects were randomized to either placebo or glucagon infusion on the first study visit and crossed over to the other treatment during the second treatment visit. Investigators were masked to subject assignment. In study visits, an MMTT was employed and subjects were treated based on CGM-based measurements of low blood glucose. Subjects were treated with study drug (ready-to-use glucagon or placebo) at a dose of 300 mcg followed by 150 mcg if needed. Of the 12 subjects that completed the trial, seven experienced severe hypoglycemia in response to an MMTT. Ready-to-use glucagon effectively treated hypoglycemia in comparison to placebo ($p = 0.0082$ glucagon vs. placebo). Rescue glucose was needed in 7 of 7 visits for subjects who received placebo and 0 of 7 visits for subjects who received ready-to-use glucagon. Both drug and placebo were well tolerated with no reported severe adverse events. An abstract of these study results was presented at the 2019 Endocrine Society annual meeting, and full results were published in the peer-reviewed *Journal of Clinical Endocrinology and Metabolism*.

This randomized controlled trial data supported the new IND and informed the design of our ongoing Phase 2 clinical trial using a vial/syringe to evaluate ready-to-use glucagon in PBH.

XSGR-PBH-201: A Phase 2, Interventional, Randomized, Double-Blind, Placebo-Controlled Pilot Study of Glucagon RTU in Subjects Who Experience Hyperinsulinemic Hypoglycemia After Bariatric Surgery

Following our IND clearance in October 2018, we initiated a new Phase 2 clinical trial at five clinical research centers in North America. This study 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 parallel comparison in the outpatient setting. The purpose of the trial was to evaluate the logistics of implementing an efficacy and safety study of ready-to-use glucagon ("Glucagon RTU") via vial/syringe to treat symptomatic postprandial hypoglycemia in subjects with PBH. The study collected safety and efficacy information to help inform a future Phase 3 clinical trial.

During the CRC crossover stage, subjects underwent two high-carbohydrate, solid/liquid-meal tests. After each meal, subjects self-administered blinded study drug (Glucagon RTU 300 mcg or placebo) when any postprandial autonomic symptom was experienced or when hypoglycemia was confirmed with a blood glucose measurement of less than 70 mg/dL using a blood glucose meter.

We reported topline results from the completed CRC crossover stage of this trial in December 2019, which demonstrated that most subjects experienced postprandial hypoglycemia within 90-120 minutes after finishing the meal. Of patients that successfully

completed the meal challenge, all subjects were also able to self-administer 300 mcg (a "mini-dose") of the study drug, as directed, during the setting of declining blood glucose. A mini-dose of Glucagon RTU was adequate to restore or maintain normal blood glucose levels within 15 minutes of administration. This effect was maintained at 30 minutes, and hyperglycemia was not observed. The incidence of a follow-on episode of hypoglycemia (rebound hypoglycemia) requiring oral glucose for rescue was less with Glucagon RTU compared to placebo. After CRC study-related procedures were completed, subjects were assigned the blinded study drug (Glucagon RTU 300 mcg or placebo) and entered the 12-week outpatient stage. Subjects also were trained to self-administer their assigned study treatment, with the presence of any postprandial autonomic symptoms. In situations where hypoglycemia (blood glucose ≤ 70 mg/dl) was present at mini-dosing or continued after treatment, oral glucose tabs were recommended in addition to the study drug.

In May 2020, we reported positive topline results from the 12 subject, 12-week outpatient stage of the trial. More than 200 postprandial hypoglycemia episodes were reported across both treatment arms. Subjects frequently experienced postprandial episodes within 90-120 minutes after finishing meals and were able to successfully self-administer RTU glucagon during these events. Similar to the in-clinic stage, the sole use of a 300 µg RTU glucagon was adequate to restore or maintain normal blood glucose levels within 15 minutes of administration and was maintained up to 120 minutes. During episodes when blood sugar was >70mg/dL at drug dosing, RTU glucagon and placebo were comparable in maintaining blood sugar within normal levels, and RTU glucagon did not elicit hyperglycemia. During episodes when blood sugar was <70 mg/dL at drug dosing and without the use of glucose tabs, RTU glucagon successfully restored blood glucose levels to normal levels (blood sugar ≥70 mg/dL) within 15 minutes, at a higher frequency when compared to placebo. When failures were observed, subjects in both treatment arms exhibited near-normal counterregulatory responses to hypoglycemia, sufficient to avoid severe hypoglycemia. Subjects' use of glucose tablets, both during and after drug dosing as a follow-on rescue, was observed only within the placebo treatment arm. In this placebo arm, glucose tablet use during postprandial hypoglycemia episodes resulted in rebound hypoglycemia. Rebound hypoglycemia was not observed in the RTU glucagon treatment arm.

In both the CRC crossover and outpatient stages, treatment emergent adverse events with mini-doses of Glucagon RTU were comparable to placebo, including negligible injection site reactions. Mini-doses of Glucagon RTU appear well tolerated, and no serious adverse events occurred.

We are currently finalizing with the FDA expectations for a registration program to support a mini-dose indication for Glucagon RTU in PBH, including the study design for a Phase 3 clinical trial.

Ready-to-Use Glucagon for Exercise-Induced Hypoglycemia in Diabetes

Exercise-induced 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. If approved, our ready-to-use glucagon would represent a significant market opportunity in the treatment for EIH.

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 which 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. Currently Gvoke and glucagon rescue kits are only indicated at an emergency dose of 1 mg for rescue from severe hypoglycemia. In addition, Eli Lilly's Baqsimi is a one-time use intranasal powder, the administration of which delivers a full 3 mg rescue dose of glucagon.

We have been awarded $2.1 million in grants from organizations such as the Leona M. and Harry B. Helmsley Charitable Trust and the NIH National Institute of Diabetes and Digestive and Kidney Diseases, and we have worked with institutions including the Joslin Diabetes Center and the University of Pennsylvania for clinical development of our mini-dose glucagon product candidates.

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.

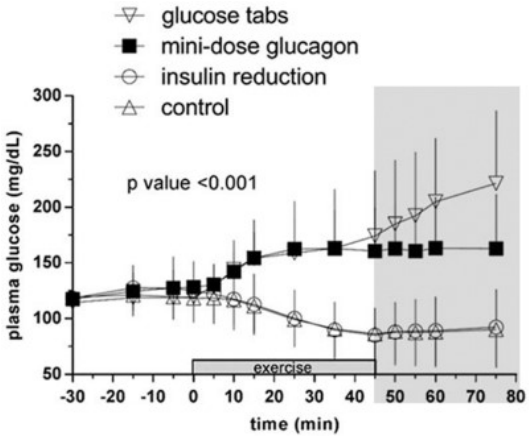
Phase 2 Clinical Trials

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. In particular, this was a four-session, randomized crossover trial involving 15 adults with T1D who exercised at 50-55% VO2max for 45 minutes under conditions of no intervention (control), 50% basal insulin reduction, 40 g oral glucose tablets, or 150 µg subcutaneous mini-dose glucagon, all administered five minutes before exercise. Secondary endpoints were to investigate the safety profile of this product candidate.

During the exercise sessions conducted in this study, plasma glucose increased slightly with mini-dose glucagon compared to a decrease with control and insulin reduction, as depicted in the figure below. Plasma glucose increased more greatly with glucose tablets. Hypoglycemia (<70 mg/dL) was experienced by six subjects during control, five during insulin reduction and none with glucose tablets or mini-dose glucagon; however, five subjects experienced hyperglycemia (>250 mg/dL) with glucose tablets and one with mini-dose glucagon. The study was well-controlled, as insulin levels were not different among sessions, while glucagon levels increased only in the mini-dose glucagon arm, as expected.

In a Phase 2 randomized, controlled clinical study, T1D subjects (n=16) administered mini-dose glucagon completed a 45-minute exercise session without adjusting basal insulin or ingesting glucose tabs (calories).



The Phase 2 study concluded that mini-dose glucagon (150 µg) may have the potential to prevent EIH in adults with T1D. In addition, mini-dose glucagon may be 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 may result in less post-intervention hyperglycemia than ingestion of carbohydrates and avoids the consumption of unnecessary calories. The results of this study were published 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. T1D subjects who receive daily insulin treatment via a subcutaneous infusion

pump performed at least 45 minutes duration of exercise in a CRC setting and at least 30 minutes duration of moderate-to-high intensity exercise in the outpatient setting and were monitored for hypoglycemia in the exercise recovery period. In January 2020, we reported positive results from the CRC setting of this Phase 2 study. Results from this stage of the Phase 2 study showed that a mini-dose of RTU glucagon was adequate to maintain normal blood glucose levels during prolonged, moderate-to-high intensity aerobic exercise.

For persons with diabetes, standard of care for aerobic exercise includes 50% insulin pump reduction. 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. Subjects were randomly assigned to RTU Glucagon with 50% insulin pump reduction (RTU Glucagon + standard of care); placebo injection with 50% insulin pump reduction (standard of care); or RTU Glucagon without insulin pump reduction (Open Label RTU Glucagon). In June 2020, we reported positive results from the outpatient stage of this Phase 2 study. Results from this stage of the Phase 2 study showed that a mini-dose of RTU glucagon was adequate to maintain normal blood glucose levels during prolonged, moderate-to-high intensity aerobic exercise in a real-world setting with or without adjustment to insulin.

During the 12-week outpatient stage, 45 subjects completed 795 aerobic exercise sessions. 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.

We are currently finalizing with the FDA expectations for a registration program to support a mini-dose indication for Glucagon RTU in EIH, including the study design for a Phase 3 clinical trial.

Ready-to-Use Glucagon for Gastroenterology

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

Ready-to-Use Glucagon for Congenital Hyperinsulinism

We have decided not to proceed with a planned Phase 3 CHI study based on the challenging regulatory pathway coupled with the limited market opportunity. Instead, we will consider requests to make our liquid-stable glucagon available for approved Expanded Access requests at no cost to eligible patients. (Expanded Access is a potential pathway for a patient with an immediately life-threatening condition or serious disease to gain access to an investigational drug for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.)

Non-Glucagon Programs

XeriSol Pramlintide-Insulin Co-formulation

Leveraging our XeriSol platform, we are developing a ready-to-use fixed dose combination of insulin and pramlintide to be delivered via a vial and syringe. Pramlintide is an injectable amylin analog for both Type 1 and 2 diabetes. In normal physiology, amylin is a hormone that is co-secreted into the bloodstream at a fixed ratio with insulin by the beta cells of the pancreas. The U.S. approval and launch of pramlintide (Symlin®) brought significant interest because of its ability, when used in combination with mealtime insulin, to flatten post-prandial blood glucose levels, reduce glucose excursions, and cause weight loss. Short-term and long-term clinical trials have found that adding pre-prandial pramlintide injections to insulin therapy reduced post-prandial glucose excursions and improved overall glycemic control (hemoglobin A1c levels) in patients with T1D. Clinically, pramlintide accomplishes this by reducing food intake, delaying gastric emptying, and reducing endogenous glucose production in the liver by suppressing glucagon secretion. The use of pramlintide also allows for approximately 30% less insulin utilization due to differential efficacy.

Pramlintide is indicated in people with diabetes for use at all major meals where patients already administer bolus insulin. The addition of a pramlintide regimen adds three or more separate injections daily which could be a challenging proposition in this patient population. We believe current use of pramlintide is quite limited because the injection burden issues outweigh the perceived benefits. To date, co-formulation/mixtures of pramlintide and insulin have experienced technical difficulties due to the physico-chemical incompatibility of a native mixture of each of these components. We believe our ready-to-use, room-temperature stable XeriSol co-formulation of pramlintide and regular insulin as well as pramlintide and lispro insulin can benefit patients by reducing the number of required injections. We address the co-formulation problem by utilizing our XeriSol technology to develop stable pramlintide and regular insulin formulations as well as stable pramlintide and lispro insulin formulations. XeriSol forms a stable co-formulation of pramlintide and insulins (regular or lispro) without the need for novel excipients. XeriSol pramlintide-insulins can be presented as a variable-fixed-ratio combination of either six or nine µg pramlintide per unit of insulin. These ratios have been shown to have beneficial clinical efficacy profiles in previous studies.

XeriSol pramlintide-insulin has several potentially valuable stability properties from a patient use perspective, namely potential two-year stability when refrigerated and up to 90 days at room temperature. This stability profile is comparable to current insulin products and would not introduce new handling challenges for existing insulin patients.

In preclinical studies, we characterized the PK and PD of pramlintide and various insulin formulations in normal and streptozotocin induced diabetic rats (mimicking T1D) given as separate injections or as a XeriSol pramlintide-insulin combined dose. Consistent with pramlintide's known pharmacological action, there was no glucose lowering with pramlintide alone. Profiles for pramlintide were similar to either saline or XeriSol vehicle administered by subcutaneous injection in rats. XeriSol pramlintide-insulin demonstrated a longer duration of glucose lowering compared to separate injections of pramlintide (Symlin) and insulin (Humulin®). Figures 1 and 2 below show a comparison of efficacy based on changes in glucose levels after injection of XeriSol pramlintide-insulin and pramlintide-lispro in comparison with separate injections of Symlin and Humulin or Symlin and Humalog® in a rodent model. In a preclinical study, XeriSol pram-insulin maintained glucose control for approximately four hours as compared to separate injections of commercially available product combinations (mimicking human subcutaneous administration) that begin to lose glucose control after approximately two hours.

Figure 1 Glucose Levels after Injection of XeriSol Pramlintide-Insulin and Humulin/Symlin Co-Injection

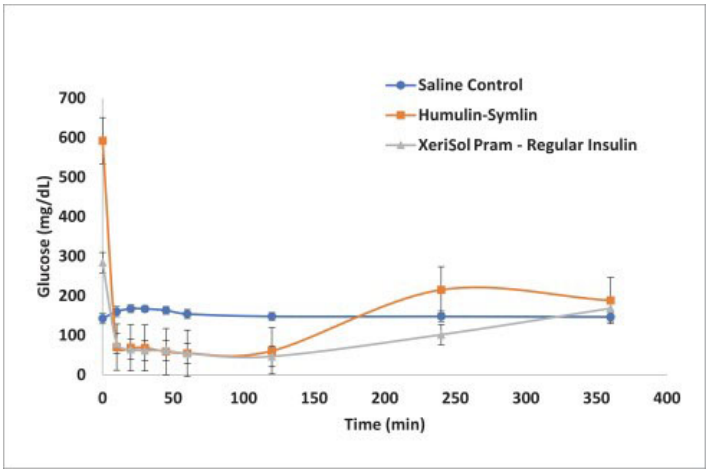
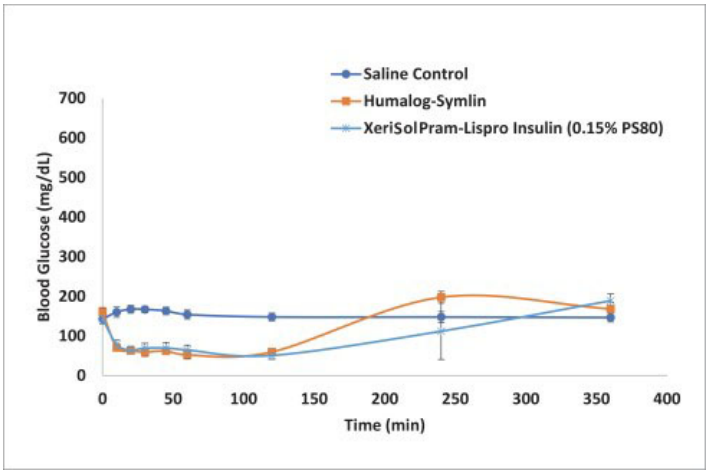


Figure 2 Glucose Levels after Injection of XeriSol Pramlintide-Lispro and Humalog/Symlin Co-Injection



We initiated a study of our novel XeriSol pramlintide-insulin co-formulation in a Phase 2 clinical trial in T1D in the third quarter of 2019. This study compares XeriSol pramlintide-insulin versus separate injections of Symlin and Humulin in diabetic subjects. According to recent guidance from the FDA, the insulin component of our XeriSol pramlintide-insulin co-formulation is subject to the FDA's "deemed to be a license" provision of the Biologics Price Competition and Innovation Act of 2009, which may necessitate that we submit a Biologics License Application ("BLA") for any future marketing authorization by the FDA.

XP-3924: A Phase 2, Randomized, Open-Label, Crossover, PD/PK Study of a Novel Pram-Insulin Co-Formulation in Adults With T1D

In June 2020, we announced positive results from our proof-of-concept Phase 2 study of our novel XeriSol pramlintide-insulin co-formulation in adults with T1D. The completed Phase 2 study was a randomized, open-label, active comparator-controlled, three-period cross-over study, which enrolled 18 adult participants with T1D. This study aimed to investigate the PK and PD of pramlintide, and the safety and tolerability of a single dose of XP-3924 (administered based upon the subjects' insulin:carbohydrate ratio), when compared to co-administration of regular insulin (Humulin) and pramlintide (Symlin) and to an injection of regular insulin alone (Humulin). Subjects were randomly allocated to a sequence of three treatments: XP-3924 (with 50% insulin reduction), regular insulin, or regular insulin (with 50% insulin reduction) plus pramlintide co-administered as separate injections. The study drugs were administered SC before the intake of a standardized 75-gram oral glucose challenge. The subjects' blood glucose levels were monitored for six hours after drug dosing. Treatment with XP-3924 resulted in a 62.3% reduction of hyperglycemia (blood glucose >180 mg/dL) after the glucose challenge when compared to Humulin ($p<0.001$). Additionally, XP-3924 exhibited comparable postprandial glycemic control to that of the co-administered injections of Humulin and Symlin. The mean absolute change in blood glucose was less in XP-3924 when compared to both Humulin and co-administered injections of Humulin and Symlin after the oral glucose challenge. The glucose variability after treatment with XP-3924 was less than both Humulin and co-administered injections of Humulin and Symlin, as defined by the comparison of the coefficient of variation of all plasma glucose readings across the six-hour duration of study treatments. The incidence and severity of treatment emergent adverse events was comparable across all treatment arms, as were the overall number of hypoglycemic events during dosing visits. There were minimal gastrointestinal side effects reported in any treatment arm. There was a comparable incidence of injection site reactions, and no edema was noted across all treatment arms. XP-3924 was safe and well tolerated, and no serious adverse events occurred in this study.

We are currently finalizing with the FDA expectations for a registration program to support a BLA, including the study design for a Phase 3 clinical trial program.

Ready-to-Use Diazepam

Leveraging our XeriSol formulation technology, we are developing a ready-to-use diazepam formulation for which we were 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. Dravet syndrome is a rare form of intractable epilepsy that begins in infancy with an estimated incidence rate of 1:16,000 to 1:21,000 in the United States.

Immediate treatment of epileptic seizures is critical to avoid increased risks of morbidity and mortality, including permanent neuronal damage, behavioral abnormalities and an increased probability in the need for life-long care.

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.

Our ready-to-use diazepam formulation has demonstrated rapid onset and high bioavailability in preclinical models. We were awarded grants totaling $2.3 million from the Epilepsy Foundation and the NIH for this program. An IND application for our ready-to-use diazepam injectable rescue pen for ARS went into effect on November 28, 2018. This IND authorized us to initiate a study (XSDZ-101) evaluating the PK and PD of our ready-to-use, room-temperature stable liquid diazepam formulation in normal volunteers. Below is a description of this study.

XSDZ-101: A Randomized Crossover Study of the Comparative Bioavailability, Pharmacokinetics, and Tolerability of Diazepam After Subcutaneous, Intramuscular, and Rectal Administration in Healthy Subjects

In May 2019, we announced positive results from our Phase 1 study of our novel formulation of diazepam. The open-label, three-treatment, three-way crossover, randomized controlled study was conducted among 24 healthy volunteers to assess the bioavailability and PK of our novel formulation of diazepam (XP-0863) after IM and SC administration compared to an administration of commercial diazepam rectal gel (Diastat). Secondary objectives were to assess the safety and tolerability of our diazepam after SC and IM administration. Our IM and SC administration of 10 mg diazepam yielded higher exposure as compared to an equivalent dose of diazepam rectal gel as assessed by AUC "(zero to infinity)". In individual comparisons, our administration resembled Diastat for both Cmax and Tmax. Additionally, both arms were safe and well-tolerated as a single dose. The study found no safety trends in any treatment group.

Based on these results, in the second half of 2019 we initiated a Phase 1b weight-based dosing study with IM administration of diazepam in healthy volunteers to assess the pharmacokinetics, safety and tolerability of two different weight-based doses of IM XP-0863 diazepam when compared to a weight-based dose of Diastat rectal gel. In April 2020, we reported positive topline results, and in July 2020 we reported complete results from this Phase 1b study.

XP-0863 is a highly concentrated liquid diazepam for IM injection that is intended for the treatment of seizure emergencies in patients ≥ 2 years of age, with partial onset or generalized convulsive seizures, who are identified jointly by their caregivers and physicians as suffering intermittent and periodic episodes of markedly increased seizure activity. XP-0863 uses the XeriSol technology platform to overcome the solubility problems associated with diazepam, reduces injection burden, provides comparable pharmacokinetics to diazepam rectal gel (Diastat), and may support the prompt and full-dose drug delivery of diazepam during seizure emergencies.

The Phase 1b study was an open-label, weight-based dose, three-treatment, three-way crossover study in healthy adult subjects. This study aimed to investigate the pharmacokinetics, safety, and tolerability of two different weight-based doses of intramuscular XP-0863 when compared to a weight-based dose of Diastat rectal gel. Subjects were randomly allocated to a sequence of three treatments: XP-0863 IM (0.25 mg/kg), XP-0863 IM (0.125 mg/kg), or Diastat (0.2 mg/kg). The subjects' diazepam blood levels were monitored over 21 days after drug dosing. XP-0863 showed comparable pharmacokinetics to Diastat, with similar partial AUCs of XP-0863 (0.25 mg/kg) to Diastat early after dosing and with increased overall exposure (zero to infinity) when compared to Diastat. XP-0863 (0.25 mg/kg) had comparable Cmax when compared to Diastat. The weight-based doses of XP-0863 were safe and well tolerated, with minimal sedation and injection site reactions, and no serious adverse events occurred.

In October 2020, we were granted Fast Track designation by the FDA for our novel formulation of diazepam, which could advance directly into a Phase 3 registration study in both pediatric and adult patients with epilepsy.

Ready-to-Use Product for Endocrinology

We are currently in Phase 1 development with product candidate XP-8121, an early-stage program for endocrinology.

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 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 requirements for Gvoke and other pipeline products utilizing ready-to-use glucagon, 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 in their 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 intend to source the device from a single supplier over the life of the product.

We believe that a number of CMOs can provide suitable secondary packaging services for Gvoke, 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. wholesale customers, and we have a commercial distribution agreement with one such vendor.

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. We believe the key competitive factors that will affect the development and commercial success of our products and product candidates include likelihood of successful dose delivery, ease of administration, therapeutic efficacy, safety and tolerability profiles and cost. 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. 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.

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, the ANDA for which was approved by the FDA on December 29, 2020 for the treatment of severe hypoglycemia. 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 because once the lyophilized glucagon is combined with water, the solution becomes unstable and can fibrillate, rendering it potentially inactive. We believe that the drawbacks of traditional kits and the lack of conversations regarding glucagon limit their adoption. Innovative glucagon products, including our Gvoke and Eli Lilly's intranasal glucagon dry powder, Baqsimi, were both approved by the FDA and launched in 2019.

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.

Zealand Pharma is developing dasiglucagon, a stable analog of human glucagon, in an auto-injector for subcutaneous administration. Zealand's New Drug Application ("NDA") for their dasiglucagon HypoPal® Rescue Pen for the treatment of hypoglycemia in people with diabetes is under review by the FDA with a PDUFA date of March 27, 2021.

While there are currently no FDA-approved products indicated for treatment of PBH, we are aware of a number of product candidates in development. Eiger Biopharmaceuticals is developing its product candidate avexitide (exendin 9-39), a glucagon-like peptide-1 receptor antagonist, to be administered subcutaneously once or twice daily. Eiger completed a Phase 2 clinical study with avexitide and an end-of-Phase 2 FDA meeting and received guidance from the FDA on Phase 3 clinical requirements. Additionally, Zealand Pharma has announced positive topline results from its Phase 2 trial with dasiglucagon in patients with PBH.

Currently, the first-line emergency treatment of epileptic seizures in the outpatient setting is the administration of diazepam rectal gel marketed as Diastat by Valeant Pharmaceuticals. UCB’s midazolam nasal spray Nayzilam, indicated for seizure clusters and ARS, launched in December 2019, and Neurelis, Inc. received approval in January 2020 for their nasal diazepam product, VALTOCO™ (previously known as NRL-1), for the treatment of seizure clusters and ARS. VALTOCO became commercially available in March 2020. The FDA issued a Complete Response Letter for Aquestive’s NDA for buccal soluble diazepam Libervant™ (previously known as AQST-203), also for the treatment of seizure clusters and ARS. Aquestive has reported that they will continue to have follow-up meetings with the FDA to discuss a path to approval. In June 2020, UCB Inc. acquired the worldwide rights to Staccato® Alprazolam from Engage Therapeutics, who was developing an inhaled alprazolam (known as STAP-001) for ARS. UCB Inc. will continue the development of this product, which is currently in Phase 2 development.

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

As of December 31, 2020, we owned 117 issued patents globally, of which 14 are issued U.S. patents. As of December 31, 2020, three of our U.S. issued patents have pending continuations or divisionals in process which may provide additional intellectual property protection if issued as U.S. patents. Our issued patents expire between December 22, 2023 and April 22, 2036, subject to payment of required maintenance fees, annuities and other charges. The subset of our patent estate directed specifically to our ready-to-use glucagon consists of one U.S. composition of matter patent that is scheduled to expire in year 2036, two pending U.S. patent applications and 18 pending international patent applications. Patents that issue based on these applications would also expire in year 2036.

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 U.S. registered trademarks for the marks Xeris Pharmaceuticals, GVOKE, GVOKE HYPOPEN and HYPOPEN, and the registered trademark for OGLUO in the EU. We also own pending trademark applications for XERISOL, XERIJECT and GVOKE HYPOPEN 2-PACK in the U.S.; for XERISOL and XERIJECT in the EU; and pending trademark applications and/or registered trademarks for GVOKE and GVOKE HYPOPEN in other 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.

Grant Agreements

Through December 31, 2020, we have received $1.9 million in grant proceeds for the development of a stable liquid glucagon for use in an artificial pancreas. Under the terms of one of the grant agreements, we will be required to pay up to four times the $0.9 million award received upon commercialization of glucagon for use in the artificial pancreas. If we undergo a change in control, then we will be required to pay a mid-single digit percentage of the gross proceeds, capped at four times the award amount less any amounts already paid. Additionally, if sales of glucagon for use in the artificial pancreas exceed $750 million in the first five years after the first commercial sale, then we would be required to make an additional payment equal to the original award amount.

Through December 31, 2020, we received $2.0 million in grant proceeds to help fund our EIH program. Under terms of one of the agreements, we will be required to pay up to two times the $0.9 million award amount upon the commercialization of an EIH product. These amounts are a low double-digit percentage of annual gross sales of an EIH product, capped at $0.5 million annually. If we undergo a change in control, then we will pay a mid-single digit percentage of the consideration capped at two times the award amount less any amounts already paid. Additionally, if sales exceed $1 billion, we will be required to pay an additional amount equal to two times the award amount.

Through December 31, 2020, we received $1.0 million in grant proceeds to help fund our T1D chronic glucagon programs. Under terms of this agreement, we will be required to pay up to two times the award amount upon the commercialization of any chronic glucagon program. These amounts are a low double-digit percentage of annual gross sales of all T1D chronic glucagon programs, capped at $0.5 million annually. If we undergo a change in control, then we will pay a mid-single digit percentage of the consideration capped at two times the award amount less any amounts already paid. Additionally, for each chronic glucagon program where sales exceed $500 million, we will be required to pay an additional amount equal to two times the award amount.

We also have received awards from the NIH National Institute of Diabetes and Kidney Diseases, which awards are not subject to any repayment obligations.

Long-Term Debt

In June 2020, the Company completed a public offering of $86.3 million aggregate principal amount of the Company'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. A total principal amount of $39.1 million of Convertible Notes converted into equity in the second half of 2020. As of December 31, 2020, the outstanding balance of Convertible Notes was $47.2 million.
In addition, as of December 31, 2020, we have $43.5 million outstanding under our Amended and Restated Loan and Security Agreement with Oxford Finance LLC, as the collateral agent and a lender, and Silicon Valley Bank, as a lender.

See “Management’s Discussion and Analysis of Financial Condition and Results of Operations - Liquidity and Capital Resources” for additional details.

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.

Our products and certain of our product candidates are subject to regulation as combination products, which means that they are composed of both a drug product and device product. If 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 has primary jurisdiction over the premarket development, review and approval. 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, 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 good clinical practices ("GCPs"), 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 current good manufacturing practice requirements ("cGMP");
- potential FDA audit of the clinical trial sites 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.

FDA Review Process

The results of product development, preclinical studies 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, the submission of most NDAs or BLAs are subject to an application user fee, which for federal fiscal year 2021 is $2,875,842 for an NDA or BLA requiring clinical data. The sponsor of an approved NDA or BLA

is also subject to an annual program fee, which for fiscal year 2021 is $336,432 for each product presentation. 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.

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 will 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 two full clinical studies which 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 alternate 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, 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 the prescription drug user fee amendments ("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, 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.

European Orphan Designation and Exclusivity

In the EU, the EMA's Committee for Orphan Medicinal Products ("COMP") grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions that affect not more than five in 10,000 persons in the EU Community, or when, without incentives, it is unlikely that sales of such products in the EU would be sufficient to justify the necessary investment in developing the products. Additionally, orphan drug designation is only available where no satisfactory method of diagnosis, prevention, or treatment of the condition has been authorized (or the product would be a significant benefit to those affected).

In the EU, orphan drug 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. 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 drug that is shown to be safer, more effective or otherwise clinically superior.

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 both the federal government and the states in which we conduct our business. 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 any remuneration (including any kickback, bribe or certain rebate), directly or indirectly, overtly or covertly, 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 programs. This law applies to our marketing practices, educational programs, pricing policies and relationships with healthcare providers, by prohibiting, among other things, soliciting, receiving, offering or providing remuneration intended to induce the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare or Medicaid programs. On December 2, 2020, the Office of Inspector General ("OIG") published further modifications to the federal Anti-Kickback Statute in the Federal Register. Under the final rule, the OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. On the same day, CMS published a final rule that provides a safe harbor for value-based compensation agreements under the Stark Law. However, the U.S. Government Accountability Office ("GAO") found that these final rules did not meet the sixty-day delay required under the Congressional Review Act. Additionally, on January 20, 2021, the Biden Administration issued a moratorium on all Trump-era rules that have not yet taken effect. The interplay between the GAO's findings and the Biden Administration's moratorium, which will determine whether these two rules are in effect, is unclear;
- federal civil and criminal false claims laws and civil monetary penalties laws, such as the federal False Claims Act ("FCA"), which impose criminal and civil penalties and authorize civil whistleblower or qui tam actions, against individuals or entities (including manufacturers) for, among other things: knowingly presenting, or causing to be presented, to a federal government healthcare program, 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 payment of 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. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Companies that submit claims directly to payors may also 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. Our marketing and activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products and any future product candidates are subject to scrutiny under this law;
- the anti-inducement law, which 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 provider, practitioner or supplier of items or services reimbursable by a federal or state healthcare program;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), and its implementing regulations, which prohibit 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 statements 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;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses (“covered entities”) as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information, including mandatory contractual terms and required implementation of technical safeguards of such 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 pursing federal civil actions;
- 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 Affordable Care Act, including the Physician Payments Sunshine Act, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program to report annually to the HHS, information related to payments or other “transfers of value” made or distributed to certain healthcare professionals and teaching hospitals, as well as ownership and investment interests held by the healthcare professionals described above 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 additional healthcare professionals;
- 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.

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 Affordable Care Act ("ACA") was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced 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; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs; imposed a new federal excise tax on the sale of certain medical devices; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and established the Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

Since its enactment, some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial, administrative, executive, and legislative challenges. We expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court. The Trump Administration issued various Executive Orders that eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices.

Additionally, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 ("Tax Act") includes a provision that decreased the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, commonly referred to as the "individual mandate," to $0, effective January 1, 2019. On December 14, 2018, a federal district court in Texas ruled the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional, and remanded the case to the lower court to reconsider its earlier invalidation of the full ACA. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case, and held oral arguments on November 10, 2020. Pending a decision, the ACA remains in effect, but it is unclear at this time what effect these developments will have on the status of the ACA.

Former President Trump signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. On January 20, 2017, he signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, he signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. 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. 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 were owed to them. This decision was appealed to the U.S. Supreme Court, which on April 27, 2020, 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. To date, at least $6 billion has been paid out to health plans and insurers, and follow-up class action and other litigation is pending. The viability of the ACA marketplace and subsequent impacts on providers, and potentially our business, are not yet known. It is unclear what impact these rulings may have on our business.

The Bipartisan Budget Act of 2018 also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D from 50% to 70%, effective January 1, 2019, and closing the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.” On December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865). This law repeals the so called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. It is impossible to determine whether similar taxes could be instated in the future. Additionally, CMS published a final rule that gives states greater flexibility, starting in 2020, 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.

In addition, the Budget Control Act of 2011 and the Bipartisan Budget Act of 2015 led to aggregate reductions of Medicare payments to providers of up to 2% per fiscal year that will remain in effect through 2030 unless additional Congressional action is taken. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, and subsequent legislation, these reductions will be suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. As the legislation currently stands, the reductions will go back into effect April 2021 and will remain in effect through 2030; however, proposed legislation, if passed, would extend this suspension until the end of the pandemic. Further, on January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. Individual states in the United States also have become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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. The previous administration’s budget proposal for fiscal year 2021 included a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the previous administration sent “principles” for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Further, the previous administration released a “Blueprint” to lower drug prices and reduce out-of-pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out-of-pocket costs of drug products paid by consumers. However, it is unclear whether the Biden Administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions after January 20, 2021.

HHS already has started the process of soliciting feedback on some measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS’s policy change that was effective January 1, 2019. On July 24, 2020 and September 13, 2020, former President Trump announced several executive orders related to prescription drug pricing that seek to implement several of his administration's proposals. The FDA also released a final rule on September 24, 2020, which went into effect on November 30, 2020, creating a process for states to build and submit to the FDA importation plans for drugs from Canada. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation ("MFN") Model under which Medicare Part B reimbursement rates will 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. The MFN Model regulations mandate participation by identified Part B providers and was intended to apply in all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. However, on December 28, 2020, a judge in the U.S. District Court for the Northern District of California granted a preliminary injunction prohibiting CMS from implementing the MFN Model.

On December 2, 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. Implementation of the amendments to the discount safe harbor has been delayed to January 1, 2023 pending litigation. 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, Congress has indicated that it 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.

Moreover, 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 I 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 drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act or FDA’s expanded access program authorities, but the manufacturer must develop and make publicly available its policy on expanded access availability and respond to patient requests according to that policy.

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 Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national drug rebate agreement with the Secretary of HHS as a condition for state Medicaid coverage of the manufacturer's outpatient drugs furnished to Medicaid patients. Effective in 2010, 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 from 15.1% of average manufacturer price ("AMP") to 23.1% of AMP, 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. In addition, the ACA also modified the statutory definition of AMP which created a new calculation methodology by which rebates owed by manufacturers are determined for drugs that are inhaled, infused, instilled, implanted or injected and thereby potentially impacting manufacturers' rebate liability. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010 and by expanding the population potentially eligible for Medicaid drug benefits. Pricing and rebate programs also must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990.

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.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the Medicaid unit rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children's hospitals) will not be eligible to receive discounted 340B pricing on a drug designated by the Secretary under section 526 of the Federal Food, Drug, and Cosmetic Act for a rare disease or condition. As 340B drug pricing is determined based on Medicaid rebate data, the revisions to the Medicaid rebate formula described above could cause the required 340B discount to increase.

However, on December 27, 2018, the District Court for the District of Columbia invalidated a recent Medicare reimbursement formula change instituted by CMS when 340B hospitals purchase drugs under the 340B program for use in the hospital outpatient setting. For the 2019 and 2018 fiscal years, CMS altered the reimbursement formula from Average Sale Price ("ASP") plus 6% to ASP minus 22.5% on specific-covered outpatient drugs. 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, and such a dramatic change was beyond the scope of the Secretary's authority. On May 6, 2019, the district court reiterated that the rate reduction exceeded the Secretary's authority and declared that the rate reduction for 2019 also exceeded the Secretary's authority and remanded the issue to HHS to devise an appropriate remedy. On July 10, 2019, the district court entered its final judgment and CMS filed an appeal. 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); the court denied this Petition on October 16, 2020. It is unclear how the invalidation of the formula could affect pharmaceutical manufacturers and hospitals who prescribe their products, but litigation is still pending on the issue. 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. On November 20, 2020, the HHS

Office of Inspector General finalized its 2019 proposal to exclude certain rebates paid by drug manufacturers from the discount safe harbor of the federal anti-kickback statute. The final rule is entitled “Fraud and Abuse; Removal of Safe Harbor Protection for Rebates Involving Prescription Pharmaceuticals and Creation of New Safe Harbor Protection for Certain Point-of-Sale Reductions in Price on Prescription Pharmaceuticals and Certain Pharmacy Benefit Manager Service Fees”. Under the final rule, discount safe harbor protection for Part D rebates is eliminated. The rule establishes a new safe harbor for point-of-sale price reductions and establishes a new safe harbor for pharmacy benefit manager service fees.

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.

Further, there have been several recent U.S. congressional inquiries, proposed federal legislation, and proposed and enacted state legislation designed to, among other things, bring more transparency to 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. At the federal level, Congress and the Executive Office of the President of the United States have each indicated that it will continue to pursue new legislative and/or administrative measures to control drug costs. Individual state legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing. Some of these measures include price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products or product candidates, once approved, or put pressure on our product pricing. For example, on October 1, 2020, the FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, States and Native American Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. Since the issuance of the final rule, several industry groups have filed federal lawsuits challenging multiple aspects of the final rule, and authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. 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. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code ("NDC") for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. Since the issuance of the final rule, on November 23, 2020, several industry groups filed federal lawsuits in the U.S. District Court for the District of Columbia, requesting injunctive relief to prevent certification from the Secretary of HHS from taking effect and challenging multiple aspects of the final rule. This litigation has not progressed. The market implications of the final rule and guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted and implemented, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

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 Management

As of December 31, 2020, we had 180 full-time employees in the United States, 76 of whom were primarily engaged in sales and marketing, 70 of whom were primarily engaged in administration and finance, and 34 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 scientific, technical, and managerial personnel, as we expand the commercialization of Gvoke and continue development of our product candidates. Our President and Chief Operating Officer and Executive Director, 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 and the design of employee compensation and benefits programs. In addition, the Chief Executive Officer and President and Chief Operating Officer regularly update our board of directors and its committees on the operation and status of these human capital trends and activities.

Employee health and safety in the workplace is one of our core values. The COVID-19 pandemic has underscored for us the importance of keeping our employees safe and healthy. 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 addition to the other information set forth in this Annual Report for the year ended December 31, 2020 and in other documents that we file with the SEC, 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 Coronavirus

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, has evolved into a global pandemic. The coronavirus has spread to most regions of the world.

As a result of the coronavirus 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 our product, Gvoke, 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 are engaging with these customers remotely, via webinar programs and virtual meetings, as we seek 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 resurgence of COVID-19 in many areas, our ability to connect with our customers in person became much more limited and we are currently back to almost exclusively remote interactions. In addition, several conferences and other programs at which we intended to market Gvoke have been postponed, canceled and/or transitioned to virtual meetings. Remote interactions may be less effective than in-person interactions. 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 for the manufacture of Gvoke as well as to perform third-party logistics functions, including warehousing and distribution of Gvoke. 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, including staffing shortages, production slowdowns and disruptions in delivery systems, our supply chain may be disrupted, limiting our ability to manufacture commercial quantities of Gvoke.
- 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 reopened our offices in mid-June on a limited, voluntary basis for those personnel who prefer to work from the office. 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 cyber-security 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. In addition, we have implemented certain measures to reduce spending and have delayed or suspended projects. Although we have implemented such cost reducing measures, we may not realize, in full or in part, the anticipated benefits, savings and improvements in our cost structure from such measures due to unforeseen difficulties, delays or unexpected costs. If we are unable to realize the expected cost savings from such measures, our operating results and financial condition would be adversely affected.
- 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.

- We have previously and may in the future conduct clinical trials for product candidates in geographies which are affected by the coronavirus pandemic. Potential impacts of the coronavirus pandemic on our various clinical trials may include disruptions or delays in patient enrollment, standard study monitoring practices, sample shipments, data analysis and reporting of results due to changes in policies at various clinical sites or in federal, state, local or foreign laws, rules and regulations. Other impacts could include quarantines or other travel restrictions and prioritization of healthcare resources toward pandemic efforts, including diminished attention of physicians serving as our clinical trial investigators and reduced availability of site staff supporting the conduct of our clinical trials. Interruption or delays in the operations of the FDA could also impair our ability to discuss ongoing or future clinical programs. If the coronavirus pandemic continues, other aspects of our clinical trials could be adversely affected, delayed or interrupted, including, for example, site initiation, patient recruitment and enrollment, and availability of clinical trial materials. It is unknown how long these pauses or disruptions could continue.
- 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 de-prioritization 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.

To date, three vaccines for COVID-19 were granted Emergency Use Authorization by the FDA. 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 ultimate geographic spread of the disease, 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 several 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 issuance of debt. We commercially launched Gvoke PFS in November 2019 and Gvoke HypoPen in July 2020. We are in the early stages of commercializing our first pharmaceutical product and have a limited operating history. Pharmaceutical 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 pharmaceutical 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 pharmaceutical 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 complete the transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition. 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 years ended December 31, 2020 and 2019, we reported a net loss of $91.1 million and $125.6 million, respectively. In addition, our accumulated deficit as of December 31, 2020 was $337.4 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 and more recently the commercial launch of Gvoke.

We expect to continue to incur significant operating expenses as we continue the commercialization of Gvoke, develop, enhance and commercialize new products 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 commercial strategy in the U.S. and our Ogluo commercial strategy outside the U.S.;
- continue our research and development efforts;
- seek regulatory approval for new product candidates and product enhancements; and
- continue to operate as a public company.

Our first product, 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. On February 11, 2021 the European Commission ("EC") granted a marketing authorization for Ogluo for the treatment of severe hypoglycemia in adults, adolescents, and children aged two years and over with diabetes mellitus. We currently plan to commercially launch Ogluo in select European countries beginning in the fourth quarter of 2021. Our ability to generate revenue from Gvoke, Ogluo and our product candidates and to transition to profitability and generate positive cash flows is uncertain and depends on the successful commercialization of Gvoke and our product candidates. 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 PFS and Gvoke HypoPen, 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 depends on a number of factors, including, but not limited to, our ability to:

- obtain commercial quantities of Gvoke 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. Regardless of these expenditures, Gvoke and our product candidates, if approved, may not be commercially successful. Although we generate revenue from Gvoke PFS and Gvoke HypoPen, 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.

Pharmaceutical 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 and expect to continue to incur such expenses for Gvoke as well as for any of our product candidates, if approved. Accordingly, we may need to obtain substantial additional funding in connection with our continuing operations. For example, due to the impacts of the COVID-19 pandemic on our business, including those discussed in the risk factor titled "Our business may be adversely affected by the ongoing coronavirus pandemic," we applied for and received a PPP Loan on April 22, 2020 for $5.1 million, of which $0.9 million was repaid on May 4, 2020 and the remaining $4.2 million on June 30, 2020. While we initiated a variety of cost reduction initiatives, we sought and obtained the PPP Loan due to our belief that such funds were necessary to support payroll costs, rent and utilities in order to avoid more drastic measures, such as deep workforce reductions, that would have likely significantly impaired our financial viability. 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. We will be required to expend significant funds in order to commercialize Gvoke as well as any of our product candidates that receive marketing approval.

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 the Amended and Restated Loan and Security Agreement dated June 30, 2020, that certain Third Amendment to the Amended and Restated Loan and Security Agreement dated August 5, 2020 and that certain the Fourth Amendment to the Amended and Restated Loan and Security Agreement dated October 23, 2020, collectively, the "Amended Loan Agreement") with Oxford Finance LLC, as the collateral agent and a lender, and Silicon Valley Bank, as a lender, and the Company, 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 Gvoke 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. Adequate additional financing may not be available to us on acceptable terms, or at all. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. 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.

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, 2020, 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 (the “Base Indenture”), as supplemented by the first supplemental indenture thereto (the “Supplemental Indenture” and together with the Base Indenture, the “Indenture”), each dated as of June 30, 2020, 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 while still pursuing our current business strategy.

In addition, we have $43.5 million outstanding under our Amended Loan Agreement as of December 31, 2020. 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 the company’s business, including its prospect of repayment of its 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 while still pursuing our current business strategy. In addition, our lenders could seek to enforce their security interests in any collateral securing such indebtedness.

We may be unable to raise the funds necessary to repurchase the Convertible Notes for cash following a fundamental change, and our existing and future indebtedness may limit our ability to repurchase the Convertible Notes.

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 future indebtedness, which may result in that other indebtedness becoming immediately payable in full. A fundamental change 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.

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") Paycheck Protection Program (the "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 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 first product, Gvoke, in the United States. Our business and future success are substantially dependent on our ability to generate product revenues in the near term and will depend on our ability to successfully commercialize Gvoke. Our product candidates are in earlier 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. We may not be able to successfully launch or commercialize our products or meet our expectations with respect to revenues. We began to commercially launch our first pharmaceutical product, Gvoke PFS, in November 2019, and commercially launched Gvoke HypoPen in July 2020. There is no guarantee that the infrastructure, systems, processes, policies, relationships and materials we have built for the commercialization of Gvoke 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.

Even if all regulatory approvals are obtained, the commercial success of our products and product candidates, if approved, depends 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 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;
- we may be subject to litigation or product 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.

The market opportunity for Gvoke and our product candidates may be smaller than we estimate.

The potential market opportunity for Gvoke and our product candidates is difficult to precisely estimate. Our estimates of the potential market opportunity for Gvoke 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. Industry publications and third-party research generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. For example, our projections for the potential size of the market for Gvoke are based on our belief that we would be able to increase the adoption of emergency glucagon products by patients and care providers. 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. If the actual market for Gvoke and our product candidates is smaller than we expect, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

Our company has limited experience marketing and selling drug products and has recently developed our sales organization. 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 recently developed our commercial infrastructure for the sales, marketing and distribution of Gvoke. In order to successfully commercialize Gvoke and 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 recently established a sales force to market Gvoke 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, 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 could delay or limit the success of any product launch, which would adversely impact the commercialization of our products, including Gvoke.

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.

Factors that may inhibit our efforts to commercialize our products include:

- our inability to recruit, train and retain adequate numbers of sales and marketing personnel;
- the inability of sales personnel to obtain access to or to persuade adequate numbers of physicians to prescribe any of our product candidates that receive regulatory approval; and
- unforeseen costs and expenses associated with maintaining an independent sales and marketing organization.

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' Action on Market Acceptance

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

We do not currently own or operate manufacturing facilities for the production of Gvoke or our product candidates. We rely on third-party suppliers to manufacture and supply our products. 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. 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, including Gvoke, 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 ability to procure sufficient supplies for the manufacture of Gvoke or development of our product candidates will depend on the severity and duration of the spread of the virus and the actions undertaken to contain COVID-19 or treat its effects.

For us to be successful, our third-party suppliers must be able to provide us with raw materials, components and products in substantial quantities, in compliance with regulatory requirements, in accordance with agreed upon specifications, at acceptable costs and on a timely basis. Reliance on third-party suppliers entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility that products will not be delivered on a timely basis, the possibility of increases in pricing for our products, and the possibility of breach or termination of a manufacturing agreement or purchase order by the third party.

Gvoke and some of our product candidates are drug-device combination products that are regulated under the drug regulations of 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 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 foreign regulatory authorities do not approve these facilities for the manufacture of Gvoke and if the FDA or such foreign regulatory authorities do not approve these facilities for the manufacture of our 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. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or may not be able to maintain compliance with the applicable cGMP and QSR requirements. Any failure to comply with cGMP or QSR requirements or other FDA, EMA and comparable foreign regulatory requirements could adversely affect our research and development activities and our ability to develop our product candidates and market our products and any future products following approval.

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; and
- 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.

If any of the above risks materialize and we are unable to satisfy commercial demand for our products in a timely manner, our ability to generate revenue would be impaired, market acceptance of our products could be adversely affected, and customers may instead purchase or use our competitors' products. 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 CMO 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. We are also unable to predict how changing global economic conditions or global health concerns such as the COVID-19 pandemic will affect our third-party suppliers and manufacturers. 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. On March 27, 2020, former

President Trump signed into law the CARES Act in response to the U.S. COVID-19 pandemic. Throughout the COVID-19 outbreak, there has been public concern over the availability and accessibility of critical medical products, and the CARES Act enhances FDA's existing authority with respect to drug shortage measures. 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.

We may in the future elect to manufacture certain new or existing products ourselves, without the assistance of third-party suppliers. However, in order to make that election, we will need to invest substantial additional funds and recruit qualified personnel in order to operate our own manufacturing facility on a commercial basis. There can be no assurance that we will be able to successfully manufacture our own products, and if we are not able to make or obtain adequate supplies of our raw materials, components or products, it will be more difficult for us to launch new products, supply our current markets and compete effectively.

Reimbursement decisions by third-party payors 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.

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 to the 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 them 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. 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. On December 27, 2018, the District Court for the District of Columbia invalidated a reimbursement formula change under the 340B program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain healthcare facilities. CMS altered the reimbursement formula for fiscal years 2018 and 2019, but the court ruled this change was not an "adjustment" that was within the Secretary's discretion to make. On May 6, 2019, the district court reiterated that the rate reduction exceeded the Secretary's authority and declared that the rate reduction for 2019 also exceeded the Secretary's authority and remanded the issue to the U.S. Department of Health and Human Services ("HHS") to devise an appropriate remedy. On July 10, 2019, the district court entered its final judgment and CMS filed an appeal. On July 31, 2020, the United States Court of Appeals for the District of Columbia Circuit ruled that CMS and HHS did not exceed their authority when it instituted the new reimbursement formula and reversed the judgment of the district court. On September 14, 2020, the plaintiffs-appellees filed a Petition for Rehearing En Banc (i.e., before the full court), and the court denied this Petition on October 16, 2020. It is unclear how this could affect covered hospitals who might purchase our products in the future and affect the rates we may charge such facilities for our approved products.

Market acceptance and sales of our products and product candidates that we develop, if approved, will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and establish payment levels. In the United States, no uniform policy of coverage and reimbursement for drugs exists among third-party payors. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, obtaining coverage and reimbursement approval of a drug from a government or other third-party payor is a time consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our drugs on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. We cannot be certain that reimbursement will be available for any of our product candidates or that reimbursement rates will not change for our current products. Also, we cannot be certain that reimbursement policies will not reduce the demand for, or the price paid for, our products. If reimbursement is not available or is available on a limited basis, we may not be able to successfully commercialize any of our products or product candidates. Further, due to the COVID-19 pandemic, millions of individuals have lost or will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize Gvoke or our product candidates even if there is adequate coverage and reimbursement from third-party payors.

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. Furthermore, third-party payors are increasingly requiring that companies provide them with predetermined discounts from list prices

and are challenging the prices charged for medical products. 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.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the ACA became law in the United States and is significantly impacting the provision of, and payment for, healthcare. With regard to pharmaceutical products specifically, the ACA, among other things, expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare prescription drug benefit. Among other things, the 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. On July 24, 2020 and September 13, 2020, former President Trump signed a series of Executive Orders aimed at lowering drug prices and at implementing several of the administration's proposals. In response, the FDA released a final rule on September 24, 2020, which went into effect on November 30, 2020, creating a process providing guidance for states to build and submit to the FDA importation plans for drugs from Canada, as further discussed below. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation ("MFN") Model under which Medicare Part B reimbursement rates will 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. The MFN Model regulations mandate participation by identified Part B providers and was intended to apply in all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. However, on December 28, 2020, a judge in the U.S. District Court for the Northern District of California granted a preliminary injunction prohibiting CMS from implementing the MFN Model. The Interim Final Rule has not been finalized and is subject to revision and challenge. On December 2, 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. Implementation of the amendments to the discount safe harbor has been delayed to January 1, 2023 pending litigation. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, and the Biden Administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. On October 1, 2020, the FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, states and Indian tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. 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. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code ("NDC") for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. Since the issuance of the final rule, on November 23, 2020, several industry groups filed federal lawsuits in the U.S. District Court for the District of Columbia, requesting injunctive relief to prevent certification from the Secretary of HHS from taking effect and challenging multiple aspects of the final rule. This litigation has not progressed. The regulatory and market implications of the Executive Orders, the final rules and final guidance, and any future actions by the Biden Administration are unknown at this time, but legislation, regulations or policies allowing the reimportation of drugs, if enacted and implemented, could decrease the price we receive for any products that we may develop and commercialize and could adversely affect our future revenues and prospects for profitability.

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.

Pricing pressure from healthcare industry consolidation and our competitors may impact our ability to sell our products at prices necessary to support our current business strategies.

Our market is subject to competitive pricing pressure as a result of product competition and a trend of consolidation in the healthcare industry to aggregate purchasing power as healthcare costs increase and reforms initiated by legislators, regulators and third-party payors to curb these costs are implemented.

For example, Eli Lilly's GEK has approximately 85% coverage, with unrestricted access across commercial, Medicare, Managed Medicaid and state Medicaid plans. 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. However, 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.

The success of Gvoke will be dependent on its proper use by patients, healthcare practitioners and caregivers.

While we have designed Gvoke 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 Gvoke was 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 Gvoke by patients, healthcare practitioners and caregivers, we may not be able to achieve market acceptance or effectively commercialize Gvoke. In addition, even in the event of proper use of Gvoke, 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.

Guidelines and recommendations can reduce the use of our products.

Government agencies and industry associations such as the American Diabetes Association promulgate guidelines applicable to certain drug classes which may include our products and product candidates that we are developing. Recommendations from these organizations may relate to such matters as usage, dosage, route of administration and use of concomitant therapies. Regulations or guidelines affecting our products and product candidates that we are developing or the use of competitive or alternative products as the standard of care to be followed by patients and healthcare providers could result in decreased use of our products or negatively impact our ability to gain market acceptance and market share.

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. 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.

If our third-party manufacturers of Gvoke or our product candidates are unable to increase the scale of their production of our products or our product candidates, or increase the product yield of manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed or interrupted.

In order to produce sufficient quantities to meet the demand for the commercialization of Gvoke, and the clinical trials and subsequent commercialization of any of our product candidates in our pipeline or that we may develop, our third-party manufacturers will be required to increase their production and automate and otherwise optimize their manufacturing processes while maintaining the quality of the product. The transition to larger scale production could prove difficult. In addition, if our third-party manufacturers are not able to automate and otherwise optimize their manufacturing process to increase the product yield for Gvoke and other components of Gvoke or our product candidates, or if they are unable to produce increased amounts of Gvoke or our product candidates while maintaining quality, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate revenues and have a material adverse impact on our business and results of operations. Any delay in our third-party manufacturers' ability to produce any of our products could have a material adverse effect on our launch plans, our business, our results of operations and financial condition.

We expect to seek to establish collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

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. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of a number of factors. Those factors may include the potential differentiation of our product or product candidate from competing products or product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product or product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative products or product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product or product candidate. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product or product candidates or bring them to market and generate product revenue.

Collaborations are complex and time consuming to negotiate and document. Further, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Any collaboration agreements that we enter into in the future may contain restrictions on our ability to enter into potential collaborations or to otherwise develop specified product candidates. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

We may be adversely affected by any disruptions to third-party suppliers that manufacture and supply our products.

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, or any other cause could materially impair our ability to manufacture our products and to distribute our products to customers. We could incur significantly higher costs and longer lead times associated with distributing our products to our customers. If we are unable to arrange for third-party suppliers of our materials and products, or to do so on commercially reasonable terms, we may not be able to market our products or product candidates that may be approved in the future. Additionally, our business could be temporarily adversely affected by higher costs for materials, increased shipping and storage costs, increased labor costs, and scheduling issues. Any interruption in the production or delivery of our supplies could reduce sales of our products and increase our costs.

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.

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 new 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 and might require that our XeriSol pramlintide-insulin co-formulation be approved under the PHS Act rather than in a 505(b)(2) NDA. If our product candidates do not meet the requirements of Section 505(b)(2) or are otherwise 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.

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.

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.

Delays in conducting clinical trials could result in increased costs to us and delay our ability to obtain regulatory approval for our product candidates.

Any delays in conducting clinical trials and related drug development programs could materially affect our product development costs and delay regulatory approval of our product candidates. We do not know whether planned clinical trials will begin on time, will need to be redesigned, or will be completed on schedule, if at all. A clinical trial can be delayed for a variety of reasons, including:

- delays or failures in obtaining regulatory authorization to commence a trial because of safety concerns of regulators relating to our product candidates or similar product candidates, competitive or comparator products or supportive care products or failure to follow regulatory guidelines;
- delays or failures in obtaining clinical materials and manufacturing sufficient quantities of the product candidate for use in a trial;
- delays or failures in reaching agreement on acceptable terms with CROs and prospective study sites;
- delays or failures in obtaining approval of our clinical trial protocol from an institutional review board ("IRB") to conduct a clinical trial at a prospective study site;
- receipt by a competitor of marketing approval for a product targeting an indication that our product candidate targets, such that we are not “first to market” with our product candidate;
- delays in recruiting or enrolling subjects to participate in a clinical trial, particularly with respect to our product candidates for certain rare indications, including those for which we have obtained, or plan to seek, orphan drug designation;
- failure of a clinical trial or clinical investigators to be in compliance with current Good Clinical Practices ("cGCPs");
- unforeseen safety issues;
- inability to monitor subjects adequately during or after treatment;
- difficulty monitoring multiple study sites;
- the FDA requiring alterations to any of our study designs, our nonclinical strategy or our manufacturing plans;
- failure of our third-party clinical trial managers to satisfy their contractual duties, comply with regulations, or meet expected deadlines;
- determination by regulators that the clinical design of a trial is not adequate; and
- disruptions caused by global health concerns, such as the COVID-19 pandemic.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRBs at the sites where the IRBs are overseeing a trial, a data safety monitoring board overseeing the clinical trial at issue, or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities;
- unforeseen safety issues, including serious adverse events associated with a product candidate, or lack of effectiveness; and
- lack of adequate funding to continue the clinical trial.

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.

Gvoke 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. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. 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 product liability claims. 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 or Gvoke:

- 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 product 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 our product candidates with respect to certain indications and intend to 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. 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. Two of our products, diazepam and glucagon, have been granted separate orphan drug designations by the FDA. A grant of orphan drug exclusivity related to the approval of the same active moiety and orphan drug indication may prevent us from seeking FDA approval for marketing in the United States during the exclusivity period except in the case where we are able to demonstrate, and the FDA concludes, that our drug is “clinically superior” to the approved products, e.g., safer, more effective, or providing a major contribution to patient care within the meaning of FDA regulations and guidance. 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. 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. 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 our first product, Gvoke, in the United States and the EMA approval of Ogluo in the European Union, we may not be able to obtain or maintain foreign regulatory approvals to market our products in other countries.

We do not have any product candidates other than Gvoke 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. 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.

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.

In March 2010, former President Obama signed into law the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA of importance to our products and product candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- 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;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the federal AKS which include, among other things, new government investigative powers and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% effective January 1, 2019 pursuant to the Bipartisan Budget Act of 2018) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- the requirements under the federal open payments program and its implementing regulations;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial, congressional, and executive challenges. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the ACA. The U.S. Supreme Court has upheld certain key aspects of the legislation, including a tax-based shared responsibility payment imposed on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly known as the requirement that all individuals maintain health insurance coverage or pay a penalty, referred to as the "individual mandate." However, as a result of tax reform legislation passed in December 2017, the individual mandate's penalty was decreased to $0, effective January 1, 2019. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was decreased to $0 as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held the individual mandate is unconstitutional but remanded the case to the lower court to reconsider its earlier invalidation of the full ACA. In March 2020, the U.S. Supreme Court agreed to hear this case, and oral arguments were held on November 10, 2020. Pending review, the ACA remains in effect, but it is unclear at this time what effect the latest ruling will have on the status of the ACA. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise.

On January 20, 2017, former President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, former President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. The Trump administration concluded that cost-sharing reduction ("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 may have on our business.

In addition, CMS finalized regulations that gives states greater flexibility, as of 2020, 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. Additionally, CMS finalized a rule, effective January 1, 2020, that allows Medicare Advantage Plans the option of using step therapy for Part B drugs. This final rule codified CMS's policy change that was effective January 1, 2019. It is unclear what effect such changes will have on our business.

Other legislative changes have been proposed and adopted since the ACA was enacted including aggregate reductions to Medicare payments to providers of 2% per fiscal year through 2030. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, and subsequent legislation, these reductions will be suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. As the legislation currently stands, the reductions will go back into effect April 2021 and will remain in effect through 2030; however, proposed legislation, if passed, would extend this suspension until the end of the pandemic. In January 2013, former President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Since 2016, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing or delaying penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance, delaying the implementation of certain ACA-mandated fees, and increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D.

Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business. We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies, and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

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.

At the federal level, the former Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Additionally, in 2018, the Trump administration released a "Blueprint" to lower drug prices and reduce out-of-pocket costs of drugs that contains additional proposals to increase manufacturer competition and increase the negotiating power of certain federal healthcare programs. Regarding legislation, on September 25, 2019, the Senate Finance Committee introduced a bill, the Prescription Drug Pricing Reduction Action of 2019, which is intended to reduce Medicare and Medicaid prescription drug prices. The proposed legislation would restructure the Part D benefit, modify payment methodologies for certain drugs, and impose an inflation cap on drug price increases. An even more restrictive bill was introduced in the House of Representatives on September 19, 2019, House Resolution 3, the Lower Drug Costs Now Act of 2019, which would require HHS to directly negotiate drug prices with manufacturers. On December 12, 2019, the Lower Drug Costs Now Act of 2019 passed the House. It is unclear whether either of these bills will make it through both chambers and be signed into law, and if either is enacted, what effect it would have on our business. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological 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.

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, 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 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. 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. Our first product, 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 advance 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. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies 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. 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 have submitted a response to the FDA regarding our plan to revise the advertisement at issue and are in discussions with the FDA.

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. These include the following:

- Anti-Kickback Statute. 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 programs. On December 2, 2020, the OIG published further modifications to the federal Anti-Kickback Statute in the Federal Register. Under the final rule, the OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. On the same day, CMS published a final rule that provides a safe harbor for value-based compensation agreements under the Stark Law. However, the GAO found that these final rules did not meet the sixty-day delay required under the Congressional Review Act. Additionally, on January 20, 2021, the Biden Administration issued a moratorium on all Trump-era rules that have not yet taken effect. The interplay between the GAO's findings and the Biden Administration's moratorium, which will determine whether these two rules are in effect, is unclear;

- False Claims Laws. The federal civil and criminal false claims and civil monetary penalties laws, including the federal 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.
- Anti-Inducement Law. 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.
- *HIPAA.* The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by HITECH and their respective implementing regulations, imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program (including private payors) or making false or fraudulent statements relating to healthcare matters. Similar to the federal AKS, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Additionally, HIPAA, as amended by HITECH and its implementing regulations, also imposes obligations on certain covered healthcare providers, health plans, and healthcare clearinghouses ("covered entities") and their business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information, including mandatory contractual terms and technical safeguards, with respect to maintaining 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.
- *Transparency Requirements.* 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 additional healthcare professionals.
- *Analogous State and Foreign Laws*. Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements, and claims involving healthcare items or services reimbursed by non-governmental third-party payors, and are generally broad and are enforced by many different federal and state agencies as well as through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources, and some state laws require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

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, reputational harm and the curtailment or restructuring of our operations. 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.

European data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

We have conducted and may in the future conduct clinical trials in the European Union ("EU") subjecting us to additional privacy restrictions. The collection and use of personal health data in the EU are governed by the provisions of the General Data Protection Regulation ("GDPR"). This regulation imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data.

The GDPR also regulates the transfers of EU and European Economic Area ("EEA") individuals' personal data to other countries that have been deemed by the European Commission not to provide adequate protection to personal data. The U.S. is not deemed to have adequate laws to protect personal data. We had relied upon the EU-U.S. Privacy Shield program to legitimize certain transfers of personal data from the EU and EEA to the U.S. However, on July 16, 2020, the European Court of Justice ("ECJ") invalidated the EU-U.S. Privacy Shield program that we (along with thousands of other companies) have utilized to transfer data from the EU and EEA to the U.S. in compliance with GDPR. As a result of this decision, companies like us that previously relied upon Privacy Shield will be required to use another GDPR-approved method to legitimize transfers of personal data to the U.S. and other third countries in compliance with the GDPR. Although in its ruling about the Privacy Shield, the ECJ deemed that the Standard Contractual Clauses ("SCCs") approved by the European Commission for transfers of personal data between EU controllers and non-EU processors are valid, the Court also noted that transfers made pursuant to the SCCs need to be analyzed on a case-by-case basis to ensure EU standards of data protection are met in the jurisdiction where the data importer is based, and there continue to be concerns about whether the SCCs (including SCCs for controller-to-controller transfers) will face additional challenges. Further, EU member state data protection authorities are empowered to evaluate the adequacy of the SCCs adopted by businesses in any specific case and they are required to suspend or ban data transfers to a third country if, in the light of all the circumstances of that transfer, the SCCs are not or cannot be complied with in that country. Until the remaining legal uncertainties regarding how to legally continue these transfers are settled, we will continue to face uncertainty as to whether our efforts to comply with our obligations under European privacy laws will be sufficient. 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. This and other future developments regarding the flow of data across borders could increase the cost and complexity of delivering our products and services in some markets and may lead to governmental enforcement actions, litigation, fines and penalties or adverse publicity, which could have an adverse effect on our reputation and 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.

We will need to obtain FDA approval of any proposed product names, and any failure or delay associated with such approval may adversely impact our business.

Any name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a trademark registration from the U.S. Patent and Trademark Office ("USPTO"). The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. The FDA may object to any product name we submit if it believes the name inappropriately implies medical claims. If the FDA objects to any of our proposed product names, we may be required to adopt an alternative name for our product candidates. If we adopt an alternative name, we would lose the benefit of any existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

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

We are 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 resulting from the use of hazardous materials, 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.

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, we have 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 has submitted a New Drug Application for their dasiglucagon auto-injector HypoPal® which has been accepted by the FDA with a PDUFA target action date of March 27, 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.

If the FDA approves a competitor’s application for a product candidate or drug-device combination product before our application for a similar product candidate or drug-device combination product, and grants such competitor a period of exclusivity, the FDA may take the position that it cannot approve our 505(b)(2) application for a similar product candidate until the exclusivity period expires. Additionally, even if our 505(b)(2) application for a product candidate is approved first, and we receive three-year marketing exclusivity, we may still be subject to competition from other companies with approved products or approved 505(b)(2) NDAs for different conditions of use that would not be restricted by a grant of exclusivity to us.

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. 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.

Recent federal legislation and actions by federal, state and local governments may permit reimportation of drugs from foreign countries into the United States, including foreign countries where the drugs are sold at lower prices than in the United States, which could materially adversely affect our operating results.

We may face competition in the United States for products and development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the Medicare Modernization Act ("MMA") contains provisions that call for the promulgation of regulations that expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. Further, the MMA provides that these changes to U.S. importation laws will not take effect, unless and until the Secretary of the HHS certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. On September 23, 2020, the Secretary of the HHS made such certification to Congress, and on October 1, 2020, FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, States and Indian Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. 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. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code ("NDC") for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The market implications of the final rule and guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

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 our proprietary product candidates and their use. 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.

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 of our 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.

In the future, we may enter into license agreements with 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.

It is difficult and costly to protect our intellectual property and our proprietary technologies, and we may not be able to ensure their protection.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for the use, formulation and structure of our 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.

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.

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.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside the United States in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction.

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.

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

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.

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

A third party 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. Ultimately, we could be prevented from commercializing a product candidate or be forced to cease some aspect of our business operations as a result of claims of patent infringement or violation of other intellectual property rights. Further, 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.

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 will depend in part on not infringing the patents or violating the proprietary rights of third parties. Significant litigation regarding patent rights exists in our industry. Our competitors in both the United States and abroad, many of which have

substantially greater resources and have made substantial investments in competing technologies, may have applied for or obtained or may in the future apply for and obtain patents that will prevent, limit or otherwise interfere with our ability to make and sell our products. 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. In the future, we may receive communications from various industry participants alleging our infringement of their patents, trade secrets, or other intellectual property rights and/or offering licenses to such intellectual property. Any lawsuits resulting from such allegations could subject us to significant liability for damages and invalidate our proprietary rights. 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.

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. In connection with such litigation or claims, we may be required to obtain licenses or make changes to our products or technologies, and if we fail to do so, we may have to withdraw existing products from the market or may be unable to commercialize one or more of our products, all of which could have a material adverse effect on our business, results of operations and financial condition.

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.

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 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).

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.

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. Patent reform legislation in the United States, including the Leahy-Smith America Invents Act ("America Invents Act") signed into law in September 2011, could increase those uncertainties and costs. The America Invents Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefining prior art and providing more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the America Invents Act has reformed the United States patent law in part by changing the U.S. patent system from a "first to invent" system to a "first inventor to file" system. The first inventor to file provision, however, only became effective on March 16, 2013, so it is still not yet clear what, if any, impact the America Invents Act will have on the operations of our business. The America Invents Act and its implementation 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.

Further, the America Invents Act created new procedures to challenge the validity of issued patents in the United States, including post-grant review and inter partes review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents. 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. A petition for inter partes review can be filed immediately following the issuance of a patent if the patent has an effective filing date prior to March 16, 2013. A petition for inter partes review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with an effective filing date of March 16, 2013 or later. 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 invalidated 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 would result in a loss of the challenged patent right to us. 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.

Risks Related to Enforcement of Intellectual Property Rights

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

Filing, prosecuting, enforcing and defending patents on our 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 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.

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.

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 Employee Matters, Managing Growth and Ongoing Operations

Risks Related to Ongoing Operations

If product 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 product liability claims against us. We maintain total product liability insurance coverage of $15.0 million.

Although we maintain product 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 product liability claims, which could materially harm our business, financial condition or results of operations.

Product 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. Product 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.

Fluctuations in insurance cost and availability could adversely affect our profitability or our risk management profile.

We hold a number of insurance policies, including product liability insurance, directors’ and officers’ liability insurance, general liability insurance, property insurance and workers’ compensation insurance and such policies contain customary conditions and

exclusions. If the costs of maintaining adequate insurance coverage increase significantly in the future, our operating results could be materially adversely affected. Likewise, if any of our current insurance coverage should become unavailable to us or become economically impractical, we would be required to operate our business without indemnity from commercial insurance providers. Additionally, even if we maintain insurance coverage for a type of liability, a particular claim may not be covered if it is subject to a coverage exclusion or we do not otherwise meet the conditions for coverage. If we operate our business without insurance, or with inadequate insurance, we could be responsible for paying claims or judgments against us, which could adversely affect our results of operations or financial condition.

Laws and regulations governing international operations may preclude us from developing, manufacturing and selling certain products outside the United States or require us to develop and implement costly compliance programs.

We have conducted some clinical trials in international countries. For any operations outside the United States, we must comply with numerous laws and regulations in each jurisdiction in which we operate. The FCPA prohibits any U.S. individual or business from paying, offering, authorizing payment or offering 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.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. 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.

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. If we expand our presence outside the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

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. Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities while local, national and international conditions warrant. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials which the FDA continues to update. As of June 23, 2020, the FDA noted it was conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. On July 10, 2020, the FDA announced its goal of restarting domestic on-site inspections during the week of July 20, 2020, but such activities will depend on data about the virus' trajectory in a given state and locality and the rules and guidelines that are put in place by state and local governments. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. 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, FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. 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 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, Barry Deutsch, 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, Clinical Development, Regulatory, Quality Assurance and Medical Affairs, and Beth Hecht, our Senior Vice President, General Counsel 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 develop and commercialize our product candidates will be limited.

Our employees, independent contractors, consultants, collaborators and contract research organizations 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 contract research organizations 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.

Risks Related to Managing Growth

We may need to increase the size of our organization, and we may encounter difficulties managing our growth.

As of December 31, 2020, we had 180 employees. As we commercialize Gvoke and development of our product candidates continues to progress, we may need to hire additional employees as required to add depth and specialized expertise to our team. This growth could place a strain on our administrative and operational infrastructure. If the product candidates that we are developing continue to advance in clinical trials, we will need to expand our development, regulatory, manufacturing, quality, compliance, recordkeeping, information technology, training, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to develop additional relationships with various collaborators, CROs, suppliers, manufacturers and other organizations. We may not be able to establish such relationships or may incur significant costs to do so. Our ability to manage our growth will also require us to continue to improve our operational, financial and management controls, reporting systems and procedures, and other compliance programs and processes, which will further increase our operating costs. Failure to manage our growth effectively could cause us to over-invest or under-invest in infrastructure and result in losses or weaknesses in our infrastructure, which could adversely affect us. Additionally, our anticipated growth will increase the demands placed on our suppliers, resulting in an increased need for us to monitor our suppliers carefully for quality assurance, and our business could suffer.

We may be required to maintain high levels of inventory, which could consume a significant amount of our resources and reduce our cash flows.

As a result of the need to maintain substantial levels of inventory due to single third-party sourcing and long lead-times to develop alternate third-party sources, we intend where feasible to carry a high level of inventory for strategic materials and products and are subject to the risk of inventory obsolescence. In the event that a substantial portion of our inventory becomes obsolete, it could have a material adverse effect on our earnings and cash flows due to the resulting costs associated with the inventory impairment charges and costs required to replace such inventory.

We may seek to grow our business through acquisitions of or investments in new or complementary businesses, products or technologies, and the failure to manage any acquisitions or investments, or the failure to integrate them with our existing business, could have a material adverse effect on us.

From time to time we expect to consider opportunities to acquire or make investments in other technologies, products and businesses that may enhance our capabilities, complement our current products or expand the breadth of our markets or customer base. Potential acquisitions and strategic investments involve numerous risks, including:

- problems assimilating the purchased technologies, products or business operations;
- issues establishing and maintaining uniform standards, procedures, controls and policies;
- unanticipated costs associated with acquisitions;
- diversion of management’s attention from our core business;
- adverse effects on existing business relationships with suppliers and customers;
- risks associated with entering new markets in which we have limited or no experience;
- potential loss of key employees of acquired businesses; and
- increased legal and accounting compliance costs.

We have no current commitments with respect to any acquisition or investment, and we have never entered into or completed an acquisition. We do not know if we will be able to identify suitable acquisitions, complete any such acquisitions on favorable terms or at all, successfully integrate any acquired business, product or technology into our business or retain any key personnel, suppliers or distributors. Our ability to grow through acquisitions successfully depends upon our ability to identify, negotiate, complete and integrate suitable target businesses and to obtain any necessary financing. These efforts could be expensive and time consuming and may disrupt our ongoing business and prevent management from focusing on our operations. If we are unable to integrate any acquired businesses, products or technologies effectively, our business, results of operations and financial condition could be materially adversely affected.

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;
- 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 as well as 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.

Risks Related to Future Financial Condition

The conversion of any of the Convertible Notes into shares of 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.

During the second half of 2020, $39.1 million in principal amount of Convertible Notes were converted into 13,171,791 shares of the Company's common stock. As of February 28, 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.

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, 2020, we had federal net operating loss carryforwards of $284.8 million and various state net operating loss carryforwards of $220.6 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, 2020. As of December 31, 2020, we had $8.0 million and $1.7 million of federal and state income tax credits, respectively, to reduce future tax liabilities. If not utilized, these carryforwards will expire at various dates between 2025 and 2038, 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. For example, on March 27, 2020, former President Trump signed into law the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 coronavirus outbreak, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. 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, 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 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. In addition, our amended and restated bylaws further provide that the United States District Court for the Northern District of Illinois will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision"). We have chosen the United States District Court for the Northern District of Illinois as the exclusive forum for Securities Act causes of action because our principal executive offices are located in Chicago, Illinois. Our amended and restated 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.

On December 19, 2018, in Sciabacucchi v. Salzberg, C.A. No. 2017-0931-JTL (Del. Ch.), the Delaware Court of Chancery issued a decision declaring that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are ineffective and invalid under Delaware law. However, that decision was appealed to the Delaware Supreme Court, and on March 18, 2020, the Delaware Supreme Court reversed the Court of Chancery and ruled that such federal forum selection provisions are "facially valid" under Delaware Law. In light of the Delaware Supreme Court's ruling, we intend to enforce our Federal Forum Provision designating the Northern District of Illinois as the exclusive forum for Securities Act claims.

We also 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 or the Northern District of Illinois. 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 Federal Forum Provision may also impose additional litigation costs on stockholders who assert the provision is not enforceable. The Court of Chancery of the State of Delaware or the United States District Court for the Northern District of Illinois 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.

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 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, which could cause significant damage to our reputation, lead to claims against the Company and ultimately harm our business.

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. As a newly public company, the analysts who publish information about our common stock will have had 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 enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically have entered, and in the future may enter, into academic, commercial, service, collaboration, licensing, feasibility, consulting and other agreements that contain indemnification provisions. 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. We may also agree to indemnify our vendors from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party.

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.

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 nonaffiliates 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

The Company has no unresolved written comments regarding its 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. In the fourth quarter of 2020, we relocated our research and development laboratory site from San Diego, California to Chicago. Our research and development laboratory site in Chicago 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

Our common stock has been publicly traded on The Nasdaq Global Select Market under the symbol “XERS” since June 21, 2018. Prior to that time, there was no public market for our common stock.

Holders of Record

On March 5, 2021, there were approximately 47 stockholders of record of our common stock and the closing price of our common stock was $4.84 per share as reported by The Nasdaq Global Select Market. 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, 2020.

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, 2020.

ITEM 6. SELECTED FINANCIAL DATA

Reserved.

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.

We are a specialty pharmaceutical company delivering innovative solutions to simplify the experience of administering important therapies that people rely on every day around the world. With novel technology platforms, XeriSol™ and XeriJect™, that enable ready-to-use, room-temperature stable formulations of injectable and infusible therapies, we are advancing a portfolio of solutions in various therapeutic categories. Our first product, Gvoke®, delivers ready-to-use glucagon via a pre-filled syringe ("Gvoke PFS") or auto-injector ("Gvoke HypoPen®") for the treatment of severe hypoglycemia, a potentially life-threatening condition, in people with diabetes. Gvoke was approved in September 2019 by the U.S. Food & Drug Administration ("FDA") for the treatment of severe hypoglycemia 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, and each is 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 February 11, 2021 the European Commission ("EC") granted a marketing authorization for Ogluo® (glucagon) for the treatment of severe hypoglycemia in adults, adolescents, and children aged two years and over with diabetes mellitus. We currently plan to commercially launch Ogluo in select European countries beginning in the fourth quarter of 2021. We are also continuing to evaluate additional applications of our ready-to-use glucagon formulation to address needs in hypoglycemia and related conditions. In addition, we are applying our technology platforms to other commercially available drugs to enable more convenient and patient-friendly subcutaneous ("SC") and intramuscular ("IM") routes of administration, including the development of products to address unmet needs in both diabetes and epilepsy. We own the rights to our proprietary formulation technology platforms, Gvoke, and our product candidates domestically and internationally, with 117 patents issued globally, including a composition of matter patent covering our ready-to-use glucagon formulation that expires in 2036.

Our formulation technologies have broad applicability across many therapeutic areas. There is increasing interest in our technology platforms by other drug development companies that seek higher drug concentrations and drug combinations in subcutaneous forms. In addition to use of these technologies for development of our own product candidates, we are currently conducting three technology platform collaboration projects with top tier pharmaceutical companies. Additional projects are under discussion with both large pharmaceutical and specialized biotech companies.

Our key priority is continuing the successful commercialization of our first product, Gvoke, for the treatment of severe hypoglycemia, while increasing the adoption and penetration of emergency glucagon therapy, by offering a glucagon product that better meets the needs of patients and caregivers.

We have built a commercial organization, including hiring individuals in commercial operations and sales and marketing, to support the commercialization of Gvoke in the United States. Outside the United States we may commercialize Ogluo with internal resources and/or pursue a commercialization partner in order to broaden the availability of Ogluo to more European countries. We currently contract with third parties for the manufacture, assembly, testing, packaging, storage and distribution of our products.

Since our inception in 2005, we have devoted substantially all of our resources to research and development initiatives, undertaking preclinical studies of our product candidates, conducting clinical trials of our most advanced product candidates, organizing and staffing our company, raising capital and commercializing our first product, Gvoke.

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 $226.0 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 $60.0 million from the Amended and Restated Loan and Security Agreement (as amended, the "Amended Loan Agreement"), of which $20 million was repaid in June 2020. In August 2019, we filed a shelf registration statement on Form S-3 with the U.S. Securities and Exchange Commission ("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, which we refer to as the "Shelf". 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.

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. There currently remains $96.1 million available for future offerings under the Shelf. During the second half of 2020, $39.1 million in principal amount of Convertible Notes were converted into 13,171,791 shares of the Company's common stock. As of December 31, 2020, 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, 2020, the outstanding balance under the Amended Loan Agreement was $43.5 million.

For the years ended December 31, 2020 and 2019, we reported net losses of $91.1 million and $125.6 million, respectively. We have not been profitable since inception, and, as of December 31, 2020, our accumulated deficit was $337.4 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;
- 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 began our field launch of Gvoke in January 2020 and have not yet generated significant product revenue from sales of Gvoke. 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 current novel coronavirus ("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 to date 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 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 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.

We believe that customer demand for Gvoke 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 are engaging with these customers remotely, via webinar programs and virtual meetings, as we seek 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 resurgence of COVID-19 in many areas, our ability to connect with our customers in person became much more limited and we are currently back to almost exclusively remote interactions. Remote interactions generally are not as effective as in-person interactions. In addition, several conferences and other programs at which we intended to market Gvoke have been postponed, canceled and/or transitioned to virtual meetings. We also have 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.

As the COVID-19 pandemic unfolded, we moved quickly to transition our employees to a remote work-from-home environment excluding essential services, such as personnel in our laboratory. For those employees, we 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 $337.4 million at December 31, 2020. Although we believe that our cash, cash equivalents, investments, and expected revenue from sales of Gvoke 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 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. 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. In addition, in order to conserve cash, we implemented measures to reduce spending, we delayed or suspended projects, and we adopted a deferred compensation plan under which a select group of management and our non-employee directors may defer receiving all or a portion of their cash compensation. Our chief executive officer, Paul Edick, deferred approximately 85% of his cash compensation for the majority of 2020 to reduce cash burn, and other members of our executive team and board of directors also deferred a significant portion of their compensation. In addition, in April 2020, we entered into the U.S. Small Business Administration (the “SBA”) Paycheck Protection Program (the “PPP”) Note (the “Note”) with Silicon Valley Bank (the “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”) to retain employees, maintain payroll and make lease and utility payments in accordance with the relevant terms and conditions of the CARES Act. In May 2020, we repaid $0.9 million of the PPP Loan, and in June 2020 we repaid the remaining $4.2 million outstanding under the PPP Loan out of proceeds from our concurrent convertible debt and equity offerings.

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 amounts, 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

Net Sales

Net sales 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 will be required to make adjustments to these allowances in the future. See "Critical Accounting Policies and Use of Estimates and Assumptions" for further information regarding the significant judgments and estimates involved in the determination of net sales.

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 incurred for Gvoke PFS and Gvoke HypoPen 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 continue to 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 our first product, Gvoke, and as we have concluded ongoing clinical programs and not initiated any new studies as we finalize our discussions with the FDA on go-forward development requirements. We expect to continue to incur research and development expenses as we continue to advance our pipeline candidates.

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 both in and outside 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 as a public reporting company.

Other Income (Expense)

Other income (expense) consists primarily of interest expense related to our convertible debt and loan agreements, 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, 2020, we had $284.8 million in federal net operating loss carryforwards, $220.6 million of various state net operating loss carryforwards, $8.0 million in federal research and orphan drug credits that begin to expire in 2025, and $1.7 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, 2020 and 2019 (in thousands):

	Years Ended December 31,		
	2020	2019	$ Change
Net sales	$ 20,155	$ 1,627	$ 18,528
Grant and other income	280	1,095	(815)
Cost of goods sold	9,328	1,603	7,725
Gross profit	11,107	1,119	9,988
Operating expenses:			
Research and development	20,921	60,438	(39,517)
Selling, general and administrative	73,732	63,061	10,671
Total operating expenses	94,653	123,499	(28,846)
Loss from operations	(83,546)	(122,380)	38,834
Other income (expense):			
Interest and other income	2,965	2,813	152
Interest expense	(10,660)	(7,163)	(3,497)
Change in fair value of warrants	(9)	692	(701)
Total other income (expense)	(7,704)	(3,658)	(4,046)
Net loss before benefit from income taxes	(91,250)	(126,038)	34,788
Benefit from income taxes	110	458	(348)
Net loss	$ (91,140)	$ (125,580)	$ 34,440

Net Sales

We commercially launched Gvoke PFS and Gvoke HypoPen for the treatment of severe hypoglycemia in people with diabetes in November 2019 and July 2020, respectively. Total net sales of Gvoke were $20.2 million and $1.6 million for the years ended December 31, 2020 and 2019, respectively. Net sales represent gross product sales less estimated allowances for patient copay assistance programs, prompt payment and other 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 will be required to make adjustments to these allowances in the future.

Grant and Other Income

Grant and other income decreased by $0.8 million for the year ended December 31, 2020 when compared to the year ended December 31, 2019, primarily due to the completion of grant programs in the first quarter of 2020.

Cost of Goods Sold

Cost of goods sold was $9.3 million for the year ended December 31, 2020, which included $2.3 million related to excess and obsolete inventory and under-absorbed overhead costs of $1.5 million. Cost of goods sold was $1.6 million for the year ended December 31, 2019, which included under-absorbed overhead costs of $0.6 million. Manufacturing costs for Gvoke incurred prior to approval and initial commercialization were expensed as incurred as research and development expenses.

Research and Development Expenses

Research and development expenses decreased $39.5 million for the year ended December 31, 2020 when compared to the year ended December 31, 2019. The decrease was primarily driven by expenses incurred in the prior year for the manufacturing of Gvoke prior to commercialization of $14.0 million, decreased expenses associated with our clinical trials of $13.7 million, a reduction of manufacturing batches and supplies needed for preclinical and clinical trials of $10.3 million, and an increase in the allocation of

certain personnel and facilities costs to costs of goods sold of $2.3 million, partially offset by restructuring expenses of $1.0 million in the current year related to the relocation of our laboratory from San Diego to Chicago.

Selling, General and Administrative Expenses

Selling, general and administrative costs increased $10.7 million for the year ended December 31, 2020 when compared to the year ended December 31, 2019. The increase was primarily driven by an increase in compensation and related personnel costs of $12.0 million due to additional headcount to support commercialization efforts of Gvoke and increased FDA registration fees of $1.0 million, partially offset by decreases in marketing and selling expenses of $3.9 million due to the costs incurred in the prior year for the initial launch of Gvoke and decreased expenses related to conferences and programs due to the COVID-19 pandemic.

Other Income (Expense)

For the year ended December 31, 2020, interest and other income increased $0.2 million in comparison to the year ended December 31, 2019, primarily as a result of a legal settlement of $1.5 million, partially offset by lower interest income as a result of lower average balances in cash equivalents and investments and lower interest rates.

For the year ended December 31, 2020, interest expense increased $3.5 million in comparison to the year ended December 31, 2019, primarily due to a loss on conversion of convertible debt of $2.6 million in the current year, interest on the convertible notes issued in the June 2020 offering of $1.9 million, a loss on extinguishment of debt of $0.7 million in the current year, and increased borrowing levels under the Amended Loan Agreement, partially offset by a loss on extinguishment of debt of $2.3 million in the prior year.

Liquidity and Capital Resources

Our primary uses of cash are to fund costs related to the manufacturing, marketing and selling of Gvoke, 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 provides 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. We become eligible to draw the second tranche of $15.0 million and the third tranche of $10.0 million if certain revenue targets are achieved prior to March 31, 2021 and June 30, 2021, respectively. We currently do not anticipate that such milestones will be 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, which we refer to as the "Shelf". 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 December 31, 2020, 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.

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 also was 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 the Company’s common stock. As of December 31, 2020, 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, 2020, the outstanding balance under the Amended Loan Agreement was $43.5 million.

Capital Resources and Funding Requirements

We have incurred operating losses since inception, and we have an accumulated deficit of $337.4 million at December 31, 2020. Based on our current operating plans and existing working capital at December 31, 2020, 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 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 our product development and clinical operations, including completion of future clinical trials, as well as marketing and selling Gvoke and commercialization of our product candidates, if approved, will depend on the amount and timing of cash received from future financings. Our future capital requirements will depend on many factors, including:

- the costs of commercialization activities, including product marketing, sales and distribution;
- our degree of success in commercializing Gvoke;
- 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.

As we continue the marketing and selling of our first product, Gvoke, 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 and our product candidates, if approved. 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,**	
	2020	**2019**
Net cash used in operating activities	$ (80,558)	$ (104,346)
Net cash used in investing activities	(27,405)	(2,383)
Net cash provided by financing activities	126,064	80,530

The decrease in cash used in operating activities for the year ended December 31, 2020 was primarily driven by decreased spending in research and development and net sales of Gvoke, partially offset by increased marketing, selling and manufacturing costs related to the commercialization of Gvoke. For a discussion regarding the net sales of Gvoke 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."

The increase in net cash used in investing activities for the year ended December 31, 2020, as compared to the year ended December 31, 2019, was primarily due to a decrease in sales and maturities of investments.

The increase in cash provided by financing activities for the year ended December 31, 2020, as compared to the year ended December 31, 2019, was primarily due to the net proceeds of $81.2 million from the June 2020 convertible debt offering, the net proceeds of $39.9 million and $21.6 million from the February 2020 and June 2020 equity offerings of our common stock, respectively, and proceeds of $3.5 million from the drawdown on the October 2020 amendment to the Amended Loan Agreement, partially offset by the paydown of principal on the Amended Loan Agreement in June 2020 of $20.0 million, as compared to the net proceeds of $57.2 million from the 2019 equity offerings of our common stock and net proceeds from the issuance of long-term debt of $22.6 million in September 2019.

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, clinical trial expenses 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 to all contracts with customers within the scope of the standard. We sell our product, Gvoke, which is available in two presentations, a pre-filled syringe (Gvoke PFS) and an auto-injector (Gvoke HypoPen), primarily to pharmaceutical wholesalers. These wholesalers then resell our products to their customers, such as retail pharmacies. In addition, 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 in the U.S. only.

Revenue is recognized when our customer (e.g., a wholesaler) obtains control of promised goods or services, which is when our obligations under the terms of our contract with the customer are satisfied, based on the consideration we expect to receive in exchange for those goods or services. The estimated net sales price is generally based on a list or fixed price less estimates of variable consideration (e.g., patient copay assistance, prompt payment and other discounts, payor rebates, chargebacks, service fees and product returns). The estimates of variable consideration are subject to a constraint such that some or all of the estimated amount of variable consideration will only be included in the transaction price to the extent that it is probable that a significant reversal of revenue will not occur when the uncertainty associated with the variable consideration is subsequently resolved. Estimating variable consideration and the related constraint requires the use of significant management judgment and other market data.

Net sales represent gross product sales less estimated allowances for patient copay assistance programs, prompt payment and other discounts, payor rebates, chargebacks, service fees, and product returns, all of which are recorded at the time of sale to the pharmaceutical wholesalers or other customer. We apply significant judgments and estimates in determining some of these allowances. If actual results differ from our estimates, we will be required to make adjustments to these allowances in the future.

Patient Copay Assistance Program

We offer a savings program 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 levels of inventory in the distribution channel. Accrued copay fees are recorded as a reduction of revenue and included in accrued trade discounts and rebates on the consolidated balance sheets.

Prompt Payment Discounts

As an incentive for prompt payment, we offer a discount to most customers. We expect that all eligible customers will comply with the contractual terms to earn the discount and, therefore, we accrue the discount on all eligible sales. We record the discount as an allowance against trade accounts receivable on the consolidated balance sheets and as a reduction of revenue.

Commercial Rebates

We contract with certain private payor organizations, primarily insurance companies and pharmacy benefits managers, to provide rebates with respect to utilization of Gvoke and contracted formulary status. We accrue estimated rebates based on contract rates, estimated percentages of products that will be prescribed to qualified patients and estimated levels of inventory

in the distribution channel and record the rebate as a reduction of revenue. 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 based on estimated percentages of product sold to qualified patients, estimated rebate percentages and estimated levels of inventory in the distribution channel that will be prescribed to qualified patients and record the rebates as a reduction of revenue. Accrued government rebates are included in accrued trade discounts and rebates on the consolidated balance sheets.

Chargebacks

We have arrangements with certain commercial and government entities that allow them to buy our 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 acquisition cost and the discounted price back to us. We accrue estimated chargebacks based on estimated percentages of product sold to these entities, contract prices, and estimated levels of inventory in the distribution channel and record the chargebacks as a reduction of revenue. Accrued chargebacks are recorded as an allowance against trade receivables on the consolidated balance sheets.

Service Fees

We record service fees paid to our wholesaler customers for distribution and inventory management services as a reduction to revenue. We accrue estimated service fees based on contractually determined amounts. Accrued service fees are included in accrued trade discounts and rebates on the consolidated balance sheets.

Product Returns

Consistent with industry practice, our customers generally have the right to return product during the period beginning six months prior to its expiration date and up to one year after its expiration date. As our products are newly launched and we do not have history of product returns, we estimate the provision for returns based on factors related to the launch of our products, third-party industry data for comparable products in the market and estimated channel inventory data. As we distribute our products and establish historical sales over a longer period of time, we will be able to place more reliance on historical purchasing and return patterns of our customers when evaluating our reserves for product returns. 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 we were to increase or decrease the rate by 1%, it would have a $0.2 million impact on revenue in the year ended December 31, 2020. We record estimated sales returns in accrued returns reserve on the consolidated balance sheets and as a reduction of revenue.

Research and development accruals

Research and development expenses are expensed as incurred. Research and development expenses include salaries and related personnel 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 for Gvoke prior to approval and initial commercialization were expensed as research and development expenses.

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 used or the services are performed.

When preparing our financial statements, we are required to estimate our accrued clinical expenses. This process involves reviewing open contracts and communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. Payments under some of the contracts we have with parties depend on factors, such as successful enrollment of certain numbers of patients, site initiation and the completion of clinical trial milestones. When accruing clinical expenses, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If possible, we obtain information regarding unbilled services directly from our service providers. However, we may be required to estimate the cost of these services based only on information available to us. If we underestimate or overestimate the cost associated with a trial or service at a

given point in time, adjustments to research and development expenses may be necessary in future periods. Historically, our estimated accrued clinical expenses have approximated actual expense incurred.

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,	
	2020	2019
Cost of goods sold	$ 151	$ —
Research and development	1,229	1,168
Selling, general and administrative	6,893	5,316
Total stock-based compensation expense	$ 8,273	$ 6,484

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, 2020 would increase or decrease interest income by approximately $1.3 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, 2020, 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, 2020 was 0.14%, 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, 2020, 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, 2020.

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 Pharmaceuticals, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Xeris Pharmaceuticals, Inc. and subsidiaries (the Company) as of December 31, 2020 and 2019, 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, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2020, 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 9, 2021

XERIS PHARMACEUTICALS, INC.
Consolidated Balance Sheets
(in thousands, except share and par value)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 37,598	$ 19,519
Short-term investments	96,190	56,030
Trade accounts receivable, net	6,875	4,693
Inventory	8,353	2,176
Prepaid expenses and other current assets	3,196	5,065
Total current assets	152,212	87,483
Investments	—	13,231
Property and equipment, net	6,707	7,853
Other assets	232	420
Total assets	$ 159,151	$ 108,987
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,117	$ 5,603
Other accrued liabilities	15,895	18,119
Accrued trade discounts and rebates	5,984	1,375
Accrued returns reserve	2,889	1,957
Other current liabilities	322	284
Total current liabilities	28,207	27,338
Long-term debt, net of unamortized debt issuance costs	87,021	58,305
Deferred rent	6,629	7,076
Other liabilities	3,533	1,832
Total liabilities	125,390	94,551
Commitments and contingencies (Note 9)		
Stockholders' Equity:		
Preferred stock—par value $0.0001, 10,000,000 shares authorized and no shares issued and outstanding as of December 31, 2020 and 2019, respectively	—	—
Common stock—par value $0.0001, 150,000,000 shares authorized as of December 31, 2020 and 2019, respectively; 59,611,202 and 27,214,523 shares issued and outstanding as of December 31, 2020 and 2019, respectively	6	3
Additional paid in capital	371,134	260,635
Accumulated deficit	(337,385)	(246,245)
Accumulated other comprehensive income	6	43
Total stockholders' equity	33,761	14,436
Total liabilities and stockholders' equity	$ 159,151	$ 108,987

The accompanying notes are an integral part of the consolidated financial statements.

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

	Years Ended December 31,	
	2020	**2019**
Net sales	$ 20,155	$ 1,627
Grant and other income	280	1,095
Cost of goods sold	9,328	1,603
Gross profit	11,107	1,119
Operating expenses:		
Research and development	20,921	60,438
Selling, general and administrative	73,732	63,061
Total operating expenses	94,653	123,499
Loss from operations	(83,546)	(122,380)
Other income (expense):		
Interest and other income	2,965	2,813
Interest expense	(10,660)	(7,163)
Change in fair value of warrants	(9)	692
Total other income (expense)	(7,704)	(3,658)
Net loss before benefit from income taxes	(91,250)	(126,038)
Benefit from income taxes	110	458
Net loss	$ (91,140)	$ (125,580)
Other comprehensive income (loss), net of tax:		
Unrealized gains (losses) on investments	(10)	93
Foreign currency translation adjustments	(27)	2
Comprehensive loss	$ (91,177)	$ (125,485)
Net loss per common share - basic and diluted	$ (2.14)	$ (4.81)
Weighted average common shares outstanding - basic and diluted	42,642,901	26,110,297

The accompanying notes are an integral part of the consolidated financial statements.

XERIS PHARMACEUTICALS, 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, 2018	20,808,366	$ 2	$ 196,121	$ (52)	$ (120,665)	$ 75,406
Net loss	—	—	—	—	(125,580)	(125,580)
Issuance of common stock upon equity offerings	6,201,202	1	57,226	—	—	57,227
Exercise and vesting of stock options	128,307	—	254	—	—	254
Exercise of warrants	3,041	—	18	—	—	18
Stock-based compensation	—	—	6,484	—	—	6,484
Issuance of common stock through employee stock purchase plan	73,607	—	532	—	—	532
Other comprehensive income	—	—	—	95	—	95
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 offerings	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 and vesting 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 loss	—	—	—	(37)	—	(37)
Balance, December 31, 2020	59,611,202	$ 6	$ 371,134	$ 6	$ (337,385)	$ 33,761

The accompanying notes are an integral part of the consolidated financial statements.

XERIS PHARMACEUTICALS, INC.
Consolidated Statements of Cash Flows
(in thousands)

	Years Ended December 31,	
	2020	**2019**
Cash flows from operating activities:		
Net loss	$ (91,140)	$ (125,580)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,467	1,078
Amortization of investments	84	(686)
Amortization of debt issuance costs	980	948
Stock-based compensation	8,273	6,484
Loss on conversion of convertible debt	2,124	—
Loss on extinguishment of debt	443	2,324
Change in fair value of warrants	9	(692)
Changes in operating assets and liabilities:		
Trade accounts receivable	(2,182)	(4,693)
Prepaid expenses and other current assets	925	(960)
Inventory	(5,143)	(2,176)
Accounts payable	(2,486)	4,737
Other accrued liabilities	(2,207)	8,912
Accrued trade discounts and rebates	4,609	1,375
Accrued returns reserve	932	1,957
Deferred rent	(447)	1,012
Other	3,201	1,614
Net cash used in operating activities	(80,558)	(104,346)
Cash flows from investing activities:		
Capital expenditures	(377)	(1,107)
Purchases of investments	(101,773)	(102,472)
Sales and maturities of investments	74,745	101,196
Net cash used in investing activities	(27,405)	(2,383)
Cash flows from financing activities:		
Proceeds from equity offerings	65,891	61,692
Payments of equity offering costs	(4,315)	(4,465)
Proceeds from issuance of debt	94,839	60,000
Repayment of debt	(25,089)	(35,000)
Payments of debt issuance costs	(5,603)	(2,381)
Payments of debt conversion costs	(400)	—
Proceeds from issuance of employee stock purchase plan shares	669	532
Proceeds from exercise of stock awards	135	152
Repurchase of common stock withheld for taxes	(63)	—
Net cash provided by financing activities	126,064	80,530
Effect of exchange rate changes on cash and cash equivalents	(22)	2
Increase (decrease) in cash and cash equivalents	18,079	(26,197)
Cash and cash equivalents, beginning of period	19,519	45,716
Cash and cash equivalents, end of period	$ 37,598	$ 19,519
Supplemental schedule of cash flow information:		
Cash paid for interest	$ 4,555	$ 3,717
Supplemental schedule of non-cash investing and financing activities:		
Tenant improvement allowance	$ —	$ 5,658
Issuance of stock for conversion of debt	$ 37,812	$ —
Accrued debt issuance costs	$ 347	$ 1,800

The accompanying notes are an integral part of the consolidated financial statements.

Note 1. Organization and Nature of the Business

Nature of business

Xeris Pharmaceuticals, Inc. ("Xeris" or the "Company") is a specialty pharmaceutical company that was incorporated in Delaware in 2005. Xeris is dedicated to the development of ready-to-use injectable and infusible drug formulations that address important unmet medical needs, are easier to use by patients, caregivers and health practitioners, and reduce costs for payors and the healthcare system.

Since its inception, the Company has devoted substantially all of its resources to research and development initiatives, undertaking preclinical studies of its product candidates, conducting clinical trials of its most advanced product candidates, organizing and staffing the Company, raising capital and commercializing its first product, Gvoke®, which was approved by the FDA in September 2019. Gvoke delivers ready-to-use glucagon via a commercially available pre-filled syringe or auto-injector for the treatment of severe hypoglycemia, a potentially life-threatening condition. The Company commercially launched Gvoke pre-filled syringe ("Gvoke PFS") in November 2019 and auto-injector ("Gvoke HypoPen®") in July 2020. The Company has financed its operations primarily through the issuance of its common stock, convertible debt, convertible preferred stock, and debt financing.

The Company has incurred operating losses since inception and has an accumulated deficit of $337.4 million as of December 31, 2020. The Company expects to continue to incur net losses for at least the next 12 months. Based on the Company's current operating plans and existing working capital at December 31, 2020, the Company believes its cash resources are sufficient to sustain operations and capital expenditure requirements for at least the next 12 months.

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 its products and any future products, if and when approved, successful development of its product candidates, the development of new technological innovations by its competitors, and protection of intellectual property.

The ongoing global outbreak of the novel 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 its business practices (including remote work for most of its employees). While we cannot predict their scope and severity, these developments and measures could materially and adversely affect our business, our results of operations and our financial condition. We are closely monitoring the impact of the COVID-19 pandemic on all aspects of our business and are taking steps to minimize its impact on our business. However, the extent to which COVID-19 impacts our 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 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.

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 and its 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 Pharmaceuticals, Inc. and its subsidiary, Xeris Pharmaceuticals Australia Pty Ltd. All intercompany transactions have been eliminated.

Note 2. Summary of Significant Accounting Policies

The accompanying financial statements have been prepared in conformity with GAAP. Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the ASC and ASUs of the FASB.

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 to all contracts with customers within the scope of the standard. The Company sells its product, Gvoke, which is available in two presentations, a pre-filled syringe (Gvoke PFS) and an auto-injector (Gvoke HypoPen), primarily to pharmaceutical wholesalers. These wholesalers then resell the Company’s products to their customers, such as retail pharmacies. In addition, 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 in the U.S. only.

Revenue is recognized when the Company's customer (e.g., a wholesaler) 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 the Company expects to receive in exchange for those goods or services. The estimated net sales price is generally based upon a list or fixed price less estimates of variable consideration (e.g., patient copay assistance, prompt payment and other discounts, payor rebates, chargebacks, service fees and product returns). The estimates of variable consideration are subject to a constraint such that some or all of the estimated amount of variable consideration will only be included in the transaction price to the extent that it is probable that a significant reversal of revenue will not occur when the uncertainty associated with the variable consideration is subsequently resolved. Estimating variable consideration and the related constraint requires the use of significant management judgment and other market data.

Net sales represent gross product sales less estimated allowances for patient copay assistance programs, prompt payment and other 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, the Company will be required to make adjustments to these allowances in the future.

Patient Copay Assistance Program

The Company offers a savings program 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 revenue and included in accrued trade discounts and rebates on the consolidated balance sheets.

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, we accrue 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 revenue.

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 Gvoke and contracted formulary status. The Company accrues estimated rebates based on contract rates, estimated percentages of products that will be prescribed to qualified patients and estimated levels of inventory in the distribution channel and records the rebate as a reduction of revenue. 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 estimated percentages of product sold to qualified patients, estimated rebate percentages and estimated levels of inventory in the distribution channel that will be prescribed to qualified patients and records the rebates as a reduction of revenue. Accrued government rebates are included in accrued trade discounts and rebates on the consolidated balance sheets.

Chargebacks

The Company's arrangements with certain commercial and government entities allow them to buy their 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 acquisition cost 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 revenue. Accrued chargebacks are recorded as an allowance against trade receivables on the consolidated balance sheets.

Service Fees

The Company records service fees paid to its wholesaler customers for distribution and inventory management services as a reduction to revenue. 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.

Product Returns

Consistent with industry practice, the Company's customers generally have the right to return product during the period beginning six months prior to its expiration date and up to one year after its expiration date. As the Company's products are newly launched and the Company does not have a history of product returns, the Company estimates the provision for returns based on factors related to the launch of its products, third-party industry data for comparable products in the market and estimated channel inventory data. As the Company distributes its products and establishes historical sales over a longer period of time, it will be able to place more reliance on historical purchasing and return patterns of its customers when evaluating its reserves for product returns. 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 its 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 $0.2 million impact on revenue in the year ended December 31, 2020. The Company records estimated sales returns in accrued returns reserve on the consolidated balance sheets and as a reduction of revenue.

Bad debt expense

The Company’s products are primarily sold to wholesalers. The Company monitors its accounts receivable balances to determine the impact, if any, of such factors as changes in customer concentration, credit risk and the realizability of its accounts receivable, and records a bad debt reserve when applicable.

Concentration of credit risk

For the years ended December 31, 2020 and 2019, three customers accounted for 92% and 94% of the Company's gross sales, respectively. These same three customers accounted for 98% and 97% of the trade accounts receivable at December 31, 2020 and December 31, 2019, 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 our contract manufacturing organizations, and manufacturing overhead costs, as well as 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 incurred prior to approval and initial commercialization were expensed as research and development expenses.

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.

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 to be cash equivalents.

Inventories

Inventories are stated at the lower of cost or net realizable value, using the first-in, first-out convention. Inventories consist 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 inventories include the direct purchase cost of materials and supplies, charges from our contract manufacturing organizations and manufacturing overhead costs. The Company reviews its inventory balance quarterly to assess if it has obsolete or excess inventory and records a charge to cost of goods sold if and when applicable. Manufacturing costs for Gvoke prior to approval and commercialization were expensed as research and development expenses.

Prepaid expenses and other current assets

Prepaid expenses and other current assets include prepaid expenses for general business purposes, which are stated at cost and amortized on a straight-line basis over the related period of benefit. Prepaid expenses also include supplies and materials used in several development projects. These supplies and materials are expensed as they are consumed.

Investments

The Company classifies its 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.

Investments in available-for-sale securities are reported at estimated fair value. Available-for-sale securities consist primarily of corporate securities, U.S. government securities and commercial paper. Unrealized gains and losses related to changes in the fair value of debt securities are recognized in other comprehensive income (loss). Changes in the fair value of available-for-sale securities impact the statements of operations and comprehensive loss only when such securities are sold or an other-than-temporary impairment is recognized. Realized gains and losses on the sale of securities are determined by specific identification of each security's cost basis. The Company regularly reviews its investment portfolio to determine if any security is other-than-temporarily impaired, which would require an impairment charge to be recorded in the period any such determination is made. The Company considers factors such as the

duration, severity of and reason for the decline in value, the financial condition of the issuer and any changes thereto, the potential recovery period and intent to sell.

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 (the "Amended Loan 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 and warrants.

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 its long-lived assets for potential impairment in accordance with ASC Topic 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 material impairment charges for the years ended December 31, 2020 and 2019, respectively.

Equity financing costs

The Company capitalizes costs directly associated with equity financings until such financings are consummated, at which time such costs are recorded in additional paid in capital against the gross proceeds of the equity financings. The Company recognized $4.3 million and $4.5 million of direct costs associated with the public equity offerings in additional paid in capital for the years ended December 31, 2020 and 2019, respectively. Costs associated with the shelf registration statement on Form S-3, filed with the U.S. Securities and Exchange Commission's ("SEC") on August 6, 2019 and declared effective on August 21, 2019 have been capitalized and are being reclassified to additional paid in capital on a pro rata basis when the Company completes offerings under the shelf registration. At the end of the three-year life of the shelf registration, the remaining deferred offering costs, if any, will be charged to the results of operations. As of December 31, 2020 and 2019, $0.2 million and $0.4 million, respectively, of such deferred costs are included in other assets on the consolidated balance sheets.

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 provided for tenant improvement allowances whereby the landlord funded the cost to build out the space. The Company recorded a liability for

such lease incentives which is being amortized to rent expense such that rent expense is recognized on a straight-line basis throughout the lease term.

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, are deducted from the carrying value of the related debt.

Warrants

The Company's 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.

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 our 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 its 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, 2020 and 2019, the Company did not accrue any interest or penalties on uncertain tax positions.

Foreign currency translation

Our functional currency is the United States Dollar. Monetary assets and liabilities of our non-US subsidiary are remeasured using the exchange rate in effect at the end of the period. Costs in local currency are remeasured using the average exchange rate for the period. The resulting remeasurement gains and losses are included in other comprehensive income (loss).

Comprehensive loss

Comprehensive loss is defined as the change in equity during a period from transactions and other events, excluding changes resulting from investments from owners and distributions to owners. Comprehensive loss includes net loss, unrealized (gains) losses on available-for-sale investments and foreign currency translation adjustments.

Reclassifications

Certain prior period amounts on the balance sheet have been reclassified to conform to the current year presentation. These reclassifications had no impact on current assets, total assets, current liabilities or total liabilities.

New accounting pronouncements

Recently issued accounting pronouncements

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 will be effective for the Company for annual and interim periods 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 its 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 LIBOR or other reference rates that are expected to be discontinued because of reference rate reform. The amendments in this update are effective through December 31, 2022. The Company does not currently expect the adoption of this new standard to have a material impact on its 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 intraperiod 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, with early adoption permitted. The Company does not currently expect the adoption of this new standard to have a material impact on its financial statements.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, as further updated by ASU 2018-19, 2019-04, 2019-05, 2019-10 and 2020-03. 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 will be effective for the Company for annual and interim periods beginning after December 15, 2022, with early adoption permitted. The Company is currently evaluating the impact the adoption of this new standard will have on its 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. The FASB has recently extended the effective date of this standard for certain companies. 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 its balance sheet.

Note 3. Inventory

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

	December 31, 2020	December 31, 2019
Raw materials	$ 2,874	$ 1,321
Work in process	4,247	662
Finished goods	1,232	193
Inventory	$ 8,353	$ 2,176

Inventory reserves were $2.2 million and $0 at December 31, 2020 and December 31, 2019, respectively.

Note 4. Property and Equipment

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

	December 31, 2020	December 31, 2019
Lab equipment	$ 2,684	$ 2,528
Furniture and fixtures	1,355	1,611
Computer equipment	277	232
Office equipment	8	80
Software	307	347
Leasehold improvements	4,627	4,543
	9,258	9,341
Less: accumulated depreciation and amortization	(2,551)	(1,488)
Property and equipment, net	$ 6,707	$ 7,853

Depreciation and amortization expense relating to property and equipment was $1.5 million and $1.1 million for the years ended December 31, 2020 and 2019, respectively.

Note 5. Other Accrued Liabilities

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

	December 31, 2020	December 31, 2019
Accrued employee costs	$ 7,989	$ 6,818
Accrued supply chain costs	1,702	—
Accrued marketing and selling costs	1,114	1,973
Accrued research and development costs	678	7,062
Accrued restructuring charges	811	—
Accrued interest expense	1,527	449
Accrued other costs	2,074	1,817
Other accrued liabilities	$ 15,895	$ 18,119

Note 6. Long-term Debt

Convertible Senior Notes

In June 2020, the Company completed a public offering of $86.3 million aggregate principal amount of the Company'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. The Company incurred debt issuance costs of $5.1 million in connection with the issuance of the Convertible Notes. The Company 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, as supplemented by the first supplemental indenture thereto, each dated as of June 30, 2020, by and between the Company 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 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. The Company 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 the Company'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 the Company is not a holder thereof) preferred equity, if any, of its subsidiaries.

Senior Secured Loan Facility

In February 2018, the Company entered into the Loan and Security Agreement, dated as of February 28, 2018 (as amended, the “Original Loan Agreement”), with Oxford Finance LLC, as the collateral agent and a lender (“Oxford”), 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"). The Company also issued warrants to the Lenders to purchase common stock, which is further discussed in Note 8, "Warrants."

In September 2019, the Company 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 the Company 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”) will become available to the Company if certain revenue targets are achieved prior to March 31, 2021 and June 30, 2021, respectively. The Company currently does not anticipate that such revenue targets will be 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, the Company entered into that certain First Amendment to the Amended and Restated Loan and Security Agreement with the Lenders (the “First Amendment”) to amend the Loan Agreement to allow the Company to incur indebtedness under the U.S. Small Business Administration (the “SBA”) Paycheck Protection Program (the “PPP”) 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, the Company entered into that certain Second Amendment to the 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 the Company's underwritten public offering of the Company's 5.00% Convertible Senior Notes due 2025 and permit the Company to prepay its 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 will be payable in 30 equal monthly installments. However, if the Company achieves a certain revenue milestone prior to January 1, 2022, then the period for interest-only payments is extended through September 30, 2022, after which the term loans will 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, the Company 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, the Company 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, the Company entered into that certain Third Amendment to the 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 the Company’s new leased laboratory space and (ii) permit the sale of certain equipment related to the relocation of the Company’s research and development laboratory from San Diego to Chicago.

On October 23, 2020, the Company entered into that certain Fourth Amendment to the Amended and Restated Loan and Security Agreement with the Lenders (the "Fourth Amendment") to amend the Loan Agreement (as amended, supplemented or otherwise modified from time to time, including by that certain First Amendment, Second Amendment, Third Amendment and Fourth Amendment, collectively, the "Amended 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.

Pursuant to the Amended Loan Agreement, the Company has provided a first priority security interest in substantially all of the Company's assets, including intellectual property, subject to certain limited exceptions.

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. For the period from the funding date of the Term A Loan through and including December 31, 2020, the interest rate was 8.68%. The remaining balance of unamortized debt issuance costs related to the Loan Agreement and the additional debt issuance costs incurred in conjunction with the Second Amendment have been reflected as a direct reduction to the loan balance and are being amortized to interest expense over the remaining life of the loan using the effective interest method.

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.

Paycheck Protection Program Loan

In April 2020, the Company entered into the SBA PPP Note with SVB (the "PPP Lender") for the PPP Loan in the amount of $5.1 million, enabled by the CARES Act to retain employees, maintain payroll and make lease and utility payments in accordance with the relevant terms and conditions of the CARES Act. The Company repaid $0.9 million of the PPP Loan in May 2020 and the remaining $4.2 million on June 30, 2020.

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

	December 31, 2020	December 31, 2019
Senior secured loan facility	$ 43,500	$ 60,000
Convertible Notes	47,175	—
Less: unamortized debt issuance costs	(3,654)	(1,695)
Long-term debt, net of unamortized debt issuance costs	$ 87,021	$ 58,305

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

2021	$ 0
2022	17,400
2023	17,400
2024	8,700
2025	47,175
	$ 90,675

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 such 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. For the year ended December 31, 2019, the Company recognized interest expense of $7.2 million, of which $0.9 million related to the amortization of debt issuance costs. Included in such interest expense is a loss on extinguishment of debt of $2.3 million relating to the write-off of the remaining balance of unamortized debt issuance costs associated with the Original Loan Agreement.

Note 7. Stockholders' Equity

The Company's authorized shares of stock of 160.0 million are divided into 150.0 million shares of common stock, par value $0.0001 per share, and 10.0 million shares of preferred stock, par value $0.0001 per share. At December 31, 2020 none of the 10.0 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 its common stock during the periods presented.

In February 2019, the Company completed an equity offering of its common stock pursuant to a registration statement on Form S-1, as amended. The Company sold an aggregate of 5,996,775 shares of common stock at a price of $10.00 per share, including 116,775 shares of common stock pursuant to the exercise of the underwriters' option to purchase additional shares. Net proceeds from the equity offering were $55.5 million after deducting underwriting discounts and commissions as well as other public offering expenses.

On August 6, 2019, the Company filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale by the Company of up to an aggregate of $250.0 million of its common stock, preferred stock, debt securities, warrants and/or units (the "Shelf"). The Company simultaneously entered into a Sales Agreement with Jefferies LLC, as sales agent, to provide for the offering, issuance and sale by the Company of up to $50.0 million of its common stock from time to time in "at-the-market" offerings under the Shelf. The Shelf was declared effective by the SEC on August 21, 2019. In December 2019, the Company sold an aggregate of 204,427 shares of common stock under the Shelf for net proceeds of $1.7 million after deducting selling commissions as well as other public offering expenses.

In February 2020, the Company completed an equity offering of its 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 its 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.

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, 2020, 31,250 RSUs vested for which 9,801 shares were withheld to cover the minimum statutory withholding taxes of $0.1 million.

Note 8. Warrants

In 2014 the Company issued 19,931 warrants (the "2014 Warrants") to certain investors. The 2014 Warrants allow each holder to purchase one share of common stock for $5.912. Of the 2014 Warrants, 18,512 warrants were exercised and 1,419 warrants expired. There are no 2014 Warrants outstanding as of December 31, 2020.

As part of the Original Loan Agreement discussed in Note 6, "Long-term Debt," the Lenders received warrants concurrent with the borrowing. The warrants represent a right for the lender to purchase shares of the Company's common stock at an exercise price of

$11.169 per share. The Company issued 53,720 warrants (the "2018 Term A Warrants") upon the drawdown of the 2018 Term A Loan in February 2018, and the Company issued 40,292 warrants (the "2018 Term B Warrants") upon the drawdown of the 2018 Term B Loan in September 2018. There have been no exercises of 2018 Term A Warrants or 2018 Term B Warrants.

Because the warrants are a freestanding instrument, indexed to the Company's stock, they do not meet the criteria for equity classification. Therefore, the warrants are classified as liabilities and subject to remeasurement at each reporting period until they are exercised, expired, or otherwise settled.

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. The Company recognized gains of $78,000, $351,000 and $263,000 upon the change in fair value of the warrants during the year ended December 31, 2019 related to the 2014 Warrants, the 2018 Term A Warrants and the 2018 Term B Warrants, respectively.

As of December 31, 2020, the following warrants were outstanding:

	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
	94,012		

Note 9. Commitments and Contingencies

Commitments

The Company has non-cancellable operating leases for office and laboratory space, which expire at various times through 2033. The non-cancellable lease agreements provide for monthly lease payments which increase during the term of each lease agreement.

In the third quarter of 2020, the Company signed a lease to occupy a research and development laboratory site in Chicago, Illinois in conjunction with the Company's plan to relocate such activities from the current San Diego site in the fourth quarter of 2020. The future minimum lease payments of the new lease are approximately $0 in 2021, $0.5 million in 2022, $0.7 million in 2023, $0.7 million in 2024, $0.7 million in 2025, and $6.5 million in 2026 and thereafter. In conjunction with the new lease, the Company assigned its lease for the San Diego site to a third party in the fourth quarter of 2020. Such assignment released the Company from any further minimum lease payment obligations for that site.

Future minimum lease payments under operating leases at December 31, 2020 are as follows (in thousands):

2021	$	1,277
2022		1,813
2023		2,031
2024		1,981
2025		1,931
Thereafter		13,723
Total minimum lease payments	$	22,756

Total rent expense under these operating leases was approximately $2.3 million and $2.2 million for the years ended December 31, 2020 and 2019, respectively.

As of December 31, 2020, we had unused letters of credit of $1.4 million which were issued primarily to secure leases.

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, 2020, 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 10. Restructuring Costs

In the third quarter of 2020, the Company commenced a plan to relocate its 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 expects to incur total restructuring costs of approximately $2.3 million related to the plan. Costs of $1.7 million were incurred in the year ended December 31, 2020, of which $1.0 million is included in research and development expenses, $0.6 million is included in selling, general and administrative expenses, and $0.1 million is included in costs of goods sold in the consolidated statements of operations and comprehensive loss. The Company anticipates that the restructuring will be substantially complete by the end of the fourth quarter of 2021. The restructuring reserve is included in other accrued liabilities in the consolidated balance sheet.

The following table summarizes the initial restructuring reserve and the payments made during the year ended December 31, 2020 (in thousands):

	Employee Termination and Relocation Costs	Other	Total
Restructuring costs	$ 1,215	$ 445	$ 1,660
Payments	(569)	(280)	(849)
Balance accrued at December 31, 2020	$ 646	$ 165	$ 811

Note 11. 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, 2020 and 2019, the number of shares of common stock available for issuance under the 2018 Plan was automatically increased by 1,088,580 shares and 835,728 shares, respectively. As of December 31, 2020, there were 609,757 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, 2020 and 2019, the number of shares of common stock available for issuance under the ESPP increased by 272,145 shares and 208,932 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 292,804 shares at a weighted average price of $2.29 per share during the year ended December 31, 2020. As of December 31, 2020, there were 307,666 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 intends to use 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, 2020, there were 263,794 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.

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 its 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, excluding those issued pursuant to the Option Exchange, was estimated with the following weighted average assumptions:

	Years Ended December 31,	
	2020	2019
Expected term (years)	5.9	6.0
Risk-free interest rate	0.42 %	2.14 %
Expected volatility	70.19 %	60.27 %
Expected dividends	—	—

Stock option activity under the 2011 Plan, 2018 Plan and Inducement Plan for the year ended December 31, 2020 was as follows:

	Options	Weighted Average Exercise Price	Weighted Average Contractual Life (Years)
Outstanding - January 1, 2020	4,428,985	$ 9.40	8.19
Granted	1,555,668	5.15	
Issued upon Option Exchange	832,907	4.09	
Cancelled upon Option Exchange	(1,127,906)	16.05	
Exercised and vested	(100,866)	1.68	
Forfeited	(534,691)	9.07	
Expired	(100,191)	10.15	
Outstanding - December 31, 2020	4,953,906	$ 5.84	7.46
Exercisable - December 31, 2020	2,173,599	$ 5.77	6.38
Vested and expected to vest at December 31, 2020	4,704,371	$ 5.84	7.42

The weighted average fair value of awards granted during the year ended December 31, 2020 was $3.13 per share. The total intrinsic value of options exercised during the year ended December 31, 2020 was $0.2 million. As of December 31, 2020, the aggregate intrinsic value of awards vested and expected to vest was $5.4 million.

At December 31, 2020, there was a total of $11.4 million of unrecognized stock-based compensation expense related to stock options that is expected to be recognized over a weighted average period of 2.1 years.

A summary of outstanding RSU awards and the activity for the year ended December 31, 2020 was as follows:

	Units	Weighted Average Grant Date Fair Value
Unvested balance - January 1, 2020	125,000	$ 13.88
Granted	677,800	6.12
Vested	(31,250)	13.88
Forfeited	(5,000)	6.37
Unvested balance - December 31, 2020	766,550	$ 7.07

RSUs are measured based on the fair market value of the underlying stock on the date of grant and vest over either three or four years in equal annual installments beginning on the one-year anniversary of the date of grant. Stock-based compensation expense related to RSUs is recognized on a straight-line basis over the employee's requisite service period. As of December 31, 2020, there was $3.9 million of unrecognized stock-based compensation expense related to RSUs, which is expected to be recognized over the weighted-average remaining vesting period of 2.3 years.

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,	
	2020	2019
Expected term (years)	0.5	0.5
Risk-free interest rate	1.01 %	1.85 %
Expected volatility	108.70 %	70.70 %
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,	
	2020	2019
Cost of goods sold	$ 151	$ —
Research and development	1,229	1,168
Selling, general and administrative	6,893	5,316
Total stock-based compensation expense	$ 8,273	$ 6,484

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 its 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, 2020 and 2019 (in thousands):

	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

	Total as of December 31, 2019	Level 1	Level 2	Level 3
Assets				
Cash and cash equivalents:				
Cash and money market funds	$ 19,519	$ 19,519	$ —	$ —
Investments:				
U.S. government securities	32,175	32,175	—	—
Corporate securities	22,164	—	22,164	—
Commercial paper	14,922	—	14,922	—
Total investments	$ 69,261	$ 32,175	$ 37,086	$ —
Liabilities				
Warrant liabilities	$ 150	$ —	$ —	$ 150

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 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, 2019	$ 150
Change in fair value of warrants	9
Balance at December 31, 2020	$ 159

There were no transfers between any of the levels of the fair value hierarchy during the years ended December 31, 2020 and 2019.

Note 13. Available-for-Sale Investments

The Company classifies its 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, 2020, 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, 2020 had an average remaining maturity of 0.4 years. The debt securities are reported at fair value with unrealized gains or losses recorded in other comprehensive income (loss). 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, 2020 and 2019 (in thousands):

	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

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Total Fair Value
Investments:				
Commercial paper	$ 14,922	$ —	$ —	$ 14,922
Corporate securities	22,146	20	(2)	22,164
U.S. government securities	32,152	23	—	32,175
Total available-for-sale investments	$ 69,220	$ 43	$ (2)	$ 69,261

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, we 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, 2020 and 2019, 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 14. 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,	
	2020	2019
Shares to be issued upon conversion of Convertible Notes	15,416,667	—
Vested and unvested stock options	4,953,906	4,428,985
Restricted stock units	766,550	125,000
Warrants	94,012	95,431
	21,231,135	4,649,416

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, 2020 and 2019, the Company made $0.6 million and $0.4 million of matching contributions to the plan, respectively.

Defined 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, 2020, the total deferred compensation liability under the Deferred Compensation Plan was approximately $1.7 million and was recorded in other liabilities in the consolidated balance sheets.

Note 16. 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,	
	2020	2019
Federal tax benefit at statutory rate	$ (19,162)	$ (26,468)
State tax benefit, net of federal benefit	(4,375)	(5,570)
Research and development and orphan drug credits	(480)	(2,912)
Uncertain tax positions	(16)	342
Permanent adjustments to expenses	710	169
Stock-based compensation	1,014	683
Return to provision adjustment	(1,203)	(3,278)
Changes in valuation allowance	23,543	36,288
Other	(141)	288
Total income tax benefit	$ (110)	$ (458)

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 year ended December 31, 2020, we have 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,	
	2020	2019
Deferred tax assets:		
Net operating losses	$ 74,894	$ 55,110
Federal research and orphan drug credits	8,362	8,309
Stock-based compensation	1,894	1,092
Other temporary differences	7,785	4,648
Valuation allowance	(92,493)	(68,950)
Total assets	442	209
Deferred tax liabilities:		
Fixed and intangible assets	(404)	(155)
Other deferred tax liabilities	(38)	(54)
Total liabilities	(442)	(209)
Net deferred tax assets	$ —	$ —

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. As of December 31, 2019, the Company had federal net operating loss carryforwards of $215.3 million and various state net operating loss carryforwards of $147.5 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, 2020, the Company had $8.0 million and $1.7 million of federal and state income tax credits, respectively, to reduce future tax liabilities. At December 31, 2019, the Company had $8.3 million and $1.0 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, 2020 and 2019 is as follows (in thousands):

Valuation allowance at December 31, 2018	$	(32,662)
Increase for 2019 activity		(36,288)
Valuation allowance at December 31, 2019		(68,950)
Increase for 2020 activity		(23,543)
Valuation allowance at December 31, 2020	$	(92,493)

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, 2020 and 2019, excluding interest and penalties, consisted of the following (in thousands):

	December 31,	
	2020	**2019**
Beginning balance - uncertain tax positions	$ 945	$ 603
Increases related to tax positions taken during the current year	48	246
Increases (decreases) related to tax positions taken during the prior year	(64)	96
Ending balance - uncertain tax positions	$ 929	$ 945

For the year ended December 31, 2020, 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 $0.9 million were offset against deferred tax assets. Tax years prior to 2017 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, 2020 and 2019, the Company incurred no interest and penalties related to income taxes.

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 upon such evaluation, our principal executive officer and principal financial officer have concluded that the disclosure controls and procedures were effective as of December 31, 2020 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, 2020 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, 2020.

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 have been 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, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

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, 2020 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, 2020 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, 2020 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, 2020 and is incorporated in this Annual Report on Form 10-K by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

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, 2020 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

Registrants may voluntarily include a summary of information required by Form 10-K under Item 16. We have elected not to include such summary.

INDEX TO EXHIBITS

Exhibit No.	Description
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-K filed with the SEC on June 28, 2018)
3.2	Amended and Restated By-laws of the Registrant (Incorporated by reference to Exhibit 3.2 to our Current Report on Form 8-K filed with the SEC on June 28, 2018)
3.3	Amendment No. 1 to the Amended and Restated By-laws of the Registrant (Incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K filed with the SEC on April 24, 2020)
4.1	Specimen Stock Certificate Evidencing Shares of Common Stock (Incorporated by reference to Exhibit 4.2 to our Registration Statement on Form S-1/A filed with the SEC on June 11, 2018)
4.2	Second Amended and Restated Investors' Rights Agreement (Incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
4.3	Description of Registrant's Securities (Incorporated by reference to Exhibit 4.3 to our Annual Report on Form 10-K filed with the SEC on March 12, 2020)
4.4	Base Indenture, dated as of June 30, 2020, by and between the Registrant and U.S. Bank National Association (Incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed with the SEC on July 1, 2020)
4.5	First Supplemental Indenture, dated as of June 30, 2020, by and between the Registrant and U.S. Bank National Association (Incorporated by reference to Exhibit 4.2 to our Current Report on Form 8-K filed with the SEC on July 1, 2020)
4.6	Form of 5.00% Convertible Senior Note due 2025 (included in Exhibit 4.5)
10.1#	2011 Stock Option and Incentive Plan and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.1 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.2#	2018 Stock Option and Incentive Plan and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.2 to our Registration Statement on Form S-1/A filed with the SEC on June 11, 2018)
10.3#	Senior Executive Cash Incentive Bonus Plan (Incorporated by reference to Exhibit 10.3 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.4#	Form of Director Indemnification Agreement (Incorporated by reference to Exhibit 10.4 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.5#	Form of Officer Indemnification Agreement (Incorporated by reference to Exhibit 10.5 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.6#	Form of Amended and Restated Employment Agreement, by and between the Registrant and Paul Edick (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1/A filed with the SEC on June 11, 2018)
10.7#	Form of Amended and Restated Employment Agreement, by and between the Registrant and John Shannon (Incorporated by reference to Exhibit 10.8 to our Registration Statement on Form S-1/A filed with the SEC on June 11, 2018)
10.8#	Form of Amended and Restated Employment Agreement, by and between the Registrant and Steven Prestrelski (Incorporated by reference to Exhibit 10.9 to our Registration Statement on Form S-1/A filed with the SEC on June 11, 2018)

Exhibit No.	Description
10.9#	Form of Amended and Restated Employment Agreement, by and between the Registrant and Ken Johnson (Incorporated by reference to Exhibit 10.10 to our Registration Statement on Form S-1/A filed with the SEC on June 11, 2018)
10.10#	Form of Employment Agreement, by and between the Registrant and Barry Deutsch (Incorporated by reference to Exhibit 10.11 to our Registration Statement on Form S-1/A filed with the SEC on June 11, 2018)
10.11#	Employment Agreement, by and between the Registrant and Beth Hecht (Incorporated by reference to Exhibit 10.12 to our Registration Statement on Form S-1 filed with the SEC on February 11, 2019)
10.12#	First Amendment to Employment Agreement, by and between the Registrant and Beth Hecht (Incorporated by reference to Exhibit 10.13 to our Registration Statement on Form S-1 filed with the SEC on February 11, 2019)
10.13+	API Supply Agreement, dated as of January 1, 2018, by and between the Registrant and Bachem Americas, Inc. (Incorporated by reference to Exhibit 10.12 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.14+	Quality Assurance Agreement, dated as of November 20, 2015, by and between Bachem AG and the Registrant, as amended by (i) Amendment 1 to the Quality Assurance Agreement, dated as of October 31, 2016, by and between Bachem AG and the Registrant and (ii) Amendment 2 to the Quality Assurance Agreement, dated as of January 26, 2017, by and between Bachem AG and the Registrant (Incorporated by reference to Exhibit 10.13 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.15+	Commercial Supply Agreement, dated as of May 14, 2018, by and between Pyramid Laboratories Inc. and the Registrant (Incorporated by reference to Exhibit 10.14 to our Registration Statement on Form S-1/A filed with the SEC on June 14, 2018)
10.16+	Joint Development Agreement, dated as of January 29, 2016, by and between the Registrant and Scandinavian Health Limited (Incorporated by reference to Exhibit 10.15 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.17	Loan and Security Agreement, dated as of February 28, 2018, by and between Oxford Finance LLC, Silicon Valley Bank and the Registrant (Incorporated by reference to Exhibit 10.16 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.18+	Quality Agreement, dated as of November 16, 2016, by and between Pyramid Laboratories Inc. and the Registrant (Incorporated by reference to Exhibit 10.17 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.19#	2018 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.18 to our Registration Statement on Form S-1/A filed with the SEC on June 11, 2018)
10.20+	Product Supply Agreement by and between SHL Pharma, LLC and the Registrant, dated August 1, 2018 (Incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q filed with the SEC on November 8, 2018)
10.21#	Inducement Equity Plan (Incorporated by reference to Exhibit 99.1 of our Registration Statement on Form S-8 filed with the SEC on February 8, 2019)
10.22	First Amendment to Office Lease Agreement, dated as of November 20, 2018, by and between 180 N LaSalle Property Owner LLC and the Registrant (Incorporated by reference to Exhibit 10.22 of our Registration Statement on Form S-1 filed with the SEC on February 11, 2019)
10.23	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 our Current Report on Form 8-K filed with the SEC on September 10, 2019)
10.24	Second Amendment to Loan and Security Agreement, dated as of May 15, 2019, by and among Oxford Finance LLC, Silicon Valley Bank and the Registrant (Incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q filed with the SEC on August 6, 2019)

Exhibit No.	Description
10.25#	Consulting Agreement between the Registrant and Jonathan Rigby, dated March 26, 2019 (Incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q filed with the SEC on May 9, 2019)
10.26	U.S. Small Business Administration Paycheck Protection Program Note, entered into April 21, 2020 by the Registrant (Incorporated herein by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the SEC on April 24, 2020)
10.27#	Deferred Compensation Plan (Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the SEC on April 10, 2020)
10.28+	Amendment 3 to the Quality Assurance Agreement, dated as of February 26, 2020, by and between the Registrant and Bachem AG (Incorporated by reference to Exhibit 10.3 of our Quarterly Report 10-Q filed with the SEC on May 7, 2020)
10.29	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 the Registrant (Incorporated by reference to Exhibit 10.4 of our Quarterly Report 10-Q filed with the SEC on May 7, 2020)
10.30+	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 the Registrant (Incorporated by reference to Exhibit 10.1 of our Quarterly Report 10-Q filed with the SEC on August 10, 2020)
10.31+	First Amendment to the Product Supply Agreement, dated as of June 24, 2020, by and between the Registrant and SHL Pharma LLC (Incorporated by reference to Exhibit 10.2 of our Quarterly Report 10-Q filed with the SEC on August 10, 2020)
10.32+	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 the Registrant (Incorporated by reference to Exhibit 10.2 of our Quarterly Report 10-Q filed with the SEC on November 9, 2020)
10.33#+	Amendment to Employment Agreement, by and between the Registrant and John Shannon, dated as of August 18, 2020 (Incorporated by reference to Exhibit 10.1 of our Quarterly Report 10-Q filed with the SEC on November 9, 2020)
10.34+*	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 Registrant
10.35	Form of Exchange Agreement (Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the SEC on November 16, 2020)
10.36*	Amended and Restated Quality Agreement, dated as of November 16, 2020, by and between Pyramid Laboratories Inc. and 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

Exhibit No.	Description
101.PRE	XBRL Taxonomy Extension Presentation Linkbase 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 Pharmaceuticals, Inc.

By /s/ Paul R. Edick
Paul R. Edick
Chief Executive Officer and Chairman

Date March 9, 2021

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below as of March 9, 2021, 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/ Barry M. Deutsch Barry M. Deutsch	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)
/s/ BJ Bormann BJ Bormann	Director
/s/ Dawn Halkuff Dawn Halkuff	Director
/s/ Marla Persky Marla Persky	Director
/s/ John Schmid John Schmid	Director
/s/ Jeffrey Sherman Jeffrey Sherman	Director

Exhibit 10.34

FOURTH AMENDMENT TO AMENDED AND RESTATED LOAN AND SECURITY AGREEMENT

THIS FOURTH AMENDMENT to Amended and Restated Loan and Security Agreement (this "**Amendment**") is entered into as of October 23, 2020, by and among OXFORD FINANCE LLC, a Delaware limited liability company with an office located at 133 North Fairfax Street, Alexandria, Virginia 22314 ("Oxford"), as collateral agent (in such capacity, "**Collateral Agent**"), the Lenders listed on Schedule 1.1 to the Loan Agreement (as defined below) or otherwise a party thereto from time to time including Oxford in its capacity as a Lender and SILICON VALLEY BANK, a California corporation with an office located at 3003 Tasman Drive, Santa Clara, CA 95054 ("Bank" or "SVB") (each a "**Lender**" and collectively, the "**Lenders**"), and XERIS PHARMACEUTICALS, INC., a Delaware corporation with offices located at 180 North LaSalle Street, Suite 1600, Chicago, IL 60601 ("**Borrower**").

A. WHEREAS, Collateral Agent, Borrower and Lenders have entered into that certain Amended and Restated Loan and Security Agreement dated as of September 10, 2019 (as amended, supplemented or otherwise modified from time to time, including by that certain First Amendment to Amended and Restated Loan and Security Agreement dated as of April 21, 2020, that certain Second Amendment to Amended and Restated Loan and Security Agreement dated as of June 30, 2020, and that Third Amendment to Amended and Restated Loan and Security Agreement dated as of August 5, 2020, collectively, the "Loan Agreement") pursuant to which Lenders have provided to Borrower certain loans in accordance with the terms and conditions thereof; and

B. WHEREAS, Borrower has requested that Collateral Agent and Lenders (i) make Credit Extensions to Borrower and (ii) make certain other revisions to the Loan Agreement as more fully set forth herein; and

C. WHEREAS, Borrower, Lenders and Collateral Agent desire to amend certain provisions of the Loan Agreement as provided herein and subject to the terms and conditions set forth herein.

AGREEMENT

NOW, THEREFORE, in consideration of the promises, covenants and agreements contained herein, and other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, Borrower, Lenders and Collateral Agent hereby agree as follows:

1. Definitions. Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.

2. Amendments to Loan Agreement.

2.1 Section 2.2 (Term Loans). Section 2.2(a)(iv) of the Loan Agreement is hereby amended and restated in its entirety as follows:

"(iv) Subject to the terms and conditions of this Agreement, the Lenders agree, severally and not jointly, during the Third Draw Period, to make term loans in a single disbursement to Borrower in an aggregate amount equal to Ten Million Dollars ($10,000,000.00) according to each Lender's Term C Loan Commitment as set forth on Schedule 1.1 hereto (such term loans are hereinafter referred to singly as a "**Term C Loan**", and collectively as the "**Term C Loans**"). After repayment, no Term C Loan may be re-borrowed."

2.2 Section 2.2 (Term Loans). New Section 2.2(a)(v) is hereby added to the end of Section 2.2(a) of the Loan Agreement as follows:

"(v) Subject to the terms and conditions of this Agreement, the Lenders agree, severally and not jointly, during the Fourth Draw Period, to make term loans in a single disbursement to Borrower in an aggregate amount equal to Three Million Five Hundred Thousand Dollars ($3,500,000.00) according to each Lender's Term D Loan Commitment as set forth on Schedule 1.1 hereto (such term loans are hereinafter referred to singly as a "**Term D Loan**", and collectively as the "Term D Loans"; each Term A

Loan, Term B Loan, Term C Loan or Term D Loan is hereinafter referred to singly as a "Term Loan" and the Term A Loans, the Term B Loans, the Term C Loans and the Term D Loans are hereinafter referred to collectively as the "Term Loans"). After repayment, no Term D Loan may be re-borrowed."

2.3 Section 13.1 (Definitions). The following terms and their respective definitions hereby are added or amended and restated in their entirety, as applicable, to Section 13.1 of the Loan Agreement as follows:

"**Fourth Amendment Effective Date**" is October 23, 2020.

"**Fourth Draw Period**" is the period commencing on the Fourth Amendment Effective Date and ending on the earlier of (i) November 16, 2020, and (ii) the occurrence of an Event of Default.

"**Term D Loan**" is defined in Section 2.2(a)(v) hereof.

"**Term Loan**" is defined in Section 2.2(a)(v) hereof.

2.4 Schedule 1.1 to the Loan Agreement hereby is replaced with Schedule 1.1 attached hereto.

3. Limitation of Amendment.

3.1 The amendments set forth above are effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right, remedy or obligation which Lenders or Borrower may now have or may have in the future under or in connection with any Loan Document, as amended hereby.

3.2 This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents are hereby ratified and confirmed and shall remain in full force and effect.

4. Representations and Warranties. To induce Collateral Agent and Lenders to enter into this Amendment, Borrower hereby represents and warrants to Collateral Agent and Lenders as follows:

4.1 Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except (i) to the extent such representations and warranties relate to an earlier date, in which case they are true and correct as of such date and (ii) solely with respect to the litigation representation and warranties contained in Section 5.3 of the Loan Agreement, to the extent such representations and warranties relate to (x) any actual or potential dispute between Borrower and SVB based on, arising from, relating to, or in connection with the Borrower's Paycheck Protection Program loan or (y) any settlement, release or other resolution thereof between SVB and the Borrower) and (b) no Event of Default has occurred and is continuing;

4.2 Borrower has the power and due authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

4.3 The organizational documents of Borrower delivered to Collateral Agent on the Effective Date, and updated pursuant to subsequent deliveries by or on behalf of the Borrower to the Collateral Agent, remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

4.4 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not contravene (i) any material law or regulation binding on or affecting Borrower, (ii) any material contractual restriction with a Person binding on Borrower, (iii) any material order, judgment or decree of any court or other governmental or public body or authority, or subdivision thereof, binding on Borrower, or (iv) the organizational documents of Borrower;

4.5 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not require any order, consent, approval, license, authorization or validation of, or filing, recording or registration with, or exemption by any governmental or public body or authority, or subdivision thereof, binding on Borrower, except as already has been obtained or made;

4.6 This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

5. Effectiveness. This Amendment shall be deemed effective as of the date hereof upon the due execution, by the parties thereto, and delivery to Collateral Agent and Lenders of: (a) this Amendment; and (b) the Corporate Borrowing Certificate attached hereto.

6. Counterparts. This Amendment may be executed in any number of counterparts, each of which shall be deemed an original, and all of which, taken together, shall constitute one and the same instrument. Delivery by electronic transmission (e.g. ".pdf") of an executed counterpart of this Amendment shall be effective as a manually executed counterpart signature thereof.

7. Governing Law. This Amendment and the rights and obligations of the parties hereto shall be governed by and construed in accordance with the laws of the State of New York.

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IN WITNESS WHEREOF, the parties hereto have caused this Fourth Amendment to the Amended and Restated Loan Agreement to be executed as of the date first set forth above.

BORROWER:

XERIS PHARMACEUTICALS, INC.

By /s/ Barry M. Deutsch
Name: Barry M. Deutsch
Title: Chief Financial Officer

COLLATERAL AGENT AND LENDER:

OXFORD FINANCE LLC

By /s/ Colette H. Featherly
Name: Colette H. Featherly
Title: Senior Vice President

LENDER:

SILICON VALLEY BANK

By /s/ Kristine Rohmer
Name: Kristine Rohmer
Title: Vice President

SCHEDULE 1.1

Lenders and Commitments

Term A Loans

Lender	Term Loan Commitment	Commitment Percentage
OXFORD FINANCE LLC	$48,000,000.00	80.00%
SILICON VALLEY BANK	$12,000,000.00	20.00%
TOTAL	**$60,000,000.00**	**100.00%**

Term B Loans

Lender	Term Loan Commitment	Commitment Percentage
OXFORD FINANCE LLC	$12,000,000.00	80.00%
SILICON VALLEY BANK	$3,000,000.00	20.00%
TOTAL	**$15,000,000.00**	**100.00%**

Term C Loans

Lender	Term Loan Commitment	Commitment Percentage
OXFORD FINANCE LLC	$8,000,000.00	80.00%
SILICON VALLEY BANK	$2,000,000.00	20.00%
TOTAL	**$10,000,000.00**	**100.00%**

Term D Loans

Lender	Term Loan Commitment	Commitment Percentage
OXFORD FINANCE LLC	$0.00	0.00%
SILICON VALLEY BANK	$3,500,000.00	100.00%
TOTAL	**$3,500,000.00**	**100.00%**

Aggregrate (all Term Loans)

Lender	Term Loan Commitment	Commitment Percentage
OXFORD FINANCE LLC	$68,000,000.00	76.8362%
SILICON VALLEY BANK	$20,500,000.00	23.1638%
TOTAL	**$88,500,000.00**	**100.00%**

Exhibit 10.36

AMENDMENT AND RESTATEMENT TO QUALITY AGREEMENT

This Amendment and Restatement Agreement (this "Amendment") has been made and entered into as of November 16, 2020 (the "Effective Date") to that certain Quality Agreement, dated as of November 16, 2016 (as amended, supplemented or otherwise modified from time to time and in effect as of the date hereof, the "Agreement"), by and between Xeris Pharmaceuticals, Inc. ("Xeris") and PYRAMID Laboratories, Inc. ("PYRAMID"). Capitalized terms used but not otherwise defined herein shall have the meanings ascribed to them in the Agreement.

NOW, THEREFORE, the parties intending to be legally bound, hereby agree as follows:

Amendment and Restatement. The Agreement is hereby amended and restated, effective as of the Effective Date, to read as set forth in Annex 1.

Miscellaneous.

(i) Governing Law. Section 25.9 of the Commercial Supply Agreement dated May 1, 2018, as amended by that certain Amendment No. 1 dated September 1, 2018, shall apply to this Amendment directly as if incorporated herein.

(ii) Counterparts. This Amendment and Restatement may be executed by one or more of the parties to this Amendment and Restatement on any number of separate counterparts, and all of said counterparts taken together shall be deemed to constitute one and the same instrument. Delivery of an executed signature page of this Amendment and Restatement by email or facsimile transmission shall be effective as delivery of a manually executed counterpart hereof.

(iii) Headings. The headings of this Amendment and Restatement are inserted merely for convenience and ease of reference and will not affect or modify the meaning of any of the terms, covenants or conditions of this Amendment and Restatement.

* * *

IN WITNESS WHEREOF, the parties hereto have caused this Amendment and Restatement to be duly executed and delivered by their respective duly authorized officers as of the Effective Date.

XERIS PHARMACEUTICALS, INC.:
By: /s/ Michele Yelmene
Name: Michele Yelmene
Title: Vice President, Regulatory and Quality Assurance

PYRAMID LABORATORIES, INC.:
By: /s/ Heba Mina
Name: Heba Mina
Title: Director of Quality

Annex 1
[See attached Quality Agreement]

QUALITY AGREEMENT

By and between

Contract Vendor Name: *PYRAMID Laboratories, Inc. (PYRAMID)*
Address: *3598 Cadillac Avenue, Costa Mesa, CA 92626*

("PYRAMID")

and

Company: *XERIS Pharmaceuticals, Inc.*
Address: *180 N. LaSalle St.*
Suite 1600
Chicago, IL 60601

("XERIS")

XERIS and PYRAMID may each be referred to herein individually as a "Party" and collectively as the "Parties."

The Parties wish to further define their individual and collective responsibilities as to the quality aspects of the Product or Service to ensure compliance with applicable current Good Manufacturing Practices (cGMPs), applicable regulatory submissions for the Product, applicable regulatory submissions for the Services, other applicable regulatory requirements, and XERIS' requirements as specified by XERIS (the "XERIS Requirements").

In order to achieve this purpose, this Quality Agreement includes a detailed listing of the activities and corresponding responsibilities associated with the Product or Service. Unless otherwise indicated, responsibility for each specified activity is assigned to either XERIS or PYRAMID, or to both Parties.

Agreement by the Parties to perform the activities detailed in this Quality Agreement is indicated by each authorized representatives' signature below:

PYRAMID Laboratories, Inc.

/s/ Heba Mina
Signature
Name: Heba Mina
Title: Director of Quality

November 16, 2020
Date

XERIS Pharmaceuticals, Inc.

/s/ Michele Yelmene
Signature
Name: Michele Yelmene
Title: Vice President Regulatory and Quality Assurance

November 19, 2020
Date

TABLE OF CONTENTS

1.0 QUALITY AGREEMENT

1.1 Effective Date

This Quality Agreement shall remain effective and binding upon the date of the final signature that appears on page 1 ("Effective Date") and remain in effect until [***] after the date of the last shipment unless XERIS specifically requests an extension of the Agreement.

1.2 Scope

This Quality Agreement outlines the obligations and responsibilities of PYRAMID Laboratories, Inc. (hereinafter referred to as "PYRAMID") and XERIS (herein referred to as "XERIS") with respect to quality assurance of the Product or Service.

1.3 Other Agreements

This Quality Agreement shall complement and is without prejudice to all other agreements containing distribution, commercial, legal or other terms, which have been entered into between the Parties regarding the Product or Service covered by this Quality Agreement, including, without limitation, that a certain Master GMP Manufacture Contract between XERIS and PYRAMID Laboratories, Inc between the Parties dated May 11, 2018 (the "Master Services Agreement"). If there are any direct conflicts between the terms of this Quality Agreement and the terms of the Master Services Agreement, then (a) this Quality Agreement shall govern with respect to issues directly related to Product specifications or Service quality matters, and (b) the Master Services Agreement shall govern with respect to all other matters.

1.4 Amendments to Quality Agreement

Amendments to this Quality Agreement must be in writing and signed by the appropriate representatives of each Party before they are deemed effective.

The Parties agree to amend terms of this Quality Agreement that need to be amended in order to ensure the Product or Service continues to meet all (a) regulatory requirements of applicable jurisdictions and (b) XERIS requirements.

If an amendment to this Quality Agreement is proposed, the proposing Party will communicate the proposed amendment to the appropriate contact person at the other Party for review and approval. The appropriate contact person for each Party is listed in Appendix 1 (Contacts and Responsibilities).

1.5 Termination of Quality Agreement

Term. This Quality Agreement shall become effective as of the Effective Date and shall terminate upon the later of (a) expiration or termination of the Master Services Agreement and (b) the final date on which PYRAMID provides Products or Services to XERIS. Notwithstanding the foregoing, if the Products or Services cease to be provided by PYRAMID to XERIS, this Quality Agreement may be terminated by either Party on providing [***] advance written notice of termination to the other Party.

Survival. All regulatory obligations required of XERIS or PYRAMID by any applicable regulatory authorities and all obligations of the Parties under effective regulations shall survive expiration or termination of this Quality Agreement. Examples of such requirements include, but are not limited to: Recalls, Complaint and Adverse Event handling and reporting, deviations and investigations, completion of stability studies, provision of information to XERIS which is necessary to maintain compliance with regulatory filings. Also, those provisions of the Master Services Agreement between the Parties shall not be affected by expiration or termination of this Quality Agreement, including, without limitation, any duties regarding confidentiality or non-disclosure.

1.6 Debarment

PYRAMID warrants and represents that it is not debarred under the Generic Drug Enforcement Act of 1992, 21 U.S.C. 335[a] (the "Generic Drug Enforcement Act"), and that it has not been convicted of a crime for which it could be debarred under the Generic Drug Enforcement Act. In connection with the Product (or provision of Services), PYRAMID further warrants, represents, and covenants that it shall not use in any capacity the services of any person debarred under the Generic Drug Enforcement Act, or convicted of a crime for which a person can be debarred under the Generic Drug Enforcement Act.

1.7 Use of Third-Parties

PYRAMID may not subcontract or delegate any of its obligations under this Quality Agreement to any third-party (including, without limitation, any affiliate of PYRAMID) unless XERIS provides prior written consent to PYRAMID for such subcontracting or delegation. Before XERIS grants any such written consent, XERIS may be required to enter into a written agreement with the third-party ("Third-Party Agreement").

PYRAMID shall not be responsible for the acts and omissions of any permitted subcontractors listed in this Quality Agreement in Appendix 4 and Xeris may enter into an appropriate written contract with such subcontractors to ensure the qualification and auditing of such subcontractors.

1.8 Assignment

PYRAMID shall not assign any or all of its rights or obligations under this Quality Agreement without XERIS' prior written consent, which consent may be granted or withheld in XERIS' sole discretion. XERIS shall have the right to assign any or all of its rights or to delegate its obligations under this Quality Agreement without the consent of PYRAMID. In the event of a permitted assignment under this Quality Agreement, the assigning Party shall continue to be bound by all pre-existing obligations under this Quality Agreement including all obligations of confidentiality and non-disclosure.

2.0 PRODUCT

The Product or Service provided for XERIS by PYRAMID includes:
As described in the Master Services Agreement.

3.0 ADMINISTRATIVE INFORMATION

A XERIS and PYRAMID contact list for each project will be maintained and updated as necessary by XERIS QA and PYRAMID QA. The contact list will be in an agreed upon location and notification of changes to the list will be communicated by XERIS QA and PYRAMID QA.

4.0 DEFINITIONS

4.1 **API**
Active Pharmaceutical Ingredient.

4.2 **Batch Production Records**
Batch Production Records are a compilation of master documents and records that contain the procedures and specifications for the Product. These master documents and records are prepared for each stage of Production for a Batch of Product, and include information relating to Production and control of the Batch.

4.3 **Batch Record Package**
Batch Record Package is a compilation of records containing the Production history and control of a Product. These records are generated by Manufacturing and Quality Control (“QC”) and reviewed and approved by Quality Assurance (“QA”). The Batch Record Package consisting of: bill of materials, manufacturing instructions, formulation, appropriate packaging instructions, labeling, and deviation documentation and additional documentation which may have been processed as part of the production record of the Batch. Attachments to the Batch Record Package may include environmental monitoring reports and copies of in-process test records, as required by the Project Plan. Ancillary documents such as raw material COAs and their incoming test results are generally not part of the Batch Record Package but are kept under Good Documentation Practices on site at PYRAMID.

4.4 **BSE/TSE Certification**
Bovine Spongiform Encephalopathy (BSE) is a Transmissible Spongiform Encephalopathy (TSE) that affects cattle.

4.5 **cGMP**
Current Good Manufacturing Practices

4.6 **Certificate of Analysis (COA)**
A document issued by Quality Assurance that confirms that a drug product meets its product specification. They commonly contain the actual results obtained from testing performed as part of quality control of an individual batch of a drug product.

4.7 **Certificate of Compliance (COC)**
Certificate of Compliance or COC means the certificate to be issued by PYRAMID stating that the Product was produced and tested in compliance with: (i) applicable cGMP guidelines, (ii) terms of this Quality Agreement, (iii) PYRAMID’s internal policies and procedures, and (iv) the “XERIS” written requirements.

4.8 **Components**

Any ingredient intended for use in the manufacture of a drug product, including those that may not appear in such drug. This includes such items as filters, containers, closures and tubing.

4.9 **Date of Manufacture (DOM)**
The date of compounding.

4.10 **Drug Substance**
Drug Substance is an active ingredient for biological drug products, such as peptides, oligonucleotides and proteins.

4.11 **Expiration Date**
The date designating the time during which the Product is expected to remain within established shelf life specifications if stored under defined conditions.

4.12 **Lot Number**
Lot Number is any distinctive combination of letters, numbers, or symbols, or any combination of them, from which the complete history of the manufacture, processing, packing, holding and distribution of a batch or lot of drug product or other material can be determined.

4.13 **Material Specifications**
A composite of the specifications and testing performed on Raw Materials, Process Consumables, Components, and Bulk Drug Substance used to evaluate identity, purity, quality and safety, as appropriate for its intended use. It describes the chemical, physical, microbiological/biological test requirements, storage conditions, and handling requirements of the material. It also may contain the testing that is performed by the vendor on the Process Consumables, Components and Drug Substance as well as other requirements of the vendor's certificate of analysis/certificate of compliance.

4.14 **Non-Conformance Report (NCR)**
Any deviation which may potentially impact the safety, identity, strength, purity, efficacy, or quality of the Product is investigated. These written reports detail the specifics of an investigation resulting from a deviation to approved procedures or specifications (e.g., deviations, OOS). The investigation includes a description of the incident, investigation, root cause, conclusions and corrective action or action plan, if applicable.

4.15 **Planned Deviation Report**
The document which is used to obtain approvals of either planned changes to temporarily modify approved operating, manufacturing, testing instructions, or procedures; or to intentional document excursions from approved operating, manufacturing, testing instructions, target/informational test results, or procedures. The deviation does not permanently change existing instructions, batch records, or procedures; it is intended to be a specific/one-time use document.

4.16 **Product Specifications**
Product Specifications is a list of tests, references to analytical procedures, and appropriate acceptance criteria which are numerical limits, ranges or other criteria for the tests described for a specific product. It establishes the set of criteria to which a drug substance or drug product should conform to be considered acceptable for its intended use. "Conformance to specifications" means that the drug substance and / or drug

product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria.

For added clarity, in-process Product Specifications/requirements are documented within the Batch Production Record and final Product Specifications/requirements are documented within Material Specifications. Product Specifications are a composite of the specifications, PYRAMID instructions, and Test Methods for a drug or material and is used to evaluate its identity, purity, quality and safety, as appropriate. It describes the chemical, physical, microbiological and biological requirements for testing of the drug and storage conditions.

4.17 **Process Consumables**
One-time use items such as tubings, filters, etc. These items are very specific to a batch and will be disposed of following production of the batch.

4.18 **Raw Materials**
Raw Materials means the materials used in the Production of the Product that may become part of the finished Product such as Active Pharmaceutical Ingredient (API), excipients, and buffer components.

4.19 **Redress**
The repackaging or placement of additional labeling operation.

4.20 **Repackaging**
A repetition of a packaging step which requires a de-packaging operation such as exchange of folding box, exchange of leaflet or insert, or de-labeling/relabeling.

4.21 **Reinspection**
A visual or mechanical/physical evaluation performed to remove/correct defective units for which the process is not expected to have an adverse effect on Product quality.

4.22 **Reprocessing**
Duplication of a step or steps currently in the Production process in order to bring the Product into conformance with Product Specifications and which will not alter the safety, identity, strength, quality, or purity of the Product beyond the established Product Requirements. In addition, an extension of an approved process step is also regarded as reprocessing.

4.23 **Retest Date**
The date when a material should be reexamined to ensure that it is still suitable for use.

4.24 **Rework**
Reworking is subjecting a material or product that does not conform to a standard or specification to one or more manufacturing steps that are different from the manufacturing process described in the application to obtain acceptable material or product.

4.25 **Stickering**
An operation by which the information content of an existing packaging material is altered (changed or added). This alteration is accomplished by the addition of another label(s) or printing of additional information on the existing packaging materials.

4.26 **Sub-lot**
A unique portion or sub set of a Lot, such as a different unit size or fill volume within the same Lot.

4.27 **Test Method**
A Test Method describes chemical, microbiological, or biological testing procedures and equipment, reagents, calculations, analysis and data interpretation documentation requirements within the QC Analytical Chemistry and Microbiological laboratories.

5.0 cGMP COMPLIANCE WITH REGULATIONS

5.1 The principles detailed in the US cGMP (21 CFR 210 and 211) and the Rules Governing Medicinal Product in the European Community – Volume IV Good Manufacturing Practice for Medicinal Products will cover the standards of Production of the Product. cGMP guidelines will also cover the standards of quality assurance and quality control for the Product, including any Product license requirements only as communicated to PYRAMID by XERIS.

5.2 PYRAMID and XERIS are responsible for following all Applicable Laws including cGMP, local, state, and federal laws, as well as applicable terms of both the Master Services Agreement and this Quality Agreement.

6.0 PRODUCTION

6.1 General

The Production operations for the Product to be performed by PYRAMID are defined in the Project Plans or Work Orders.

6.2 Facility

6.2.1 PYRAMID will produce the product at the Facility as specified in the production batch record. The floor plan of the production area and corresponding room classifications are available for review during annual audits of the Facility.

6.2.2 PYRAMID will ensure that the Facility and equipment used to produce the Product will be qualified and maintained according to current regulatory requirements and in accordance with the Master Batch Records used to produce the product. The production of the product will be conducted in a suitably controlled environment and such facilities will be regularly monitored for parameters critical to the process to demonstrate compliance with cGMP guidelines and the batch production records.

6.2.3 PYRAMID will maintain controlled access to the premises as a whole including the Facility. PYRAMID will maintain all XERIS Confidential Information as defined in the Master Services Agreement.

6.3 Personnel

6.3.1 PYRAMID will provide adequate personnel with the appropriate education, training and experience to execute responsibilities defined in this Quality Agreement.

6.3.2 XERIS is responsible for providing personnel qualified to train PYRAMID personnel during technology transfer of Production processes and analytical methods.

6.4 **Materials Management**

6.4.1 PYRAMID will use only raw materials, process consumables and components approved by XERIS and sampled, tested and stored in accordance with the Materials Specifications.

6.5 Inventory Management

6.5.1 PYRAMID shall maintain an accurate inventory listing of Components, labeling, and printed labels stored at PYRAMID on behalf of XERIS. Inventory reports, including description, quantity, and receipt date shall be provided to XERIS upon request.

6.5.2 PYRAMID shall have written instructions for printing, labeling and label reconciliation.

6.6 **Supplier Qualification**

6.6.1 XERIS shall be qualify raw materials (API, etc.) and container closure components (syringe, pistons, vials, stoppers etc.) supplied to PYRAMID. Certification that XERIS has performed audits shall be furnished to PYRAMID upon request.

6.6.2 PYRAMID shall qualify container components, raw materials, and Process Consumables not supplied by XERIS.

6.6.3 Materials Procured by PYRAMID

6.6.3.1 PYRAMID is responsible for ensuring all raw materials, process consumables and components procured by PYRAMID for use in the production complies with the specifications approved by XERIS. PYRAMID is responsible for ensuring all raw materials, process consumables and components are appropriately sampled and tested upon receipt, as well as for holding the relevant Certificates of Analysis for the Raw materials, process consumables and components. PYRAMID is responsible for ensuring raw materials, process consumables and components are released prior to use. PYRAMID is responsible for notifying XERIS of any issues or change requests.

6.6.3.2 PYRAMID will ensure PYRAMID suppliers are audited, qualified and monitored per PYRAMID SOPs.

6.6.3.3 For PYRAMID sourced items, PYRAMID is responsible for maintaining a program to evaluate animal derived material and control the risk of Bovine Spongiform

Encephalopathy (BSE) and Transmissible Spongiform Encephalopathy (TSE) and other potential infectious agents.

6.6.4 Materials Sourced by XERIS

6.6.4.1 XERIS is responsible for ensuring all materials sourced by XERIS for use in the production of product comply with the specifications. XERIS will provide PYRAMID a Certificate of Analysis for all materials sourced by XERIS. If there is any change to the formulation, manufacture, testing, or specifications of any materials sourced by XERIS, XERIS will notify PYRAMID within [***] of any such change in reasonable detail including any additional hazards that result therefrom or storage parameters that are required therefore prior to sending such materials sourced by XERIS to the PYRAMID facility.

6.6.4.2 XERIS will communicate within [***], any problem confirmed by XERIS that is a change in acceptability of all materials sourced by XERIS. PYRAMID will evaluate the status change for its impact to PYRAMID systems.

6.6.4.3 For XERIS sourced items, XERIS is responsible for maintaining a program to evaluate animal derived material and control the risk of Bovine Spongiform Encephalopathy (BSE) and Transmissible Spongiform Encephalopathy (TSE) and other potential infectious agents, and shall be provided to PYRAMID

6.7 **Batch Production Records**

6.7.1 PYRAMID shall transcribe the production information into its own Master Batch Record format and will obtain written approval from XERIS for each document version before production. However, agreed upon changes to documentation will be handled as outlined by Change Policy (see Article 11.0).

6.8 **Standard Operating Procedures**

6.8.1 PYRAMID is responsible for maintaining any Standard Operating Procedures required to Produce, test, and store the product at PYRAMID and to support cGMPs.

6.9 **Dates of Production and Expiration/Retest of Product**

6.9.1 Date of Production – Date of Production is based on the date that API is added to the liquid to initiate the formulation (compounding) steps.

6.9.2 Expiration/Retest Date – XERIS will calculate the Expiration/Retest Date from the date of production (see Section 6.9.1) using the shelf life accepted by the FDA or other regulatory agency as appropriate and as communicated by XERIS to PYRAMID

6.10 **Production (Facilities) and Equipment Data**

6.10.1 PYRAMID is responsible for keeping records of equipment usage (previous product produced in non-dedicated equipment), cleaning, any maintenance, and calibration performed.

6.10.2 PYRAMID is responsible for maintaining calibration and preventive maintenance procedures and schedules for equipment/instruments used in the Production, packaging, testing and validation/qualification of the product.

6.10.3 PYRAMID, as a multi-product facility, will have specific written procedures in place to control cross contamination of products.

6.10.4 PYRAMID is responsible for labeling all Product dedicated equipment and storing this equipment appropriately to prevent its use for other products.

6.10.5 PYRAMID will have well defined written procedures in place for environmental monitoring.

6.11 **Reinspection, Redress, Reprocessing, and Rework**

6.11.1 Redress, reprocessing or rework of Product shall not be performed without prior approval by PYRAMID QA and XERIS QA. Documentation for redress, reprocessing or rework will be per approved protocol or batch production record and execution records will be included in the batch documentation submitted to XERIS upon completion.

6.11.2 Reinspection, reprocessing, or rework will require a deviation investigation except where a standard procedure or batch production record allows for such routine activity in the course of normal processing.

6.12 **Storage and Shipment**

6.12.1 Storage – PYRAMID will store the Product as per the Product Specifications approved by XERIS. PYRAMID will ensure there is no possibility of interference, theft, product contamination, or admixture with any other materials during storage before shipping of the Product. XERIS will provide details of any labeling and container requirements including container sealing and integrity.

6.12.2 Packaging and Labeling for Transit – The Product will be suitably packaged and labeled for transit. The configuration and labeling of the shipping containers shall be specified by or approved by XERIS QA. Product designated for shipment outside of the United States shall be labeled in accordance with applicable laws.

6.12.3 Shipment of Product – XERIS will authorize PYRAMID to ship product upon submission of a formal XERIS request in writing. Released product will be shipped by PYRAMID to a location designated by XERIS. Quarantined Product may only be shipped with approval of XERIS QA and PYRAMID QA. Product samples required for testing or further processing may be shipped prior to release of the product with Approval by XERIS QA. For commercial products, XERIS is responsible for ensuring that shipping configurations and containers are validated. XERIS is

responsible for ensuring that shipping configurations meet all applicable transportation legal requirements (e.g. Department of Transportation (DOT), etc.).

6.12.4 XERIS is responsible for monitoring the shipment to its destination and acquiring shipping information such as temperature data.

6.12.5 PYRAMID will ship product to designated sites following procedures approved by XERIS which conform to the regulatory submission for the product using shipping containers, temperature controls, and recorders authorized by XERIS.

6.13 Product and Process Development

6.13.1 XERIS is responsible for all product, process development and process validation including component compatibility unless specifically contracted to PYRAMID. PYRAMID will comply with the relevant requirements of this Agreement to support the realization of XERIS product development. XERIS will provide the necessary information to allow PYRAMID to manufacture and ship XERIS Products meeting the specifications set forth in this Agreement. Specifically:

6.13.1.1 Product and Process Design are XERIS' responsibility. At XERIS' request, PYRAMID will collaborate on design of development and scale up studies and process assessments designed to evaluate sources of process variability and how to control them. PYRAMID may also perform these studies at XERIS' direction. It is XERIS' responsibility to work with PYRAMID to define the process controls and operational ranges for the manufacturing process.

6.14 Risk Management

6.14.1 XERIS is ultimately responsible for product risk management. PYRAMID will collaborate with XERIS, when requested, on product risk assessments.

6.14.2 PYRAMID is responsible for the assessment, control, and mitigation of risks related to the manufacturing processes for the product. PYRAMID will provide information to XERIS on all pFMEAs, deviations, changes, test results, etc., which affect the product and may impact product risk assessments.

7.0 QUALITY CONTROL

7.1 General

7.1.1 Testing activities for the product, which are to be performed by PYRAMID, shall be determined by XERIS and specified in the Product Specifications.

7.1.2 XERIS is responsible to supply of all non-compendial reference standards. PYRAMID is responsible for the qualification of all non-compendial reference standards according to XERIS specification

7.2 Subcontracting

7.2.1 PYRAMID will notify XERIS of outsourcing of analytical testing within [***]. PYRAMID shall not outsource any testing without prior written consent by XERIS.

7.3 **PYRAMID Supplied Raw Materials, Process Consumables, and Components**

7.3.1 Quality control of raw materials, process consumables, and components supplied by PYRAMID will be undertaken by PYRAMID unless otherwise specified in writing by XERIS. PYRAMID will notify XERIS of any investigations related to the storage and handling of any raw materials, process consumables, and components supplied by PYRAMID that have been used to produce product.

7.4 **In-Process and Finished Product Testing**

7.4.1 PYRAMID will perform in-process and finished product testing as directed by XERIS using approved XERIS Product Specifications and validated, or otherwise verified, Test Methods.

7.4.2 A Certificate of Analysis, confirming that the Product has been Produced and tested in accordance with the Product Specifications, will be issued by PYRAMID, XERIS or XERIS designated laboratory.

7.4.3 XERIS may perform testing at its cost to confirm or supplement the PYRAMID data. XERIS may perform confirmatory testing to validate the PYRAMID data. Periodically thereafter, XERIS may test material to confirm the PYRAMID data. Resolution of disagreements regarding conflicting test data will be handled per Article 10.0.

7.4.4. Shipping of samples to XERIS or a third-party contract laboratory will be per a validated or otherwise qualified shipping method provided by or approved by XERIS.

7.5 **Reserve Samples (Retain Samples)**

7.5.1 XERIS is responsible for storing reserve (retain) samples of product per 21 CFR 211.170.

7.5.2 Retain samples shall consist of at least enough material to perform full testing two times.

7.5.3 PYRAMID and / or XERIS is responsible for storing reserve (retain) samples of (a) primary packaging materials, (b) Raw Materials, except water, compressed gases, highly volatile compounds and those that are not stable, and (c) Bulk Drug Substance used in the formulation of the Product for [***] past product expiration date assigned by XERIS, or for [***] after distribution of the batch, whichever is longer.

7.6 **Stability Program**

7.6.1 XERIS is responsible for maintaining a stability-testing program for the product and reference standards. PYRAMID will provide samples of product to XERIS or

XERIS' designated testing facility for placement on a stability program as directed by XERIS in this Quality Agreement. XERIS is responsible for identifying the batch number and quantity of product for each lot to be tested.

7.7 Out-of-Specification (OOS) Investigations

7.7.1 PYRAMID is responsible for investigating any testing performed by PYRAMID that fails to meet Product Specifications and notifying XERIS within [***] of the initiation of any investigation. XERIS QA retains the right to review and investigation data and reports to provide technical comments and assist with corrective action(s). Each investigation will be reviewed by PYRAMID's designated Quality representative and will follow the procedures recommended by regulatory agencies and as defined in appropriate PYRAMID Standard Operating Procedures for OOS investigations. All completed investigation reports will be included in the released, executed Batch Record Package that will be provided to XERIS QA.

7.7.2 PYRAMID must obtain XERIS quality assurance approval for retesting and/or resampling prior to the initiation of testing for any OOS not determined to be the cause of a laboratory error.

8.0 QUALITY ASSURANCE

8.1 Documentation

8.1.1 XERIS shall have the right to review and approve (such approval not to be unreasonably withheld) the following documents associated with their product prior to implementation: (i) Product Specifications, (ii) Product specific Test Methods, (iii) Master Batch Records and (iv) Raw Material, Process Consumables, Components and in-process specifications as part of the Master Batch Record approval, (v) Product specific Standard Operating Procedures (vi) stability, process validation, laboratory method validation/qualification, equipment qualification, and cleaning validation protocols and summary reports specific to their Product or XERIS dedicated-equipment.

8.1.2 Master Batch Record – PYRAMID is responsible for creating the product specific Master Batch Record. XERIS will approve each revision of the Master Batch Record prior to its use for cGMP Production. Original executed Batch Record Packages with Lot Numbers issued by PYRAMID will be maintained on-site by PYRAMID's Quality Assurance Unit.

8.1.3 Product Specific Standard Operating Procedures – PYRAMID is responsible for creating and maintaining the product specific Standard Operating Procedures based on XERIS supplied information. XERIS will review such Standard Operating Procedures and provide approval.

8.1.4 General Standard Operating Procedures – PYRAMID is responsible for creating and maintaining all Standard Operating Procedures and other documentation required to support cGMP operations at PYRAMID. XERIS will be allowed to review such Standard Operating Procedures during on-site audits.

8.1.5 Labels – PYRAMID or XERIS may generate a label proof for review. Approval will be by XERIS QA and PYRAMID prior to generation and use of labels for product.

8.2 **Deviations**

8.2.1 Deviations – Any deviation from the process during Production, including but not limited to, Batch Production Record execution, environmental monitoring excursions or processing procedures, will be carefully explained and documented in an investigation and referenced in the Batch Production Record per PYRAMID procedures. All temporary changes to Batch Production Records or Standard Operating Procedures are reviewed and approved by PYRAMID QA prior to implementation. Deviations must be justified and approved by PYRAMID's designated quality representative and, the affected area management, and be included in the released, executed Batch Record Package.

8.2.1.1 XERIS product Related Deviations – Deviations will be communicated to XERIS within [***] of the discovery of the deviation. All investigations related to Product will be forwarded to XERIS QA for review as part of the released, executed Batch Record Package. Each investigation will be reviewed and approved by PYRAMID's designated quality representative. XERIS will review and approve, such approval not to be unreasonably withheld, Deviation reports review and approval process shall not exceed [***]. XERIS retains final disposition of any Batch of Product. PYRAMID is responsible for investigating any test result or in-process test which fails to meet Product Specifications (see 7.7 OOS). XERIS, as product experts, may, at its cost, conduct its own independent failure investigation, and may participate in the PYRAMID failure investigation, as applicable.

8.2.2 XERIS will authorize the disposition of any batch of product aborted or rejected by PYRAMID.

8.2.3 PYRAMID will provide notification to XERIS if any problems are discovered that may impact product previously shipped to XERIS or its distributor(s) or licensee(s) within [***] of discovery and initiation of the investigation.

8.3 **Batch Disposition**

8.3.1 For each batch, PYRAMID will provide to XERIS the released Batch Record Package for review.

8.3.2 PYRAMID is responsible for ensuring the product has been produced according to the Product Specifications, procedures documented in the Batch Production Records, and this Quality Agreement. PYRAMID will provide to XERIS a Certificate of Compliance.

8.4 **Product Release**

8.4.1. Approval and release, or rejection, of the product is the absolute and legal responsibility of XERIS' Quality Unit. Product release will be undertaken by XERIS

based on XERIS' internal procedures, the Batch Record Package documentation provided by PYRAMID, and completion of any release testing required by XERIS.

8.4.2. Any problem discovered by XERIS likely to cause rejection of the Product will be communicated to PYRAMID promptly upon discovery and in any event within [***] following receipt of Product samples and Batch Record Package documentation.

8.5 **Records Retention**

8.5.1 PYRAMID will retain commercial Batch Production Records for the product for a minimum of [***] beyond the Expiration Date of Product. Otherwise they will be returned according to PYRAMID's retention SOP.

8.5.2 PYRAMID will return any Batch Production Records past the date in 8.5.1 after first notifying XERIS QA in writing no less than [***] in advance.

8.5.3 All other non-commercial Batch Records will be retained according to PYRAMID's SOP.

8.5.4 Electronic copies (scanned) of Batch Production Records will be stored in accordance with PYRAMID's record keeping SOP.

8.6 **Production and Quality Presence in the Production Facility**

8.6.1 PYRAMID will permit no more than two (2) XERIS representative to be present at the site in the Facility where product is being Produced. PYRAMID will permit only [***] representative in the formulation area for observational purposes only. XERIS representative while at the Facility shall at all times be subject to obligations of confidentiality set forth in Article 14 of the Master Services Agreement and all of PYRAMID's rules and procedures.

8.7 **Self-Inspection**

8.7.1 PYRAMID will operate an annual internal auditing program to drive continuous improvement of cGMP operations.

8.8 **Product Complaints**

8.8.1 XERIS is responsible for receiving and initially investigating any product complaints. XERIS will notify PYRAMID within [***] of discovery of any problems thought to be due to production, which are found during the distribution of the product and provide product samples, if applicable, representative of the complaint. PYRAMID will perform investigations for any issue thought to be due to production of product. Investigation reports will be forwarded to XERIS within [***] of initiation of the investigation or PYRAMID will notify XERIS and the Parties will agree, through good faith discussions, on a new target date for completion.

8.9 **Product Recalls**

8.9.1 Each Party will notify the other Party within [***] of (a) receipt of written notice if any batch of product is alleged or proven to be the subject of a recall, market withdrawal or correction or (b) either Party's determination that a recall is necessary. XERIS is responsible for instituting a product recall, market withdrawal or correction. XERIS will notify PYRAMID of any recall within [***] of initiation. Investigation reports regarding the defect or cause of the recall or withdrawal will be forwarded to XERIS within [***] after receipt of request. In the event that the investigation requires additional time to complete, PYRAMID will notify XERIS QA and the Parties will agree, through good faith discussions, on a new target date for completion.

8.10 Adverse Events

8.10.1 Unless otherwise defined herein, the terms used surrounding adverse experiences shall have the meanings set forth in the International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use.

8.10.2 XERIS shall advise PYRAMID of any adverse medical event or adverse drug event within [***] of XERIS' receipt of notice thereof if thought to be due to production of product. PYRAMID will perform investigations for any issue thought to be due to production of product. Investigation reports will be forwarded to XERIS within [***] of initiation of the investigation or PYRAMID will notify XERIS and the Parties will agree, through good faith discussions, on a new target date for completion.

9.0 REGULATORY COMPLIANCE

9.1 Regulatory Inspections

9.1.1 PYRAMID will permit access by the regulatory agencies to PYRAMID's premises. PYRAMID will notify XERIS QA of any announced regulatory inspections that directly involve the product within [***]. PYRAMID will immediately inform XERIS of any unannounced regulatory inspections that directly involve XERIS product. PYRAMID will permit XERIS representatives (such representatives to be reasonably acceptable to PYRAMID) to be present at the Facility for a pre-approval inspection or any subsequent inspection that directly involves XERIS product. XERIS personnel may be allowed to participate directly in the inspection.

9.1.2 PYRAMID will secure the agreement of XERIS QA prior to making any commitment to a regulatory agency specifically regarding XERIS Product. XERIS shall be provided with draft responses to regulatory observations that directly involve the Product and its Production prior to submission to the regulatory authorities. XERIS QA/RA shall have ability to provide comments to the responses and corrective actions and approve final responses which pertain directly to the product. PYRAMID shall retain the final authority for corrective actions and content of the responses to the regulatory authority for all non-product related items.

9.1.3 PYRAMID will forward to XERIS QA any observations and responses from a routine regulatory inspection relating to the Facility where XERIS' product is produced.

9.1.4 XERIS will inform PYRAMID in writing of any regulatory issue that impacts PYRAMID's ability to produce the product promptly upon the discovery or receipt thereof and in any event within [***].

9.2 **Regulatory Actions**

9.2.1 XERIS will provide PYRAMID a copy of the relevant Product sections of the Chemistry, Manufacturing, and Controls (CMC) section of their regulatory filings prior to submission for review and comment by PYRAMID's Regulatory Affairs department.

9.2.2 XERIS will notify PYRAMID of any regulatory actions related to the product that may impact PYRAMID promptly upon the discovery or receipt thereof and in any event within [***].

9.2.3 Each party agrees to supply the other Party with any production, testing, or storage data within [***] if requested, as the result of a regulatory inspection, or a potential regulatory exposure such as a recall or significant product complaint.

9.3 **Right to Audit**

9.3.1 PYRAMID will allow representatives from XERIS, or Qualified Person for EU, to have access to PYRAMID's production, warehousing, laboratory premises, records, regulatory filings (i.e., DMF) and communications (i.e., FDA 483s) solely for audit purposes listed below in Sections 9.3.2 through 9.3.4; and subject at all times to PYRAMID's obligation to protect the confidential information of its clients.

9.3.2 PYRAMID will permit XERIS to conduct a 2- day preparatory audit of cGMP Production of the product for the pre-approval inspection for product.

9.3.3 PYRAMID will permit XERIS to conduct 'for cause' audits to address product quality or safety problems as discovered through product failures or complaints related to PYRAMID's production of the product, for so long as such problems exist and are persisting or directly after the occurrence of such problem.

9.3.4 PYRAMID will permit XERIS to perform [***] cGMP compliance audit per year.

9.3.5 PYRAMID will use reasonable efforts with its critical vendors, contractors or subcontractors used in the Production of Product to facilitate audits by XERIS.

9.3.6 While at PYRAMID's premises, XERIS agrees to follow (and shall cause its representatives to follow) all of PYRAMID's rules and procedures and shall use its best efforts not to interfere with or interrupt other PYRAMID projects or PYRAMID personnel.

9.4 **Audit Closeout**

9.4.1 An exit meeting will be held with representatives from PYRAMID and XERIS to discuss significant audit observations.

9.4.2 XERIS will provide a written report of all observations within [***] to PYRAMID. Within [***] of the audit report receipt, PYRAMID will provide a written response to all findings that details corrective action to be implemented. PYRAMID will follow up to ensure all corrective actions are implemented.

10.0 RESOLUTION OF DISAGREEMENTS

10.1 Non-conformity Dispute – In the event that a dispute arises between PYRAMID and XERIS regarding the conformity of a Batch of Product, the resolution will proceed in stages. The first stage requires direct communication between the Quality units from both Parties (Appendix 2) who will in good faith promptly attempt to reach an agreement. If these actions fail to achieve resolution the second stage will employ a qualified third-party consultant to review the Batch Record Package and related documentation. This third-party consultant must be agreeable to both Parties prior to use. The results from this referee consultant will be used as final authority regarding the conformity or non-conformity of the batch of product and the responsibility therefore if non-conforming. Financial liability is determined in the Master Services Agreement.

10.2 Test Result Dispute – Notwithstanding the requirements outlined in the MSA, in the event that a dispute arises between PYRAMID and XERIS in the testing performed by PYRAMID for the product, the resolution will proceed in stages. The first stage requires direct communication between Quality units from both Parties (Appendix 2) to determine that the methods of analysis are the same and are being executed in the same manner at the applicable sites. Second, carefully controlled and split samples should be sent from one site to another in an attempt to reach agreement. Should there be a failure to achieve resolution, Quality management from the Parties will be required to meet to work through the analysis of a mutually agreeable sample. If these actions fail to achieve resolution a qualified referee laboratory will be used to analyze the samples. This laboratory must be agreeable to both Parties prior to use. The results from this referee laboratory will be used as final authority to determine conformity or non-conformity and the responsibilities therefore if non-conforming. Financial liability is determined in the Master Services Agreement.

11.0 CHANGE POLICY

11.1 All changes to approved documents will be managed via PYRAMID's change control or planned deviation processes.

11.2 All proposed changes go through a technical, regulatory, and cGMP impact assessment by the PYRAMID expert groups per PYRAMID change control procedure. The scope of this change process potentially impacting the Product (for Phase III, registration, or commercial purposes) includes but is not limited to Raw Materials, Process Consumables, Components and or their suppliers, packaging materials, labeling, Production process, equipment, XERIS specific validated

equipment, Facilities, utilities or computer systems, Product Specifications, and test methods.

11.3 The Product-specific controlled documents for Phase III, registration, or commercial purposes such as Batch Records, Product Specifications, and Product related Standard Operating Procedures or changes that may affect XERIS' regulatory submissions will also go through XERIS' review for regulatory impact, implementation requirements, and XERIS' approval. Changes must have appropriate documentation to justify the rationale behind the change.

11.4 The Parties will assess changes within [***] and for those changes marked urgent, the Parties will use commercially reasonable efforts to assess within [***].

11.5 Each Party agrees to notify the other of changes in key project personnel to ensure the effectiveness of arrangements and assure the quality of the Product.

11.6 XERIS will notify PYRAMID in writing who is authorized to make and approve changes on their behalf.

12.0 PRODUCT AND PROCESS VALIDATION

12.1 Process Validation– XERIS is responsible for ensuring the PYRAMID production process is validated for product. The validation should ensure the process is capable of effectively and reproducibly achieving the product acceptance specifications and quality attributes. PYRAMID shall provide adequate resources to execute process validations as per mutually approved protocols. XERIS is responsible for development and validation of the manufacturing process including processing hold times, formulation and process parameters, and filter validations. The activities may be contracted to PYRAMID, and if so, terms shall be outlined in the Master Services Agreement or in the Project Plan.

12.1.1 PYRAMID will work in conjunction with XERIS to support their process validation or related studies. PYRAMID may perform these studies on behalf of XERIS. XERIS holds final responsibility for the study design and execution, results, conclusions, and approval.

12.1.2 PYRAMID will provide XERIS with appropriate quality system, material, process, or product data to support XERIS' continued process verification activities. PYRAMID may also collaborate with XERIS on process assessments as a means of evaluating process variability. PYRAMID performs routine reviews of quality system, manufacturing, calibration, and maintenance data as part of the [***] management review. Where appropriate, those data may be made available to XERIS for incorporation in to their process verification activities.

12.2 Cleaning Verification– PYRAMID is responsible for ensuring adequate cleaning of product contact parts used in the Production of Product is carried out between Batches of different product to prevent contamination.

12.3 Sterilization and Depyrogenation Validation – PYRAMID is responsible for ensuring sterilization processes are validated and adequate sterilization and

depyrogenation is carried out on the Components and appropriate equipment prior to the Production of each Batch of Products.

12.4 Equipment, Computerized Systems, Facility, and Utilities Qualification – PYRAMID is responsible for ensuring any equipment, computer, Facility, utility and support systems used to produce product are qualified according to applicable regulatory requirements.

12.5 Laboratory Qualification – PYRAMID is responsible for ensuring all laboratories are in compliance with cGMPs and are qualified in all of the methodology associated with the product. If product specific analytical work is performed at PYRAMID, then XERIS will provide any relevant analytical documentation to assist in the methods transfer or methods validation. PYRAMID is responsible for third party laboratory qualification unless such laboratory is specified by XERIS. PYRAMID may be contracted to qualify third party laboratory at XERIS' expense.

13.0 PERIODIC PRODUCT REVIEW, ANNUAL REPORT AND DRUG LISTING

13.1 Annual Report

XERIS is responsible for preparing any annual report as required by applicable regulations. At least [***] before the annual report due date, XERIS shall request in writing from PYRAMID any data required for submission of the annual report. PYRAMID will provide the requested information to XERIS within [***].

13.2 Drug Listing

PYRAMID is responsible for site Establishment Registration with the appropriate agency, while XERIS is responsible for drug listing activities including listing PYRAMID as the manufacturer of the product. PYRAMID will provide XERIS with applicable information needed for drug listing, including Establishment Registration number and/or Facility Establishment Identifier (FEI) number.

14.0 QUALITY RESPONSIBILITIES TABLE

	Responsibilities	XERIS	PYRAMID
A.	**Compliance Requirements**		
1.01	Follow applicable regulations and current Good Manufacturing Practices, as well as locally imposed requirements. • 21 CFR Part 4 • 21 CFR Part 11 • 21 CFR Parts 210 and 211 • 21 CFR Part 820.20 • 21 CFR Part 820.50 • 21 CFR Part 820.100 • Eudralex – Annexes 1 and 13, the Rules Governing Medicinal Products in the European Union, Volume 4 EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use. • ICH Q9 – Quality Risk Management • ICH Q10 – Pharmaceutical Quality System • Eudralex - The Rules Governing Medicinal Products in the European Union, Volume 10, Chapter 3 Applicable compendia requirements (e.g. USP, EP), as required by XERIS and ***PYRAMID*** agreed to in writing by the Parties.	**[***]**	**[***]**
1.02	Follow all applicable laws including cGMP, local, state and federal laws.	**[***]**	**[***]**
1.03	Manufacture, package, ship, store and test the product and materials in an environment meeting the applicable cGMP regulations, which is designed, constructed and maintained in a manner that a) permits the operation therein to be performed under clean, sanitary and orderly conditions; b) permits the effective cleaning of all surfaces; and c) prevents the contamination of the Product and the addition of extraneous material to the Product.	**[***]**	**[***]**
1.04	Manufacture the product in adherence to approved Master Batch Records (MBRs) and product specifications, etc. where applicable.	**[***]**	**[***]**
1.05	Refrain from activity that could adversely affect quality of the Product.	**[***]**	**[***]**
1.06	Have management controls in place to track and trend investigations and corrective or preventative action commitments.	**[***]**	**[***]**
1.07	Maintain a Quality Unit that is independent of production and that fulfills both quality assurance and quality control responsibilities.	**[***]**	**[***]**
1.08	Disposition of product by Quality Unit or Qualified Person (QP) after review of all relevant documents (see Appendix 3) to ensure compliance.	**[***]**	**[***]**
1.09	Product failing to meet specifications may not be supplied to XERIS without XERIS' prior written consent.	**[***]**	**[***]**
1.10	Involve the Quality Unit in all cGMP related matters.	**[***]**	**[***]**
1.11	Notify XERIS within [***] of any changes not subject to cGMP change control that would affect documentation within this Quality Assurance Agreement including but not limited to PYRAMID's "Primary Contacts", "Quality Agreement Signatory", or a company name change due to a merger/acquisition.	**[***]**	**[***]**

	Responsibilities	XERIS	PYRAMID
1.12	Maintain adequate internal and external audit programs per cGMP.	[***]	[***]
1.13	Maintain effective quality systems that minimize the potential for product quality, regulatory and compliance issues.	[***]	[***]
1.14	Permit a representative of XERIS to be present during any stage manufacture of product (Person in the Plant). Reference section 8.6.	[***]	[***]
B	**Right to Audit**		
2.01	Have the right to audit PYRAMID's facilities and systems [***] per year, as they relate to the manufacture of Product, at appropriate times. XERIS retains the right to conduct "for cause" audits as necessary.	[***]	[***]
2.02	Have the right to perform 2-Day Pre-PAI audit of facilities and systems.	[***]	[***]
2.03	Schedule visits and/or audits.	[***]	[***]
2.04	Request product-specific documents for review to ensure continued adherence to the agreed upon manufacturing process, applicable cGMP and other applicable requirements during audits.	[***]	[***]
2.05	Provide documents as requested in 2.03.	[***]	[***]
2.06	Issues PYRAMID a confidential audit report summarizing audit observations within [***] of the audit date. If required by XERIS policies and procedures or by any competent authority, XERIS reserves the right to share the audit report with a third-party undertaking QC release activity in relation to Product on behalf of XERIS.	[***]	[***]
2.07	Issue responses to all observations in writing to XERIS within [***] of receipt. Responses are to include timelines and plans for closure of all commitments.	[***]	[***]
2.08	Ensure that deficiencies highlighted during these audits are remediated in accordance with a mutually agreed upon action plan.	[***]	[***]
C	**Regulatory Inspections and Exchanges**		
3.01	Coordinate all activities necessary to ensure readiness prior to regulatory agency Pre-Approval Inspections and maintain inspection readiness throughout the approval process.	[***]	[***]
3.02	Coordinate all activities necessary to ensure and maintain readiness for all announced and unannounced regulatory agency inspections.	[***]	[***]
3.03	Notify XERIS within[***] of receiving a written notification of failures to comply with cGMP after a general site inspection (i.e. an inspection not directly related to a specific XERIS product or service) from any regulatory agency.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
3.04	Notify XERIS within [***] of being notified of any pending or ongoing regulatory authority inspection or communication related to XERIS products or the facilities, equipment, or process used to produce, test or warehouse the product. In the event that the inspection pertains to XERIS product, PYRAMID shall permit a representative of XERIS to be present during any such inspection. If a XERIS representative cannot be on site for the inspection, then daily updates will be communicated to XERIS summarizing the inspector's observations.	[***]	[***]
3.05	Obtain XERIS approval for all documents and correspondence related to XERIS products, prior to providing same to any regulatory agency, provide a list or copies of all documents directly related to a XERIS Product or operations that have been shared with a regulatory agency during any inspection. Copies of PYRAMID's product related correspondence with regulatory agencies will also be provided to XERIS.	[***]	[***]
3.06	Provide copies to XERIS within [***] of correspondence received from regulatory authorities (Boards of Health, Health Authority, etc.) related to XERIS product and related operations performed by PYRAMID, other than correspondence described in item 3.03.	[***]	[***]
3.07	Notify XERIS QA by telephone, followed by written communication, within [***] of the receipt of a Regulatory Authority inspection report, deficiency letter or regulatory compliance observation, which contains any significant adverse findings that relate to XERIS products or the facilities used to produce, test, or warehouse the product. Significant adverse findings include, but are not limited to, conditions, practices, or processes that adversely affect or may potentially adversely affect product or service quality and/or the rights, safety or wellbeing of subjects/patients and/or the quality and integrity of data, documentation, or other materials or information addressed in the inspection.	[***]	[***]
3.08	Provide a copy of the EIR, regulatory inspection report, deficiency letter, or regulatory compliance observations, response and related correspondence to XERIS, edited to exclude PYRAMID proprietary information within [***] of receipt. Allow XERIS to review, comment on the response, and approve the response relevant to product supplied to XERIS QA, prior to submission of the response to the regulatory authority.	[***]	[***]
3.09	Notify PYRAMID of any regulatory compliance observation received by XERIS that pertains to operations performed by PYRAMID and requires PYRAMID information or action within [***] of receipt.	[***]	[***]
3.10	Provide XERIS with information requested to ensure compliance with regulatory requirements within [***] of notification, or as required to meet regulatory obligations.	[***]	[***]
3.11	Upon obtaining written permission from XERIS QA, sample and retain an equal amount of product if samples of XERIS product are taken by the regulatory authority, until given further written instruction from XERIS.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
3.12	Provide PYRAMID with advance written notification of new or supplemental regulatory submission/application that impacts the operations performed by PYRAMID within [***] of submission.	[***]	[***]
D.	**Regulatory Documentation**		
4.01	Provide all necessary Letters of Authorization, or other documentation, to permit reference to PYRAMID's Master File(s) to facilitate the registration of the Product, if applicable.	[***]	[***]
4.02	Maintain annual reports as required in accordance with the regulations of the applicable regulatory authority. At least [***] before the annual report due date, request in writing from PYRAMID any data required for submission.	[***]	[***]
4.03	Provide requested data for annual reports within [***].	[***]	[***]
4.04	Liaison with Regulatory Authorities for approval, maintenance and updating of regulatory submissions where required.	[***]	[***]
4.05	Notify XERIS of any regulatory application change as applicable within [***] before submitting the change to authority and prior to implementation.	[***]	[***]
4.06	Upon request, provide assistance in the preparation and review of pertinent sections of new or supplemental regulatory applications where XERIS owns the product registration and submit comments to the proposed application to XERIS.	[***]	[***]
4.07	Provide sections of product registration/regulatory submissions relevant to PYRAMID manufacture and quality control of XERIS product for review prior to submission.	[***]	[***]
4.08	Establish appropriate data verification procedures for data generated in support of regulatory documents submission by XERIS.	[***]	[***]
4.09	Ensure that XERIS is provided copies of current health authority regulatory licenses, cGMP certificates and related documents.	[***]	[***]
4.10	Secure and maintain all licenses and implement all necessary regulatory compliance procedures (e.g., compliance with DEA Regulations, Schedules 1-5) necessary to (a) receive and process active pharmaceutical ingredients and drug products relating to products and Services at PYRAMID's facilities and (b) distribute products to XERIS' designated facilities.	[***]	[***]
E.	**Animal Derived Materials**		
5.01	Have an effective program in place for PYRAMID sourced materials that is aligned with XERIS requirements to evaluate and control the risk of BSE/TSE for raw materials and components.	[***]	[***]
5.02	Notify XERIS of the use of any animal derived materials. The foregoing requirement includes any animal derived materials used in the Product manufacturing process including: (i) those used as machine lubricants, cleaning agents/aids and/or processing aids, and; (ii) any animal derived materials that have contact with product.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
5.03	Maintain appropriate records for each lot of animal derived material to ensure traceability. Where required by local regulations, the location where animals lived or were slaughtered (if applicable) must be documented.	[***]	[***]
5.04	Provide BSE/TSE certification from vendors of materials supplied to PYRAMID by XERIS.	[***]	[***]
F.	**Buildings and Facilities**		
6.01	Buildings and facilities used in the manufacture, handling or storage of the product shall be designed, constructed and maintained to facilitate cleaning, maintenance and operations and to ensure orderly placement of equipment and materials to prevent mix-up and contamination.	[***]	[***]
6.02	Ventilation systems will be designed and maintained to minimize the risk of contamination.	[***]	[***]
6.03	Dispose of sewage, refuse and other waste in a safe and timely manner following applicable environmental health and safety regulations.	[***]	[***]
6.04	Maintain a set of current drawings for critical utilities including water, electricity, compressed gasses and air handling.	[***]	[***]
6.05	Maintain and document an adequate, effective pest control program.	[***]	[***]
6.06	Notify XERIS prior to the implementation of a change in product category manufactured in the same facility and equipment as XERIS Product (such as veterinary drugs or hazardous, deleterious, potent or sensitizing materials, for example: Penicillin, beta-lactam, etc.).	[***]	[***]
6.07	Notification to XERIS within [***] of any significant shutdowns or operational interruptions of PYRAMID's facilities which may impact XERIS Products.	[***]	[***]
6.08	Notify and receive approval from XERIS prior to use of existing or expanded laboratory or storage facilities that have not been specifically reviewed for their suitability during a XERIS cGMP compliance audit or without prior written approval by XERIS.	[***]	[***]
G.	**Personnel and Training**		
7.01	Provide sufficient training, including applicable cGMPs, to meet obligations of this Quality Agreement.	[***]	[***]
7.02	Provide adequate personnel, qualified by appropriate training and experience to perform and supervise the technology transfer, manufacture, testing, packaging and disposition of the product.	[***]	[***]
7.03	Ensure training is regularly conducted, assessed and documented by qualified individuals.	[***]	[***]
7.04	Have written job descriptions for positions responsible for performing cGMP related activities.	[***]	[***]
7.05	Ensure that non-employees, including consultants, advising on the manufacture and control of the product have sufficient education, training, and experience to advise on the subject for which they are retained. Non-employees will be supervised as required and trained in cGMP.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
H.	**Material Management and Suppliers Qualification**		
8.01	XERIS shall qualify supplier and raw materials (API, etc.) and container closure components (syringe, pistons, vials, stoppers, etc.) supplied to PYRAMID. Xeris shall provide certification of vendor and material qualification to PYRAMID, upon request.	[***]	[***]
8.02	PYRAMID shall qualify components, raw materials, and Process Consumables not supplied by XERIS.	[***]	[***]
8.03	Ensure all raw materials, process consumables and components are appropriately sampled and tested upon receipt and hold the relevant Certificates of Analysis for the raw materials, process consumables and components.	[***]	[***]
8.04	Ensure raw materials, process consumables and components are released prior to use.	[***]	[***]
8.05	Ensure PYRAMID suppliers are qualified and monitored per PYRAMID SOPs.	[***]	[***]
8.06	Ensure all materials sourced by XERIS for use in the production of product comply with the specifications.	[***]	[***]
8.07	Provide PYRAMID a Certificate of Analysis for all materials sourced by XERIS.	[***]	[***]
8.08	Maintain an accurate inventory listing of components stored at PYRAMID on behalf of XERIS. Inventory reports, including description, quantity, and receipt date shall be provided to XERIS upon request.	[***]	[***]
I.	**Sub-Contracting**		
9.01	XERIS is responsible to identify and qualify any Sub-Contractors that may be required for analytical testing, third party manufacturing, sterilization, or any special studies. XERIS shall ensure these Sub-Contractors operate in compliance with current cGMP, compendial requirements and any other applicable regulations.	[***]	[***]
9.02	Not engage any Sub-Contractor without the prior written consent of XERIS QA. PYRAMID is responsible to provide samples to Subcontractors to perform finished product testing to support product release as indicated in the batch record.	[***]	[***]
9.03	Maintain Sub-Contractor as a qualified contractor following approved procedures in accordance with XERIS Requirements. Documentation should be supplied to PYRAMID to allow for confirmation by external auditors when necessary.	[***]	[***]
J.	**Change Control**		

	Responsibilities	XERIS	PYRAMID
10.01	Have approved written procedures for control of changes impacting the product including, but not limited to, manufacturing components/raw materials or process, packaging materials, labeling, computer hardware/software, product specifications, and test methods. Ensure any changes are reviewed/approved by Quality Unit. Include in written procedures the process and criteria for customer notification and approval, follow up and closure of changes.	[***]	[***]
10.02	Notify XERIS as soon as reasonable, but no later than [***] after any emergency, unplanned changes which directly impact a XERIS product or Service. In the case of emergency changes, PYRAMID and XERIS shall cooperate to expedite the review and approval process prior to final acceptance of the change.	[***]	[***]
10.03	Notify XERIS of all significant changes to facility, process, test methods, quality systems and specifications. Significant changes are those that impact Product identity, strength, safety, potency, purity, MFG. site, stability, regulatory status or validation/qualification(s).	[***]	[***]
10.04	Issue a change request for each change as soon as possible after the need for change is apparent, allowing [***] for XERIS to comment and approve or reject changes prior to implementation or for PYRAMID to comment on the feasibility of or timeline for the change.	[***]	[***]
10.05	Provide copies of change control documentation such as supporting data, validation/qualification reports and contractor approved change control forms for changes impacting product as requested by XERIS.	[***]	[***]
10.06	Implement monograph changes in order to meet new or revised compendial requirements.	[***]	[***]
10.07	Jointly establish a strategy to secure regulatory approvals as necessary and to mutually agree to an implementation timetable.	[***]	[***]
10.08	Specify to PYRAMID who is authorized to make and approve changes (per Section 11 of this Agreement) on behalf of XERIS.	[***]	[***]
K.	**Validation/Qualification**		
11.01	Define all process parameters, critical process control points and quality attributes and Specifications.	[***]	[***]
11.02	Have a written master validation/qualification plan for the facilities, equipment/instruments, manufacturing process, cleaning procedures, analytical procedures, in process control tests and computerized systems approved by the Quality Unit (as appropriate).	[***]	[***]
11.03	Prepare and maintain validation/qualification documentation approved by the Quality Unit, including protocols, reports and associated documentation. Provide such documents to XERIS upon request.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
11.04	Validate/qualify as necessary all critical systems, utilities and equipment/instruments used for the manufacture and control of product (through Installation Qualification (IQ), Operational Qualification (OQ), and/or Performance Qualification (PQ)).	[***]	[***]
11.05	Validate/qualify computer systems and associated software used in cGMP-related activities associated with the product. procedures must be in place to ensure the integrity, archiving, retrieval and destruction of the electronic data that comply with applicable regulations.	[***]	[***]
11.06	Validate/qualify methods and procedures for cleaning of equipment with acceptance criteria for residues defined and justified. Alternative evaluations of cleaning validation/qualification (dedicated equipment, matrix approach, worst case scenario, etc.) are to be approved by XERIS.	[***]	[***]
11.07	Develop and execute a plan for process and method validation/qualification including definition of roles and responsibilities between PYRAMID and XERIS for performing technology transfers, if applicable.	[***]	[***]
11.08	Where method validation is performed by PYRAMID:	[***]	[***]
	• Write method validation protocol,	[***]	[***]
	• Review and approve method validation protocol,	[***]	[***]
	• Execute method validation protocol,	[***]	[***]
	• Write method validation report, and	[***]	[***]
	• Review and approve method validation report.	[***]	[***]
11.09	For process validation:	[***]	[***]
	• Write process validation protocol,	[***]	[***]
	• Review and approve process validation protocol,	[***]	[***]
	• Execute process validation protocol,	[***]	[***]
	• Write process validation report, and	[***]	[***]
	• Review and approve process validation report.	[***]	[***]
11.10	Validate/qualify all manufacturing processes, product formulation, mixing operations and hold times for the formulation process.	[***]	[***]
11.11	Qualify time limitations for each phase of production.	[***]	[***]
11.12	Evaluate protocol deviations encountered during validation/qualification to determine impact on validation/qualification studies, including need to conduct repeat studies.	[***]	[***]
11.13	Evaluate validated/qualified systems and processes periodically to verify they are still operating in a valid manner.	[***]	[***]
11.14	Report all media simulation failures for Product related aseptic manufacturing processes.	[***]	[***]
11.15	Permit a representative of XERIS to be present during process demonstration and validation.	[***]	[***]
11.16	Validate / qualify bioburden and sterility assays.	[***]	[***]
L.	**Preventive Maintenance and Calibration**		

	Responsibilities	XERIS	PYRAMID
12.01	Maintain calibration and preventive maintenance procedures and schedules for equipment/instruments used in the manufacture, packaging, testing and validation/qualification of the Product. Include calibration tagging where appropriate.	[***]	[***]
12.02	Inform XERIS within [***] if an investigation for an out of calibration or out of tolerance instrument used for services performed for XERIS concludes that there could be impact on Product.	[***]	[***]
12.03	Document and review (including calibration performed by Sub-Contractor) manufacturing and laboratory equipment/instrumentation calibration data.	[***]	[***]
M.	**Manufacturing and Laboratory Investigations**		
13.01	Have appropriate procedures for the identification, investigation, reporting, tracking, trending and closure of deviations as per applicable cGMP requirements. Investigations must include but are not limited to known lab errors, atypical results, and Out-of-Specification (OOS) results that occur during the manufacture and testing of the Product.	[***]	[***]
13.02	Document and notify XERIS within [***] of first knowledge of any significant deviation. Significant deviations include, but are not limited to, those which have the potential to affect the quality, identity, purity and/or strength of the product; those which impact the cGMP, validation/qualification or regulatory status; any OOS test result which cannot be invalidated within *** or any deviation resulting in the product being outside of filed registration limits (see Appendix 3 for examples). XERIS retains the right to request notification of additional deviations on a case by case basis. All deviations must be resolved prior to release of Product.	[***]	[***]
13.03	Review and approve any significant deviation prior to product release.	[***]	[***]
13.04	Provide investigation/deviation documentation for approval, including original and any retest or resample results to XERIS QA with the batch record, or upon request.	[***]	[***]
13.05	Assist PYRAMID in investigations when deemed appropriate.	[***]	[***]
13.06	Complete investigations within [***] of commencement.	[***]	[***]
13.07	Approve in writing any significant deviation from PYRAMID's internal specifications or standard operating procedures that may affect XERIS products or services. The decision to approve will not be unreasonably withheld or delayed.	[***]	[***]
13.08	Complete corrective/preventive action (CAPA) commitments resulting from investigation closure within the planned timeframe. Provide evidence of closure of CAPA items to XERIS for notified deviations.	[***]	[***]
N.	**Documentation and Records**		
14.01	Document all required process and testing steps at the time such process or testing step is executed.	[***]	[***]
14.02	Record all changes to process or testing documents in a cGMP compliant fashion (e.g., by initialing and dating all changes).	[***]	[***]

	Responsibilities	XERIS	PYRAMID
14.03	Have a controlled system to initiate, review, revise, approve, obsolete and archive all cGMP documentation.	[***]	[***]
14.04	Maintain a document control system for Standard Operating Procedures.	[***]	[***]
14.05	Maintain a document control system for specifications, including: raw materials, product labeling, packaging materials and other materials that would likely affect Product quality.	[***]	[***]
14.06	Review and approve all cGMP-related records.	[***]	[***]
14.07	Retain, archive and destroy all cGMP-related documents and data pertaining to Services performed for XERIS in accordance with XERIS and regulatory requirements as defined below: • keep all original analytical records including test results, records, charts, computer reports, and graphs for a minimum period of [***] or if batch-related, one year in excess of expiration date, • keep all validation/qualification and technical transfer documents in connection with Service performed for XERIS for [***] after the life of the Product, • keep original investigation and OOS report documentation in connections with Services performed for XERIS for a minimum of [***] or [***] beyond expiration date of associated batch, at the end of retention period, notify XERIS prior to destruction of records identified above, including a specific identification of the records. XERIS retains the right to have all records transferred and to maintain any such record as it relates to product at its discretion, • ensure that original records are protected from fire and water damage in a limited access area and retain commercial Batch Records for a minimum of [***] beyond the Expiration Date of product. • retain Batch Record documentation to meet applicable regulatory requirements and any special instruction provided by XERIS.	[***]	[***]
14.08	Write Master Batch (or, as applicable, Packaging) Records.	[***]	[***]
14.09	Review and approve Master Batch Records.	[***]	[***]
14.10	Have all executed batch-related records reviewed and approved by PYRAMID's Quality Unit prior to submission to XERIS for release. Ensure records have a unique lot identification number.	[***]	[***]
14.11	Review executed Batch Records within [***].	[***]	[***]
14.12	[***]	[***]	[***]
14.13	For laboratory control records, include complete data derived from all tests conducted to ensure compliance with specifications. These records will contain the date and the signature of a second qualified person showing review and verification of the records.	[***]	[***]
14.14	Provide copies of documents or records needed to ensure compliance with regulatory requirements or filings to XERIS upon request.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
14.15	Provide copies of documents and records for XERIS disposition of product listed in Appendix 4.	[***]	[***]
14.16	Provide a Certificate of Analysis for the release of each manufactured lot.	[***]	[***]
14.17	Provide a complete Certificate of Analysis (only for tests performed by PYRAMID) for each shipment of the Product, containing at minimum the following information: • XERIS Product number, • PYRAMID Product number, (if applicable) • PYRAMID lot number, • Name of Product, • Batch size, • Quantity; • Name of the test (if applicable), • Test method (if applicable), • Specification limit (if applicable), • Expiration/Retest date (if applicable) • Actual test result (as a numerical value, unless designated Pass/Fail in the specification limit), including retest results if required (if applicable) • Date tested for each test (if applicable) • Quality Assurance approval and date, • Manufacturing site (name and address) • Manufacturing date, and • Storage conditions	[***]	[***]
14.18	Final release of the drug product.	[***]	[***]
14.19	Provide Certificate of Compliance certifying Product was manufactured in a current cGMP-compliant facility and was tested in accordance with and meets specifications and was manufactured according to its approved regulatory dossier.	[***]	[***]
14.20	Keep and make accessible to XERIS upon request all manufacturing, analytical, and distribution records. Where original documentation is in a language other than English, a direct translation to English will be provided by PYRAMID upon request by XERIS. Care should be taken that any changes made to the English version are also reflected in the original language documentation.	[***]	[***]
O.	**Production and In-Process Controls**		
15.01	Have approved written procedures in place for qualification of vendors or subcontractors that provide cGMP-materials and services.	[***]	[***]
15.02	Perform and maintain all PYRAMID qualifications in a current state as per applicable procedures and XERIS requirements.	[***]	[***]
15.03	Provide current Raw Material, API, and Product Specifications to PYRAMID.	[***]	[***]
15.04	Have a system for batch identification including assigning lot numbers.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
15.05	Implement and document specifications for raw materials, packaging materials, and product labeling and processing aids that would likely affect product quality pursuant to specification documentation provided by XERIS.	[***]	[***]
15.06	Have approved written procedures for all required in-process sampling and testing.	[***]	[***]
15.07	Procure, test (as required), and disposition raw materials, components, packaging and labeling used in manufacture and packaging of product.	[***]	[***]
15.08	Document actual yields for the product and evaluate actual yields versus theoretical in-process yield control limits.	[***]	[***]
15.09	Provide a XERIS-defined Date of Manufacture (DOM) for assigning to product.	[***]	[***]
15.10	Use a XERIS-defined Date of Manufacture (DOM) in the Master Batch Records (MBRs).	[***]	[***]
15.11	Assign Product expiration (shelf-life) date.	[***]	[***]
15.12	Have appropriate inspection process or device in place to ensure the correct product is packaged, the correct labeling is utilized, and any inline marking is completely and accurately located and legible.	[***]	[***]
15.13	Include in shipper label, at a minimum: • name and address of the manufacturer, • unique identifying code, • batch number, • quantity of contents, • storage and special transport conditions, • manufacturing date, • XERIS-assigned expiry date (if provided), and • any special requirements (if applicable).	[***]	[***]
15.14	Where appropriate, develop all labeling in accordance with applicable regulations (including for the country intended for distribution) and regulatory submission (as applicable).	[***]	[***]
15.15	Include a representative label in the batch record.	[***]	[***]
15.16	Approve label proof, generated by PYRAMID or XERIS, prior to generation and use of labels for Product.	[***]	[***]
15.17	Establish and maintain a program for environmental monitoring including tracking and trending processes.	[***]	[***]
15.18	Retain reserve samples of raw materials, packaging materials and Product label, intermediates (if applicable) in accordance with PYRAMID's written procedures.	[***]	[***]
15.19	Retain reserve samples of Final Product	[***]	[***]
15.20	Provide certification that all at-risk raw materials/components have been tested for the absence of BSE/TSE contamination for each lot of Product supplied to XERIS.	[***]	[***]
P.	**Process Equipment**		
16.01	Process equipment must be uniquely identified, status tagged and managed with an equipment history log or equivalent system. Process lines will be appropriately identified.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
16.02	Use appropriate food grade machine lubricants and oils that contain no animal derived materials.	[***]	[***]
16.03	Maintain a current set of “as-built” drawings for equipment and facilities.	[***]	[***]
Q.	**Reprocess (if applicable)**		
17.01	Where reprocessing is required and permitted, review and approve all reprocessing steps.	[***]	[***]
17.02	Document approval in specific reprocessing protocols or special batch record instructions.	[***]	[***]
17.03	Perform reprocessing only where specified in protocol or specific batch record instructions approved by XERIS.	[***]	[***]
17.04	Review and approve product requiring reprocessing.	[***]	[***]
R.	**Rework (if applicable)**		
18.01	Where rework is required and permitted, have a protocol or procedure that has been approved by both XERIS and PYRAMID, and any regulatory approval that may be required prior to implementation.	[***]	[***]
18.02	Review and approve Product requiring rework.	[***]	[***]
S.	**Laboratory Controls**		
19.01	Have written procedures for sample management, identification, testing, disposition and recording, approval, tracking, storage, retention and disposal of laboratory data.	[***]	[***]
19.02	Hold samples and dispose of them as required by specifications and procedures.	[***]	[***]
19.03	Destroy samples and sample packaging in a secure and legal manner that prevents unauthorized use or diversion in accordance with PYRAMID’s procedures. Maintain destruction records. Destruction method must render any XERIS owned registrations, logos or trademarks unidentifiable.	[***]	[***]
19.04	Have approved written procedures for management, preparation and use of reference standards, reference materials, reagents, and solutions including qualification/requalification of use period.	[***]	[***]
19.05	Mutually agree on source, grade and characterization of reference standards/materials, if not XERIS supplied.	[***]	[***]
19.06	Provide PYRAMID with qualified non-compendial standards and corresponding storage conditions, potency/purity information, and expiration/review dating.	[***]	[***]
19.07	Have appropriate specifications and test procedures for the Product, which are consistent with the applicable compendial monograph, XERIS-approved product monograph and/or Product Specifications.	[***]	[***]
19.08	Test Product in accordance with qualified or validated methods, as appropriate, and with specifications using calibrated, qualified equipment. Shall not perform reduced testing regimen without meeting requirements of an established program or protocol reviewed and agreed to by XERIS.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
19.09	Transfer all test methods qualified or validated by XERIS according to protocols (that includes roles & responsibilities) approved by PYRAMID and XERIS.	[***]	[***]
19.10	Ensure method transfers have been completed and approved prior to the generation of any cGMP test data.	[***]	[***]
T.	**Retest**		
20.01	Perform retesting, when required and approved, in accordance with approved protocols or procedures.	[***]	[***]
20.02	Approve retest protocols for retesting associated with confirmed OOSs as applicable.	[***]	[***]
U.	**Stability (if applicable)**		
21.01	Maintain a documented, ongoing stability program to monitor the stability of the Product using stability indicating procedures.	[***]	[***]
21.02	Store stability samples in containers/closures in accordance with approved protocols which include time stations and storage conditions.	[***]	[***]
21.03	Write and review stability protocol.	[***]	[***]
21.04	Approve stability protocols prior to executing stability studies.	[***]	[***]
21.05	Write and approve stability reports.	[***]	[***]
21.06	Assign and approve appropriateness of storage conditions and retest or expiry date base on stability data.	[***]	[***]
21.07	Perform stability testing of reworked/reprocessed batches or those associated with investigations or revalidations/re-qualifications as required by XERIS.	[***]	[***]
V.	**Storage and Distribution**		
22.01	Validate/qualify and maintain storage facilities appropriate for conditions specified on the Product label. Maintain records of any critical parameters.	[***]	[***]
22.02	Establish and maintain an environmental monitoring program including trending activities to ensure adherence to specified product, raw material, packaging material and component storage conditions (such as temperature and humidity).	[***]	[***]
22.03	Upon PYRAMID's receipt of sample(s) from XERIS, when samples are provided with temperature recorders, read recorder and report temperature excursions to XERIS.	[***]	[***]
22.04	Provide any special precautions to be taken during sample storage, handling, testing and disposal.	[***]	[***]
22.05	Provide PYRAMID with corresponding storage conditions and any details of labeling and container requirements including container sealing and integrity.	[***]	[***]
22.06	Receive, handle and store XERIS reference standards as defined in writing by XERIS. PYRAMID will maintain a use log (or equivalent) for all XERIS reference standards.	[***]	[***]
22.07	Have validated/qualified systems for controlling quarantined, rejected or recalled materials and segregate rejected or recalled materials.	[***]	[***]
22.08	Storage of bulk material per XERIS approved Specifications.	[***]	[***]

	Responsibilities	XERIS	PYRAMID
22.09	Storage of Finished Product per XERIS approved Specifications.	[***]	[***]
22.10	Provide Product Material Safety Data Sheet or equivalent.	[***]	[***]
22.11	Ship Product in accordance with qualified transportation requirements.	[***]	[***]
22.12	In the event of an environmental excursion affecting Product, notify XERIS QA within [***] and make subsequent investigation available to XERIS upon request.	[***]	[***]
22.13	Authorize PYRAMID to ship Product upon submission of a formal XERIS QA request in writing.	[***]	[***]
22.14	For commercial products, ensure that shipping configurations and containers are validated. Ensure that shipping configurations meet all applicable transportation legal requirements (e.g. Department of Transportation (DOT), etc.).	[***]	[***]
22.15	Monitor the shipment to its destination and acquire shipping information such as temperature data.	[***]	[***]
22.16	Have a system in place for ensuring commercial unreleased product is not shipped unless authorized by XERIS Quality Assurance unit.	[***]	[***]
22.17	Have validated/qualified systems for tracking product inventory and shipments and maintain appropriate records for such activities.	[***]	[***]
W.	**Control, Disposal and Destruction of Production Materials**		
23.01	Have a procedure for the access, control, reconciliation, disposition, disposal, and destruction of obsolete or rejected production materials proprietary to XERIS or bearing XERIS proprietary information used in the Product manufacture, packaging and labeling that include but is not limited to: • Active Pharmaceutical Ingredient/ Biological Drug Substance • Excipient Raw Materials • Tooling, dies, printing rolls, plates and associated drawings used in the manufacturing of Product. • XERIS printed components and materials used to print such component, including but not limited to: printed components, containers, closures, tools, dies, plates, drawings and artwork including all electronic files.	[***]	[***]
23.02	Dispose and destroy obsolete or rejected production materials in a secure and compliant manner that prevents unauthorized use or diversion in compliance with environmental regulations. Maintain destruction records and provide to XERIS upon request. Destruction method must render all XERIS owned trademarks, logos, or registration marks as unidentifiable.	[***]	[***]
X.	**Complaints**		
24.01	Have written procedures in place to document, investigate, issue reports, follow up, respond to XERIS and manage all product quality related complaints.	[***]	[***]
24.02	Where XERIS is the regulatory submission holder:	[***]	[***]

	Responsibilities	XERIS	PYRAMID
	• Notify PYRAMID within [***] of product complaints received by XERIS that potentially impact quality, purity, safety and effectiveness of distributed Product and could result in a product recall.	[***]	[***]
	• Manage complaint investigations and any required regulatory reporting.	[***]	[***]
	• Assist in investigations of Product-related complaints, as requested by XERIS QA and report progress of investigation to XERIS in a timely manner.	[***]	[***]
	• Retain complaint investigation records.	[***]	[***]
	• Evaluate trends and severity of complaint.	[***]	[***]
	• Implement corrective actions associated with manufacture of product.	[***]	[***]
24.03	Significant complaints (e.g. those alleging product contaminations, tampering, counterfeiting, etc. or which have been reported to a regulatory authority) require preliminary investigation and response to the other party within [***].	[***]	[***]
24.04	Should a complete investigation report not be able to be completed within [***] interim reports shall be communicated to XERIS QA until investigation is completed.	[***]	[***]
Y.	**Recalls**		
25.01	Where XERIS is the regulatory submission holder:	[***]	[***]
	• Each party will notify the other in writing within [***] of discovery of any product defects that could result in a product recall or abnormal restriction on the supply of product.	[***]	[***]
	• Sole responsibility for determining the need for recall of XERIS product. There shall be approved procedures for issuing field alerts, Biological Product Deviation Reports (as applicable), Product Defect Reports and recall that address the decision-making process, correspondence with regulatory agencies, management of recalls, and reconciliation of returned product.	[***]	[***]
	• Notify PYRAMID of any recall within [***] of initiation.	[***]	[***]
	• Cooperate and participate in the investigation to make the decision to issue field alerts, Biological Product Deviation Reports, Product Defect Reports or recalls.	[***]	[***]
	• Issue correspondence to regulatory agencies.	[***]	[***]
	• Manage recall and reconciliation of returned product.	[***]	[***]
Z.	**Adverse Experiences**		
26.01	XERIS shall be responsible for product adverse drug reaction reporting to regulatory authorities.	[***]	[***]
26.02	In the event XERIS has or receives any information regarding any adverse experience which may be related to the use of the product, XERIS shall immediately, and in no event later than within [***] of receipt by XERIS, provide PYRAMID with all pertinent information to facilitate investigation.	[***]	[***]

APPENDIX 1: Contacts and Responsibilities

Position	XERIS	PYRAMID Laboratories, Inc.
Contract Manager	**[***]**	**[***]**
Analytical	**[***]**	**[***]**
Manufacturing	**[***]**	**[***]**
Quality Assurance	**[***]**	**[***]**
Pharmaceutical Development	**[***]**	**[***]**
Product Distribution	**[***]**	**[***]**
Project Manager	**[***]**	**[***]**
Regulatory	**[***]**	**[***]**

Contact Information

PYRAMID Laboratories, Inc. Phone Number: [***]

XERIS Pharmaceuticals, Inc. Phone Number: [***]

NOTE: 1) A designee may be assigned to specific projects by the responsible personnel.
2) The designated representatives of each company will be responsible for the supply or receipt of information and controlled documents.

APPENDIX 2: Significant Deviations Requiring Notification to XERIS

Significant Deviations that require notification to XERIS (minimum expectations) *Any deviation that may potentially impact the quality, safety and efficacy of a XERIS Product*	
Significant deviations	**List of specific examples (but not limited to)**
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

APPENDIX 3: Documentation to be Supplied by PYRAMID

The following documents/records will be supplied to XERIS:

- Master Batch Records for XERIS review and approval
- Executed batch records
- Supporting environmental monitoring results and personnel monitoring as applicable to the executed record
- Any in-process and finished product testing results documented in the executed batch record
- List of all materials used in the production of a batch by lot number, including XERIS lot numbers where applicable
- All completed and approved deviations and investigations (including those approved by XERIS)
- BSE/TSE Statement for the components of the lot manufactured
- Any analytical results applicable to the release of the lot as tested by PYRAMID
- Certificate of Compliance from PYRAMID including cGMP statement
- Certificate of Analysis (if applicable)

APPENDIX 4: Authorized Subcontractors

PYRAMID may not subcontract any of its obligations under this Quality Agreement except pursuant to the provisions of Section 7.2 of the Quality Agreement. The Parties acknowledge and agree that the subcontractor(s) listed below have satisfied the requirements set forth in Section 6.6 of the Quality Agreement, have been approved by XERIS`, and may perform activities on behalf of PYRAMID under the Quality Agreement, subject to PYRAMID's and such subcontractor's continuing obligations under the Quality Agreement, including, without limitation, their respective obligations under Section 6.6.

SUBCONTRACTOR NAME:	**[***]**
ADDRESS:	**[***]**
TYPE OF SERVICE:	*ANALYTICAL TESTING LABORATORY*

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors
Xeris Pharmaceuticals, Inc.:

We consent to the incorporation by reference in the registration statement (No. 333-233061) on Form S-3 and registration statements (Nos. 333-237120, 333-229587 and 333-225802) on Form S-8 of Xeris Pharmaceuticals, Inc. of our report dated March 9, 2021, with respect to the consolidated balance sheets of Xeris Pharmaceuticals, Inc. as of December 31, 2020 and 2019, 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, 2020, and the related notes, which report appears in the December 31, 2020 annual report on Form 10-K of Xeris Pharmaceuticals, Inc.

/s/ KPMG LLP

Chicago, Illinois
March 9, 2021

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 Pharmaceuticals, 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 9, 2021

By: /s/ Paul R. Edick
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, Barry M. Deutsch, certify that:

1. I have reviewed this annual report on Form 10-K of Xeris Pharmaceuticals, 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 9, 2021

By: /s/ Barry M. Deutsch
Barry M. Deutsch
Chief Financial Officer
(Principal Financial 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 Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ended December 31, 2020 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 9, 2021

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 Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Barry M. Deutsch, 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 9, 2021

By: /s/ Barry M. Deutsch
Barry M. Deutsch
Chief Financial Officer
(Principal Financial Officer)