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, 2019

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, IL	**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, 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 is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☑

As of June 28, 2019, the aggregate market value of the Registrant's common stock held by non-affiliates of the Registrant was approximately $227.2 million based on the closing sales price as reported on the Nasdaq Exchange.

As of February 28, 2020, 37,570,080 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 2020 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, 2019.

XERIS PHARMACEUTICALS, INC.

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Year Ended December 31, 2019

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;
- our expectations related to the anticipated timing of the commercial launch of Gvoke HypoPen;
- our expectations related to the potential timing of the launch of our ready-to-use glucagon in certain European countries, if we receive marketing approval;
- 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;
- the pricing and reimbursement of Gvoke or any of our product candidates, if approved;
- 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 "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. 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 leveraging our novel non-aqueous formulation technology platforms, XeriSol™ and XeriJect™, to develop and commercialize ready-to-use injectable and infusible drug formulations. We have developed and launched the first ready-to-use, room-temperature stable liquid glucagon formulation that, unlike the current standard of care, can be administered without any preparation or reconstitution. Our first product, Gvoke™, delivers ready-to-use glucagon via a commercially available pre-filled syringe ("Gvoke PFS") or auto-injector, Gvoke HypoPen™ ("Gvoke HypoPen") for the treatment of severe hypoglycemia, a potentially life-threatening condition, in people with diabetes. Gvoke was approved 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 on September 10, 2019. We began the commercial launch of Gvoke PFS in November 2019. Gvoke PFS 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. We expect Gvoke HypoPen will be commercially available in July 2020, in the same doses as the Gvoke PFS. Additionally, in November 2019, we submitted a Marketing Authorisation Application ("MAA") to the European Medicines Agency ("EMA") for our novel ready-to-use, room temperature stable liquid glucagon formulation for the treatment of severe hypoglycemia in people with diabetes. We are also applying our novel liquid glucagon formulation to the management of hypoglycemia associated with additional intermittent and chronic conditions with significant unmet medical need. Finally, 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 114 patents issued globally, including a composition of matter patent covering our ready-to-use glucagon formulation that expires in 2036.

Our proprietary XeriSol and XeriJect non-aqueous formulation technology platforms allow for the subcutaneous and intramuscular delivery of highly concentrated, ready-to-use formulations of peptides, small molecules, and proteins (including monoclonal antibodies) using 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 intravenous ("IV") administration over long periods of time. We believe our broadly applicable platforms can provide distinct advantages over existing formulations by eliminating reconstitution and refrigeration, enabling long-term room-temperature stability, significantly reducing injection volume and enabling patient-convenient SC or IM administration versus IV infusion. 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 key priority is the commercialization of our first product, Gvoke, for the treatment of severe hypoglycemia in people with diabetes to address limitations of traditional glucagon kits. Hypoglycemia, a key concern of people with both Type 1 Diabetes ("T1D") and Type 2 Diabetes ("T2D"), occurs when a person has a deficiency of glucose in their bloodstream, often as a result of insulin treatment. Symptoms of hypoglycemia include fatigue, shakiness, anxiety, headache, nausea and vomiting, and in severe cases, hypoglycemia can result in cardiovascular disease, seizure, coma, and, if left untreated, death. 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 underuse 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.

We believe Gvoke addresses the administration challenges of traditional glucagon kits and has the potential to be the preferred emergency glucagon product. Our ready-to-use Gvoke does not require reconstitution or refrigeration and features two-year room-temperature stable liquid glucagon delivered in a pre-filled syringe or an auto-injecting device 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 traditional glucagon kits, a nasally administered glucagon powder, Eli Lilly's BAQSIMI™, was approved by the FDA in July 2019 and was launched in August 2019. While BAQSIMI offers a novel route of administration, we believe patients and caregivers in the diabetic community want greater certainty that a full dose of glucagon will be delivered in an emergency situation and so will prefer Gvoke to BAQSIMI.

Our goal is to establish Gvoke as the preferred emergency glucagon product and drive greater adoption and penetration of emergency glucagon therapy by offering a glucagon product that better meets the needs of patients and caregivers. The American Diabetes Association ("ADA") recommends that glucagon be prescribed for all individuals at increased risk of clinically significant hypoglycemia for use in

the event of an emergency. People with diabetes who are treated with insulin or substances that promote production of insulin are at increased risk of clinically significant hypoglycemia. There are an estimated 1.5 million people with T1D in the United States who are treated with insulin because their bodies do not naturally produce insulin, all of whom are clinically appropriate for glucagon. Approximately 4.7 million additional people with T2D in the United States are treated with insulin because their bodies do not use insulin properly, of which we estimate that approximately 50% are clinically appropriate for glucagon. Therefore, we estimate the potential target population for emergency glucagon therapy totals approximately 3.9 million people in the United States. Our commercial strategy is to penetrate this market efficiently with a concentrated sales force by targeting high prescribers of glucagon and mealtime insulin and to activate demand through targeted direct-to-patient promotion. We also plan to use our medical affairs and market access teams to actively drive market access and obtain payor coverage for Gvoke. The combination of our promotional efforts in this category and Eli Lilly's in support of its BAQSIMI is expected to drive a significant increase in prescription activity for glucagon in general. In fact, since the introduction of Gvoke PFS in November 2019, total monthly glucagon prescriptions across all types and formulations have been higher by 25% or more over that same month's prior year totals.

Due to the limitations of traditional glucagon kits and other factors, only approximately 567,200 total prescriptions for traditional glucagon kits were written in 2019 in the United States. In the second half of 2019, both BAQSIMI, which Eli Lilly launched in August 2019, and Gvoke PFS, which we launched in November 2019, entered the market. According to IQVIA, total prescriptions written in 2019 for BAQSIMI and Gvoke PFS were approximately 40,900 and 600, respectively. Total units reported in 2019 were approximately 906,700 traditional glucagon kits, 106,100 units of BAQSIMI, and 2,300 Gvoke units as adjusted for a consistent unit of measure. Based on our market research, we are targeting our marketing to all 3.9 million people that we believe are clinically appropriate for glucagon. In 2019, U.S. sales for emergency glucagon products were approximately $259 million, but we believe that increasing penetration, including by new entrants that address unmet patient and caregiver needs, such as Gvoke, may result in a potential sales opportunity of up to $2.2 billion. Outside of 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. In November 2019, we submitted our MAA to the EMA for our liquid glucagon formulation for the treatment of severe hypoglycemia in people with diabetes. If our MAA is approved, we could potentially launch our liquid glucagon formulation in certain European countries in 2021. 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 certain intermittent and chronic use conditions with significant unmet medical need. In 2019, the following development programs either produced positive clinical trial results or advanced into clinical trials. We plan to continue to advance these programs going forward. These additional applications are:

- 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.
- Management of diabetes via glucagon in a fully integrated, bi-hormonal artificial pancreas closed-loop system.

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 have decided not to proceed with a planned Phase 3 Congenital Hyperinsulinism ("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.

In addition, we concluded our Hypoglycemia Associated Autonomic Failure ("HAAF") program based on results from our Phase 2 clinical trial in adult T1D subjects, as no statistically significant differences between the treatment arms were observed based on percent change in plasma epinephrine concentration from baseline. While there were positive epinephrine and improved hypoglycemia awareness responses observed in some subjects, the equivocal efficacy results observed may be explained by the incomplete elimination of time spent with hypoglycemia.

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 ready-to-use, liquid-stable diazepam delivered via a commercially available auto-injector for the emergency treatment of epileptic seizures. Additionally, based on the promising data seen in some of our early clinical trials as well as formulations in our laboratory, we believe we have the potential to advance a number of additional programs in additional indications and 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.

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 CHI and our ready-to-use, liquid-stable formulation of diazepam for the treatment of Dravet syndrome and acute repetitive seizures, or ARS, in patients with epilepsy. Additionally, we have received orphan drug designation from the EMA for CHI and Noninsulinoma Pancreatogenous Hypoglycaemia 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, 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.

	Product Candidate	Indication	Development Stage	Next Milestone	
			Preclinical / Phase 1 / Phase 2 / Phase 3 / Marketed	Event	Expected Date
Ready-to-Use Glucagon for Hypoglycemia*	Gvoke™	Severe Hypoglycemia	Approved	Launch HypoPen	2H '20
	Glucagon PFS/AI - EU	Severe Hypoglycemia	MAA under review	Regulatory decision	1H '21
	Self-Administered Glucagon	Post-Bariatric Hypoglycemia**	Phase 2	Ph 2 outpatient data	1H '20
Ready-to-Use Products for Diabetes and Epilepsy	Self-Administered Glucagon	Exercise-Induced Hypoglycemia	Phase 2	Ph 2 out-patient data	1H '20
	Pramlintide-Insulin	T1D / T2D Blood Sugar Control	Phase 2	Ph 2 data	1H '20
	Diazepam	Acute Repetitive Seizures** Dravet Syndrome**	Phase 1b	Ph 1b data	1H '20

* Additionally, we have available via Expanded Access, continuous infusion glucagon for Congenital Hyperinsulinism

** Orphan Drug Designation

Additionally, we have provided ready-to-use glucagon to Oregon Health & Science University ("OHSU") for their Phase 1 closed-loop dual-hormone artificial pancreas study. OHSU presented topline results at the ADA 79th Scientific Sessions and submitted results to a peer-reviewed journal in the fourth quarter of 2019. Based on the results, we plan to support advancement of OHSU and other artificial pancreas programs with ready-to-use glucagon.

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 and epilepsy. 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 for Gvoke***. We commercially launched Gvoke PFS in the United States in November 2019 and expect Gvoke HypoPen to be commercially available in July 2020. We are initially targeting approximately 8,000 healthcare professionals who are high prescribers of traditional glucagon kits and/or mealtime insulin products, using an initial field team of 80 individuals, and activating demand through targeted direct-to-patient promotion. We have built our initial commercial organization and critical infrastructure, including individuals in operations, supply chain, pharmacovigilance, compliance, regulatory, marketing, sales leadership, market access and sales operations, as well as our medical affairs organization.
- ***Secure regulatory approval for our ready-to-use liquid stable glucagon in Europe.*** We submitted our MAA to the EMA in November 2019. We plan to pursue development and commercialization collaborations for most, if not all of the non-U.S. markets we seek to enter. If approved, we could launch our ready-to-use glucagon in certain European countries in 2021.
- ***Continue to advance our ready-to-use glucagon portfolio to address hypoglycemia associated with other conditions***. We plan to apply our ready-to-use, room-temperature stable liquid glucagon to address multiple conditions that could benefit from intermittent or chronic administration, such as PBH as well as in diabetes for EIH. We are also evaluating our liquid-stable glucagon as the glucagon component of a fully integrated, bi-hormonal artificial pancreas. Through these programs, our primary goal is to secure FDA approval of a vial of our liquid glucagon for self-administration via a syringe or transfer to a pump reservoir for continuous infusion. We plan to leverage efficiencies across our portfolio, such as our supply chain, research and development, and our commercial and medical organizations. We plan to use commercially available drug delivery devices for our liquid-stable glucagon formulation and associated intermittent and chronic glucagon programs.
- ***Continue to leverage our technology and expertise to develop a portfolio of additional product candidates***. We are exploring the application of our formulation technology platforms to other commercially available drugs for multiple conditions. We initiated and completed several preclinical studies of a fixed-ratio pramlintide-insulin co-formulation combination product for the treatment of diabetes and began a Phase 2 clinical trial in the second half of 2019. We expect topline results in the first half of 2020. In addition, we are developing an improved formulation of diazepam to be administered through a ready-to-use auto-injector for which we are evaluating indications such as the treatment of patients with Dravet syndrome and ARS. In December 2018 we initiated 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 in May 2019. Based on these results, we initiated an additional Phase 1b weight-based study in the second half of 2019 and expect topline results in the first half of 2020. Finally, we have advanced several additional programs to formulation stage and expect these to complete preclinical development over the next year.
- ***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 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 have formulated 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 treatment of hypoglycemic conditions and improve the lives of people who experience hypoglycemia.

Our Products

Gvoke

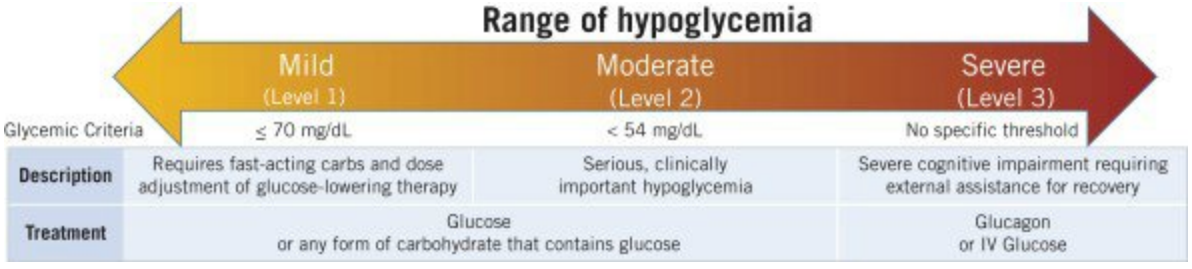
Gvoke offers a ready-to-use, room-temperature stable glucagon that is designed to be administered subcutaneously in a simple two-step process via a commercially available pre-filled syringe or auto-injector. In our human factors studies, 99% of users were able to successfully administer the full dose 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 by the FDA on September 10, 2019. We began the commercial launch of Gvoke PFS in November 2019. Gvoke PFS 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. We expect Gvoke HypoPen will be commercially available in July 2020, in the same doses as the Gvoke PFS.

Additionally, we submitted our MAA to the EMA in November 2019. We are currently evaluating plans to submit Gvoke for regulatory approval in Canada and other countries. We have a clinical trial application in place with Health Canada to allow the inclusion of Canadian clinical research sites in certain of our U.S. clinical trials related to Gvoke.

Hypoglycemia Background

Diabetes is a widespread condition that affects an estimated 425 million people worldwide with an estimated 22.1 million drug-treated people in the United States. Among people with diabetes in the United States, all of the approximately 1.5 million people with T1D and 4.7 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. In 2014, the U.S. Department of Health and Human Services National Action Plan for Adverse Drug Event Prevention highlighted diabetes agent-associated hypoglycemia as one of its three primary concerns because of the severity and increasing prevalence of the problem. In 2017, the ADA stated that hypoglycemia remains the major limiting factor in the glycemic management of T1D and T2D.

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 clinically significant hypoglycemia, defined as blood glucose <54 mg/dL, for use in the event of an emergency. 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 two episodes of severe hypoglycemia per year. On average, half of people with T2D treated with insulin experience an episode of mild or moderate hypoglycemia twice per month. People with T2D treated with insulin are also at risk of severe hypoglycemia, and approximately 21% of these individuals experience an episode of severe hypoglycemia at least once annually.

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. On September 10, 2019, Gvoke was approved by the FDA, and we commenced the commercial launch of Gvoke PFS in November 2019. In July 2019, a nasally administered glucagon powder, Eli Lilly's BAQSIMI, was approved and is currently being marketed in the U.S. Prior to this, 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.

In 2019, Eli Lilly's GEK and BAQSIMI represented approximately 68% and 11% of U.S. sales, respectively, and Novo Nordisk's GlucaGen HypoKit represented approximately 20% of U.S. sales.

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 is currently available in two doses: a 0.5 mg/0.1 mL dose for pediatric patients and a 1 mg/0.2 mL dose for adolescent and adult patients. We expect Gvoke HypoPen will be available in July 2020, in the same doses as the Gvoke PFS. These innovative formats are designed to provide the reliability of a ready-to-use liquid glucagon while making it easier for patients or caregivers to administer quickly and simply. We have designed Gvoke to be easy to administer.

The key features of Gvoke PFS and Gvoke HypoPen are:

- *Ready-to-use:* With its easy two-step administration process, the user of Gvoke PFS simply pulls off the cap, inserts the needle at a 90-degree angle and pushes the plunger down as far as it will go, or with Gvoke HypoPen, pulls off the cap and pushes down on the skin for five seconds until the viewing window turns red. There is no reconstitution required at the time of emergency.
- *Easy-to-use:* 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 and the nasal glucagon powder, Gvoke features the following benefits:

Glucagon Product Characteristics

	Gvoke™ Pre-Filled Syringe	Traditional Glucagon Kits	Nasal Glucagon Powder
Manufacturer	Xeris Pharmaceuticals	Lilly, Novo Nordisk, and Fresenius Kabi	Lilly
Active ingredient	Glucagon	Glucagon	Glucagon
Dosage strength(s)	0.5 mg/0.1 mL and 1 mg/0.2 mL	1 mg	3 mg
How supplied	Premixed, stable liquid glucagon in a single-use prefilled syringe	Lyophilized glucagon powder in a single-dose vial with diluent in a prefilled syringe	Single-use intranasal device containing glucagon powder
Administration site(s)	Subcutaneous injection to the lower abdomen, outer thigh, or outer upper arm	Intramuscular or subcutaneous injection to the upper arm, thigh, or buttock, or intravenously	Device actuation into one nostril
Shelf life	Up to 24 months	Up to 24 months; after reconstitution, shelf life is up to 24 hours (Novo)	Information not available
Storage	Controlled room temperature	Controlled room temperature	Store at up to 86° F
Needle size and placement	27-gauge 1/2" visible needle	25-gauge 5/8" visible needle (Lilly)	N/A
Dose readiness	No reconstitution required	Needs reconstitution	No reconstitution required
Premeasured pediatric & adult dose options	Yes	No	No
Indication statement	GVOKE is an antihypoglycemic agent indicated for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes **ages 2 years and above.**	Glucagon is indicated as a treatment for severe hypoglycemia (low blood sugar) which may occur in patients with diabetes mellitus. (Lilly)	BAQSIMI™ is an antihypoglycemic agent indicated for the treatment of severe hypoglycemia in patients with diabetes **ages 4 years and above.**

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 22.1 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 84 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 clinically significant hypoglycemia for use in the event of an emergency. Based on our Healthcare Professional Perceptions Study, we believe almost all people with T1D and approximately 50% of people with T2D on insulin are considered clinically appropriate for glucagon. In the United States, there is an estimated 1.5 million people with T1D who are treated with insulin because their bodies do not naturally produce insulin and approximately 4.7 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 3.9 million people in the United States. We are currently offering Gvoke PFS in packages of one or two pre-filled syringes Based on responses from our market research studies, most buyers would be expected to purchase, on average, two syringes or pens per person. We believe by increasing penetration into the market for emergency glucagon kits and based on the current price of approximately $280 per unit for traditional emergency glucagon products, the U.S. potential sales opportunity may be up to $2.2 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 567,200 total prescriptions for emergency glucagon kits were written in 2019 in the United States, resulting in the purchase of approximately 906,700 single-dose kits. In 2019, U.S. sales for emergency glucagon products totaled approximately $259 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 do 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 414,000 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

We will seek to replace traditional emergency glucagon kits with Gvoke, increase the number of at-risk people who carry emergency glucagon and promote access to emergency glucagon products. While our sales force and medical teams expect to focus on driving awareness and adoption of Gvoke by healthcare professionals, we believe accelerated growth and expanded uptake will come from targeted direct-to-patient messaging that, because the majority of people with diabetes are concentrated in 15 states, will allow us to efficiently and effectively reach our target audience.

We launched Gvoke PFS in November 2019, and we expect Gvoke HypoPen to be commercially available in July 2020. Our strategy for Gvoke includes the following:

- **Drive awareness and adoption of Gvoke**. We plan to drive awareness and adoption of Gvoke to replace traditional emergency glucagon kits in the market.
  - **Healthcare Professionals:** Having recently launched Gvoke, we are targeting high glucagon prescribing healthcare professionals. Approximately 3,000 healthcare professionals issue about 50% of current glucagon prescriptions. We intend to reach these professionals using our initial sales representatives.
  - **Patients and Caregivers:** We intend to activate patient advocacy organizations and leverage channels such as direct-to-consumer tactics, social media, digital presence, traditional offline channels and press coverage to drive awareness and communicate our value proposition to patients and caregivers. Because we do not have the first product to market in a competitive landscape, we plan to increase our spend on direct-to-consumer tactics. Epidemiology and census data indicate that 15 states account for almost 60% of people with diabetes, allowing us to be efficient and effective with our promotional activities.
- **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 the approximately 3,000 healthcare professionals who issue about half of the current glucagon prescriptions, we are targeting approximately 5,000 healthcare professionals who are high mealtime insulin prescribers but who are not high prescribers of glucagon. We hired an initial field team of 80 individuals to reach these professionals.
  - **Patients and Caregivers:** We believe there is an opportunity to activate patient and caregiver demand for Gvoke. Gvoke is designed as an easy-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.** Traditional emergency glucagon kits have favorable market access, and current trends indicate a relatively low level of management of these products by payors. For example, Eli Lilly's GEK is covered at or above 80% with unrestricted access across commercial, Medicare, Managed Medicaid and State Medicaid plans. A *Diabetes Health Coverage: State Laws and Programs* report reviewing state insurance mandated coverage, Medicaid coverage and state-sponsored diabetes programs showed that 46 states and the District of Columbia have a diabetes statutory mandate for coverage, whether as medication or supply. Of our target patient population, approximately 50% are commercially insured, one-third are covered by Medicaid and approximately 15% are covered by Medicare. However, gaining market access and formulary coverage for new products takes substantial time and resources. As a result, we plan to increase 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.

We have established a distribution channel in the United States for the commercialization of Gvoke. Gvoke PFS is currently being sold to wholesale pharmaceutical distributors, who, in turn, sell Gvoke PFS 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 of the United States, we plan to collaborate with local companies.

Our Product Candidates

Ready-to-Use Glucagon for Hypoglycemia Associated with Intermittent and Chronic Conditions

We are applying our ready-to-use liquid-stable glucagon formulation to treat other intermittent and chronic 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 intermittent and chronic applications of 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 intermittent and chronic hypoglycemic conditions, we intend to leverage our completed preclinical studies across our glucagon portfolio, which consist of five toxicology studies in rats (up to 26 weeks), three toxicology studies in pigs (up to 39 weeks), one tolerability study in rabbits, three PK studies in rats, and four PK studies in minipigs. These preclinical studies 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 intermittent and chronic 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 has also been observed following sleeve gastrectomy, a procedure that reduces the size of the stomach. In the U.S., approximately 20% of bariatric procedures performed are RYGB, while approximately 60% 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 68% to 97% 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.

From 2015 to 2017, the National Institute of Diabetes and Digestive and Kidney Diseases, which is part of the National Institutes of Health ("NIH"), awarded us $1.8 million in Fast-Track Small Business Innovation Research ("SBIR") grants to demonstrate the potential benefits of ready-to-use glucagon in these patients. Collaborators on this grant included endocrinologists at the Joslin Diabetes Center and device engineers at the Harvard University John R. Paulson School of Engineering and Applied Science.

Clinical Experience in PBH

We have completed a proof-of-concept clinical trial and a randomized controlled Phase 2a 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 dosed the first patient in this clinical trial in the second half of 2019 and received topline in-clinic results in December 2019. We expect the results from this trial, including the ongoing outpatient phase, will help enable the evaluation of ready-to-use glucagon in a future Phase 3 clinical trial using a vial/syringe.

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 is 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 is 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 will also collect 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. 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.

The Phase 2 trial will evaluate blood glucose recovery ($\geq$ 70 mg/dL) at 15 minutes after dosing with Glucagon RTU and placebo. Safety, tolerability and quality-of-life are also assessed. The trial is comprised of 12 evaluable subjects.

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. 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. This study is currently ongoing in the outpatient stage, where both subjects and investigators remain blinded.

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, since current commercially available liquid glucagon kits are unstable in aqueous solution for extended periods of time. Glucagon rescue kits exist as a lyophilized powder that must be reconstituted in diluent immediately prior to injection and are only indicated at an emergency dose of 1 mg for rescue from severe hypoglycemia. 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. 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 candidate.

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.

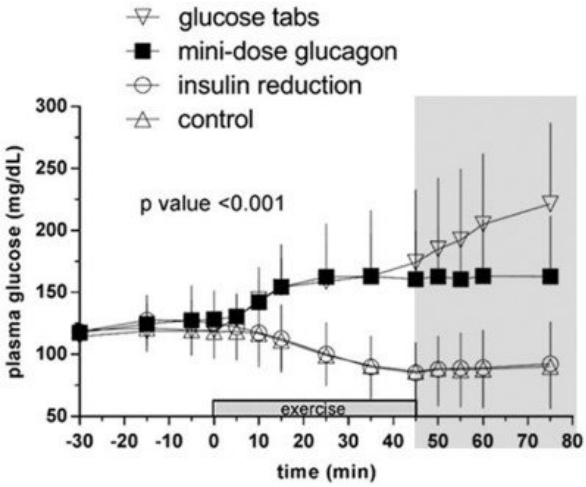
Phase 2 Clinical Trials

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 exercise-induced hypoglycemia. 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 2a 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 2a 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 exercise-induced hypoglycemia, 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*.

Ongoing Trials

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 is 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 exercise-induced hypoglycemia (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 will perform 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 will be monitored for hypoglycemia in the exercise recovery period. In January 2020, Xeris reported positive results from the CRC setting of this Phase 2 study. Results showed that a mini-dose of RTU glucagon was adequate to maintain normal blood glucose levels during prolonged, moderate-to-high intensity aerobic exercise. The outpatient stage, where subjects will be exercising on their own at home, is currently ongoing with results expected in the first half of 2020. This stage of the trial is 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.

Ready-to-Use Glucagon for Bi-Hormonal Artificial Pancreas Closed-Loop Systems

We are evaluating our ready-to-use glucagon for use in a bi-hormonal artificial pancreas closed-loop system. In mid-2019, OHSU completed a Phase 1 proof-of-concept randomized three-way crossover clinical trial to evaluate the utility of such a system. OHSU presented topline results at the ADA 79th Scientific Sessions in June 2019 and submitted results to a peer-reviewed journal. Based on the study results, we plan to support advancement of OHSU and other artificial pancreas programs with ready-to-use glucagon. In December 2013, we filed an IND application for the use of ready-to-use glucagon 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.

Insulin-Dependent Diabetes Market

Continuous subcutaneous insulin infusion from a pump ("CSII") has been shown to improve glycemic control for people with diabetes. However, data from clinical trials indicate that even when used in closed-loop, insulin analogs, pumps and CGMs have generally modest effects in reducing hypoglycemic events because they are capable of only delivering or stopping delivery of insulin. As such, CSII users are still forced to ingest carbohydrate containing foods or over-the-counter glucose products or utilize emergency glucagon products to counteract hypoglycemia.

We believe the quality of life for patients could be significantly improved by offering a bi-hormonal artificial pancreas that delivers both insulin and glucagon. While significant work has been done developing extensive algorithms and control systems needed for the bi-hormonal pump, a key limitation has been the lack of a glucagon formulation that does not require reconstitution and is stable for at least three days in a pump chamber. We believe the utilization of our ready-to-use glucagon in a bi-hormonal system has the potential to minimize the incidence of hypoglycemia, improve patient quality of life, and drive higher rates of adoption of CSII systems.

All patients utilizing an intensive insulin regimen are candidates for a bi-hormonal pump system. In the United States, this includes all 1.5 million people with T1D as well as approximately 1.0 million people with T2D. Of this population, approximately one-third of patients with T1D and a very small percentage of those with T2D are currently utilizing CSII therapy.

Xeris Offering—Liquid-Stable Ready-To-Use Glucagon for a Bi-Hormonal Artificial Pancreas

A liquid-stable glucagon formulation is a critical component to facilitate a bi-hormonal artificial pancreas. Our ready-to-use glucagon has demonstrated stability at body temperature in a patch pump chamber. Collaborators in our bi-hormonal artificial pancreas program include endocrinologists at OHSU. In addition, numerous researchers have expressed interest in using our ready-to-use glucagon in research studies with novel bi-hormonal pump systems.

To support development of our ready-to-use glucagon for this application, we have been awarded approximately $1.9 million in funding from organizations such as the NIH National Institute of Diabetes and Digestive and Kidney Diseases and the JDRF.

Clinical Experience

We have successfully completed a number of preclinical studies in multiple species, a Phase 2a dose-ranging glucagon PK/PD study and a Phase 1 proof-of-concept randomized clinical trial.

Phase 1 Clinical Trial

NCT 03424044: A Randomized, Three-Way, Cross-Over Outpatient Study to Assess the Efficacy of a Dual-Hormone Closed-Loop System with XeriSol Glucagon vs Closed-Loop System with Insulin Only vs a Predictive Low Glucose Suspend System

This was a single center, randomized, three-way, crossover investigator-initiated trial conducted by OHSU using our ready-to-use glucagon in a vial. Subjects underwent the 76-hour study with 9 hours inpatient and 67 hours outpatient using the closed-loop artificial pancreas system. The trial was completed in mid-2019 and was designed to compare glucose control resulting from the use of a bi- and single-hormone closed-loop system as compared to a predictive low glucose suspend system ("PLGS"), using the percent of time with sensed glucose below 70 mg/dl as the primary endpoint. The bi-hormonal closed-loop system is designed to reduce the time spent in the hypoglycemic range and increase the time spent in the target range, even during and after exercise, as compared to an insulin only closed-loop system and a predictive low glucose suspend system. OHSU reported study results at the ADA 79th Scientific Sessions in June 2019. They reported that dual-hormone improved overall hypoglycemia as compared to single-hormone and PLGS. Single-hormone and dual-hormone both significantly improved time in range compared to PLGS. Time in range was similar between single and dual hormone, but the dual hormone achieved this with lower hypoglycemia. Dual-hormone reduced rescue carbohydrate treatments compared to single-hormone and PLGS.

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.)*

Ready-to-Use Glucagon for Hypoglycemia-Associated Autonomic Failure

We concluded our Hypoglycemia-Associated Autonomic Failure ("HAAF") program based on results from our Phase 2 clinical trial in adult T1D subjects, as no statistically significant differences between the treatment arms were observed based on percent change in plasma epinephrine concentration from baseline. HAAF is a condition in which chronic hypoglycemia impairs the body's natural response to restore blood sugar levels and can lead to an individual becoming unaware of the onset of a severe hypoglycemic event and result in cardiovascular disease, seizure, coma, and, if left untreated, death. In previous publications, the strict avoidance of hypoglycemia in subjects with HAAF has been shown to improve counterregulatory epinephrine and autonomic symptom responses and consequently reestablish the awareness of hypoglycemia. We evaluated whether two dose levels of continuous subcutaneous glucagon infusion ("CSGI"), administered over 28 days, could similarly restore the epinephrine response to hypoglycemia in subjects with HAAF. This was a Phase 2 prospective, randomized, placebo-controlled, double-blind, parallel trial in adult T1D subjects. In this trial, 49 subjects with documented HAAF were randomized to receive 4 weeks of treatment with high rate CSGI (n=15), low rate CSGI (n=18), or placebo (n=16). Epinephrine was quantified following a stepwise hypoglycemia induction. CSGI was not sufficient to restore defective glucose counter-regulation (epinephrine response) or hypoglycemia symptom awareness. While there were positive epinephrine and improved hypoglycemia awareness responses observed in some subjects, the equivocal efficacy results observed may be explained by the incomplete elimination of time spent with hypoglycemia. The administration of both low and high rate CSGI was generally well tolerated, and no significant adverse events related to CSGI were reported.

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 about 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: 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.

We initiated a study of our novel XeriSol pramlintide-insulin co-formulation in a 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 for any future marketing authorization by the FDA.

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

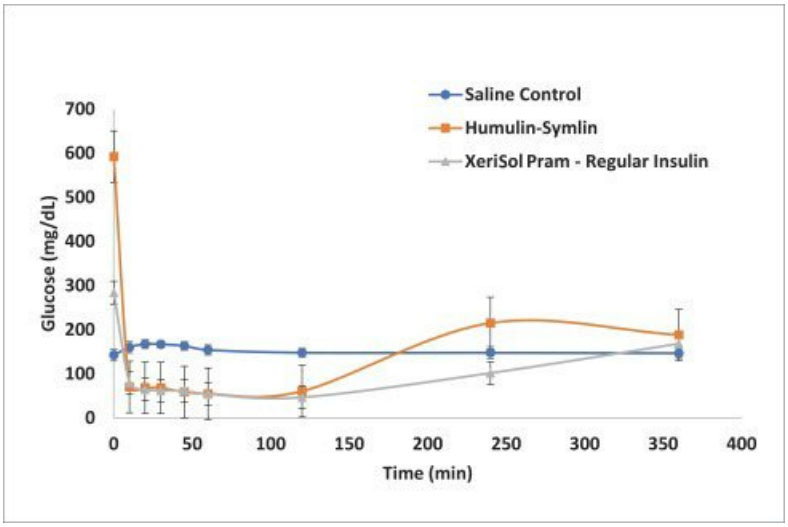
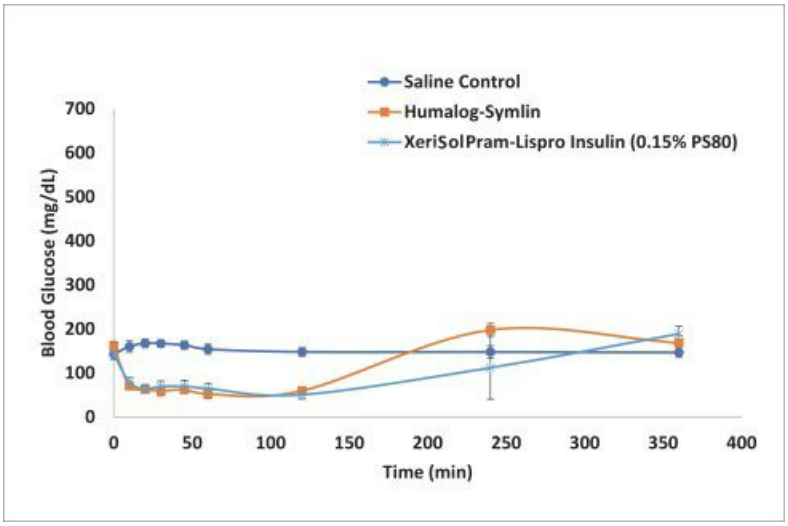


Figure 2 Glucose Levels after Injection of XeriSol Pramlintide-Lispro and Humalog/Symlin Co-Injection



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, these 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 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 received orphan drug designation for our product candidate from the FDA and 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 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. Based on these results, we initiated a second Phase 1 open-label, single-arm, weight-based dosing study with IM administration of diazepam in healthy volunteers in the second half of 2019. We expect topline results in the first half of 2020.

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 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 C_{max} and T_{max}. 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, we initiated another Phase 1 open-label, single-arm, weight-based dosing study with IM administration of diazepam in normal volunteers in the second half of 2019. We expect topline results from this trial in the first half of 2020.

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 were all involved in manufacturing our clinical supplies and commercial registration batches.

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 company-owned 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 entered into a commercial distribution agreement with one such vendor in 2019.

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.

Two emergency glucagon kits are currently available to treat severe hypoglycemia: Eli Lilly’s GEK and Novo Nordisk’s GlucaGen HypoKit. 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. In addition, Eli Lilly has developed an intranasal glucagon dry powder, BAQSIMI, that was approved by the FDA in July 2019 and launched in August 2019, and Fresenius Kabi introduced an emergency glucagon kit in February 2020. The latter is functionally indistinguishable from the Lilly GEK and Novo GlucaGen HypoKit.

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. Based on its public filings, Zealand has stated it intends to file a New Drug Application ("NDA") in early 2020. Zealand's dasiglucagon completed a Phase 3 clinical development program that studied the investigational product candidate in adults and children with T1D.

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 a Phase 3 clinical requirements. Additionally, a clinical investigator has initiated a proof-of-concept study (NCT03984370) with Zealand Pharma's 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. Aquestive's NDA for buccal soluble diazepam Libervant™ (previously known as AQST-203), also for the treatment of seizure clusters and ARS, is under review by the FDA with the PDUFA date of September 27, 2020. Engage Therapeutics is developing an inhaled alprazolam (known as STAP-001) for ARS, with the agent currently in Phase 2b 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, 2019, we owned 114 issued patents globally, of which 14 are issued U.S. patents. As of December 31, 2019, 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 international patent applications. Patents that issue based on these applications would also expire in year 2036.

Trade Secret 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 a U.S. registered trademark for the mark Xeris Pharmaceuticals. We also own pending trademark applications for XERISOL, XERIJECT, GVOKE, GVOKE HYPOPEN and HYPOPEN in the United States and XERISOL and XERIJECT in the EU for use in connection with our pharmaceutical research and development and products, as well as trade names that could be used with our potential products. The USPTO has allowed

the following trademark applications which are awaiting the acceptance by the USPTO of Statements of Use: XERISOL, XERIJECT, GVOKE, GVOKE HYPOPEN, HYPOPEN and GLUCAPEN.

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, 2019, 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, 2019, we received $2.0 million in grant proceeds to help fund our EIH program. Under terms of one of the 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, 2019, 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 have also received awards from the NIH National Institute of Diabetes and Kidney Diseases, which awards are not subject to any repayment obligations. See “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Contractual Obligations and Commitments” for additional details.

Loan and Security Agreement

In February 2018, we entered into a Loan and Security Agreement that provided a senior secured loan facility of up to an aggregate principal amount of $45.0 million. The first tranche was $20.0 million and was drawn down in February 2018. The second tranche was $15.0 million and was drawn down in September 2018. In September 2019, we entered into an Amended and Restated Loan and Security Agreement ("Amended Loan Agreement") which amended and restated the Loan and Security Agreement in its entirety and provides up to $85.0 million in term loans in three tranches. The initial tranche of $60.0 million was drawn down in September 2019 and remained outstanding as of December 31, 2019. The second tranche of $15.0 million and the third tranche of $10.0 million will become available upon achievement of certain revenue targets prior to March 31, 2021 and June 30, 2021, respectively. The $35.0 million drawn down under the Loan and Security Agreement and the related final payment fee of $2.3 million were repaid in conjunction with the execution of the Amended Loan Agreement. See “Management’s Discussion and Analysis of Financial Condition and Results of Operations - Loan Agreement” 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 Biologics License Applications ("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 also are 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 2020 is $2,942,965 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 2020 is $325,424 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 of a standard NDA and respond to the applicant is ten months from the receipt of the 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, however, authorized 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 listed drug. 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 has also 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 Biologics License Application ("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.

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

In order to market any product outside of 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.
- 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 clearinghouse ("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 health care professionals and teaching hospitals, as well as ownership and investment interests held by the health care 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 health care 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 will also 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 may also 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, Congressional, and Executive challenges. 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 referred to as the "individual mandate", the requirement that all individuals maintain health insurance coverage or pay a penalty. However, the current presidential administration has indicated that enacting changes to the ACA is a legislative priority and has discussed repealing and replacing or amending the ACA. Under the Trump Administration, there are ongoing efforts to modify or repeal all or part of the ACA or take executive action that affects its implementation. The Tax Cuts and Jobs Act of 2017 (the "TCJA"), for example, includes a provision that repealed the individual mandate effective January 1, 2019.

Since January 2017, President Trump has 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, 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, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. The Trump administration has concluded that cost-sharing reduction, or CSR, payments to insurance companies required under the ACA have not received necessary appropriations from Congress and announced that it will discontinue these payments immediately until those appropriations are made. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans 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. 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 were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known. The Bipartisan Health Care Stabilization Act of 2017 as well as the follow-on Bipartisan Health Care Stabilization Act of 2018 were introduced to appropriate funds to stabilize CSR payments; however, the future of this effort is unclear.

On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including 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 (these three provisions have been repealed, as discussed below). 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, 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. In December 2018, the CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this

risk adjustment. Additionally, CMS published a final rule that will give 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.

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. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate no longer had any monetary impact on those who did not have qualifying insurance as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. 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. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA and our business. 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. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. We continue to evaluate the effect that the Affordable Care Act and its possible repeal and replacement could have on our business.

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 2029 unless additional Congressional action is taken. 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 have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and 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. At the federal level, the Trump administration has included drug price control measures in past budget proposals that may be enacted in future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, 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, 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. HHS has already started the process of soliciting feedback on some of these 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. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative 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 health care 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, or collectively 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 health care 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 must also 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 specified covered outpatient drugs ("SCODs"). The court ruled this change was not an "adjustment" which was within the Secretary's discretion to make but was instead a fundamental change in the reimbursement calculation, 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 has filed an appeal. 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 is also possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of our drugs after approval. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

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

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

Further, there have been several recent U.S. congressional inquiries, proposed federal, 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 Trump administration 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 health care 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 health care 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 December 18, 2019, President Trump, HHS and the FDA issued a notice of proposed rulemaking that, if finalized, would allow for the importation of certain prescription drugs from Canada. The FDA also issued a Draft Guidance document outlining a potential pathway for manufacturers to obtain an additional National Drug Code, or 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 regulatory and market implications of the notice of proposed rulemaking and Draft Guidance 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.

Outside of 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 will likely continue as countries attempt to manage healthcare expenditures.

Employees

As of December 31, 2019, we had 202 employees, 97 of whom were primarily engaged in sales, marketing and medical affairs, 53 of whom were primarily engaged in administration and finance, and 52 of whom were primarily engaged in product development and research.

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, or the 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

Risks Related to our Financial Position and Need for Financing

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.

We commercially launched our first product, Gvoke PFS, in November 2019 and expect to launch 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. As of December 31, 2019, we have generated $1.6 million in product revenues. We have financed our operations primarily through private placements of our preferred stock, borrowings under the Amended Loan Agreement that we entered into with Oxford Finance LLC and Silicon Valley Bank, our initial public offering in June 2018, or our IPO, and our public offerings in February 2019 and February 2020. We have not yet demonstrated an ability to conduct sales and marketing activities necessary for successful product commercialization. We have not yet demonstrated an ability to manufacture Gvoke HypoPen on a commercial scale or arrange for a third party to do so on our behalf. 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, 2019 and 2018, we reported a net loss of $125.6 million and $60.1 million, respectively. In addition, our accumulated deficit as of December 31, 2019 was $246.2 million. Substantially all of our operating losses have resulted from costs incurred in connection with research and development, clinical and regulatory initiatives to obtain approvals for our product candidates and preparation for commercialization of Gvoke.

We expect to continue to incur significant operating expenses as we continue to build our commercial infrastructure, 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.;
- continue our research and development efforts;
- seek regulatory approval for new product candidates and product enhancements;
- hire and retain additional personnel and add operational, financial and management information systems; and
- continue to operate as a public company.

Our first product, Gvoke, was approved by the U.S. Food & Drug Administration ("FDA") for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages 2 years and above on September 10, 2019. Our ability to generate revenue from Gvoke 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 have begun to generate revenue from Gvoke PFS, we have not yet generated revenue from any of our product candidates and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. We have just begun to generate revenue from Gvoke PFS, which we commercially launched in November 2019. We do not expect to generate significant revenue until we successfully commercialize Gvoke. 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 in the United States or in other key territories 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 begin commercialization of Gvoke. Regardless of these expenditures, Gvoke and our product candidates, if approved, may not be commercially successful. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenue, we will not become profitable and may be unable to continue operations without continued funding.

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. 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. 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. 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.

Our Amended Loan Agreement provides for term loans of up to an aggregate of $85.0 million, of which $60.0 million was drawn in September 2019. We become eligible to draw the second tranche of $15.0 million and the third tranche of $10.0 million following the Company's achievement of certain revenue targets prior to March 31, 2021 and June 30, 2021, respectively.

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. This debt financing 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 of the amounts due. Events of default also include our failure to comply with customary affirmative covenants as well as our breach of customary negative covenants in the Amended Loan Agreement. Affirmative covenants include the maintenance of a minimum cash balance equal to the outstanding obligations plus $5.0 million in the event that we maintain one or more permitted accounts at other institutions. 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.

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

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 have 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 just began to commercially launch our first pharmaceutical product, Gvoke PFS, in November 2019, and we expect to commercially launch Gvoke HypoPen in July 2020. There is no guarantee that the infrastructure, systems, processes, policies, relationships and materials we have built in anticipation of 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. For example, on October 29, 2019, we identified incorrect outer carton label side serialization flaps on Gvoke PFS 2-packs. The incorrect label was part of the approval package received from the FDA on September 10, 2019. To correct the issue, we executed a market recall of the Gvoke 1 mg 2-pack cartons and 0.5 mg 2-pack cartons. Correctly printed cartons were introduced into production on November 12, 2019 and we believe no further action is required at this time. However, were such events to occur in the future, they could 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 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;
- the strength of our sales, marketing and distribution support; and
- the availability of sufficient third-party coverage and reimbursement.

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, or 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 out 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 an internal 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.

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.

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., or Bachem, for active pharmaceutical ingredient, or API, Pyramid Laboratories Inc., or Pyramid, for drug product and SHL Pharma, LLC, or 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 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, or 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, or 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. We are also unable to predict how changing global economic conditions or potential global health concerns such as the COVID-19 coronavirus 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.

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 recent reimbursement formula change under the 340B program. The 340B program imposes ceilings on prices that drug manufacturers can

charge for medications sold to certain health care facilities. It is unclear how this decision 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.

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 Health Care and Education Affordability Reconciliation Act, or collectively, the ACA, became law in the United States and is significantly impacting the provision of, and payment for, health care. 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 health care programs. In addition, on December 18, 2019, President Trump, the U.S. Department of Health and Human Services ("HHS"), and the FDA issued a notice of proposed rulemaking that, if finalized, would allow for the importation of certain prescription drugs from Canada. The FDA also issued a Draft Guidance document outlining a potential pathway for manufacturers to obtain an additional National Drug Code, or 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 regulatory and market implications of the notice of proposed rulemaking and Draft Guidance 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 80% coverage, with unrestricted access across commercial, Medicare, Managed Medicaid and state Medicaid plans. Of our target patient population, approximately 50% are commercially insured, one-third are covered by Medicare and approximately 15% are covered by Medicaid. 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 ADA 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, contract research organizations, or 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 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 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 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 candidate from competing 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 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 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 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 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 potential global health concerns such as the COVID-19 coronavirus, 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

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, 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. In addition, if any of our product candidates are approved under Section 505(b)(2) of the FDCA as of the March 23, 2020 transition date and are then "deemed to be a license" for the biological product under section 351 of the PHS Act, we could lose certain unexpired exclusivity and this could materially harm our business. 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, or MAA, to the European Medicines Agency, or 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 prospective study sites or other CROs;
- delays or failures in obtaining approval of our clinical trial protocol from an institutional review board, or 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, or 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; and
- determination by regulators that the clinical design of a trial is not adequate.

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 plan to 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 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 Noninsulinoma Pancreatogenous Hypoglycaemia Syndrome, or NIPHS, which includes patients with PBH. We intend to 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 intend

to 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. For a product that obtains orphan drug designation on the basis of a plausible hypothesis that it is clinically superior to the same drug that is already approved for the same indication, such as our diazepam for acute repetitive seizures or our ready-to-use glucagon for PBH, in order to obtain orphan drug exclusivity upon approval, clinical superiority of such product to this same drug that is already approved for the same orphan indication must be demonstrated. 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.

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, for the treatment of several intermittent and chronic conditions, 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

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, or 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.

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.

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 which received marketing approval on July 24, 2019 and is currently available for sale, Eli Lilly's GEK and Novo Nordisk's GlucaGen HypoKit. In the future, competitors may include a subcutaneous dasiglucagon auto-injector being developed by Zealand Pharma. 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, or 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.

Even with the FDA approval of our first product, Gvoke, or any potential future approval of one or more of our product candidates in the United States, we may never 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 approved for sale in any international markets, and we do not have experience in obtaining regulatory approval in international markets. 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, with respect to our liquid stable glucagon formulation for the treatment of severe hypoglycemia in people with diabetes (marketed as Gvoke in the U.S.), we submitted an MAA to the EMA in November 2019. As Eli Lilly's GEK is not approved in Europe, we have conducted an additional clinical trial comparing Gvoke to Novo Nordisk's GlucaGen HypoKit, in addition to our clinical trials involving Eli Lilly's GEK. There can be no assurance that the results that we observed from our prior clinical trials for Gvoke will be sufficient to secure approval in Europe.

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, 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 Anti-Kickback Statute, or 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. 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.

Since January 2017, President Trump has 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. One Executive Order directs 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 or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates 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. The loss of the cost share reduction payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. Further, on June 14, 2018, 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 they were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business are not yet known.

In addition, CMS finalized regulations that would give 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. 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. 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.

In addition, 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 2029. In January 2013, 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 and the Trump Administration have indicated that each will address such costs through new legislative and administrative 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 Trump administration's budget proposals for fiscal year 2020 contains further drug price control measures that could be enacted in future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, 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, 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. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, 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. 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.

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.
- *False Claims Laws.* The federal civil and criminal false claims and civil monetary penalties laws, including the federal False Claims Act ("FCA"), prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Companies that submit claims directly to payors 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.
- *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 the Health Information Technology for Economic and Clinical Health Act of 2009, or 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 health care professionals and teaching hospitals, as well as ownership and investment interests held by the health care 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 health care 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 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, or GDPR. This directive 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 imposes strict rules on the transfer of personal data out of the EU to the United States. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States may result in fines and other administrative penalties. The GDPR introduces new data protection requirements in the EU and substantial fines for breaches of the data protection rules. The GDPR regulations may impose additional responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms ensuring compliance with these and/or new data protection rules. This may be onerous and adversely affect our business, financial condition, prospects and results of operations.

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, or 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, or SEC, is involved with enforcement of the books and records provisions of the FCPA and may suspend or bar issuers from trading securities 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, or 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 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 of our patent applications will be found to be patentable, including over our own prior art patents, or 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.

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.

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, or the 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.

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 control of 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.

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 other 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.

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.

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 marks 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.

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 Employee Matters, Managing Growth and 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. We will face even greater risks upon any commercialization by us of our products and 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 $10.0 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.

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 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.

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

As of December 31, 2019, we had 202 employees. As we commercialize Gvoke and development of our product candidates continues to progress, we anticipate the 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.

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, 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 additional costs associated with our public company reporting requirements, and we expect those costs to continue to increase in the future. For example, we devoted significant resources in 2019 and expect to continue to do so in future years 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.

If we experience material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately report our financial condition or results of operations which may adversely affect investor confidence in us and, as a result, the value of our common stock.

We are required under Section 404 of the Sarbanes-Oxley Act to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting beginning with this Annual Report on Form 10-K for the year ended December 31, 2019.

As we complete the transition from a company with a development focus to a commercial entity, we will continue to enhance our processes, computer systems and related internal controls. During the ongoing evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to conclude that our internal controls are effective. The effectiveness of our controls and procedures may be limited by a variety of factors, including:

- faulty human judgment and simple errors, omissions or mistakes;
- fraudulent action of an individual or collusion of two or more people;
- inappropriate management override of procedures; and
- the possibility that any enhancements to controls and procedures may still not be adequate to assure timely and accurate internal controls.

When we cease to be an "emerging growth company" under the federal securities laws, our auditors will be required to express an opinion on the effectiveness of our internal controls. If we are unable to confirm that our internal control over financial reporting is effective, or if our auditors are unable to express an opinion on the effectiveness of our internal controls, we could lose investor confidence in the accuracy and completeness of our financial reports, which could cause the price of our common stock to decline.

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.

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. 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. If we operate our business without insurance, we could be responsible for paying claims or judgments against us that would have otherwise been covered by insurance, which could adversely affect our results of operations or financial condition.

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.

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 currently conduct 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.

Inadequate funding for the FDA, the SEC and other government agencies 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, 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. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. 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.

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.

The comprehensive U.S. tax reform bill that was passed in December 2017 could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), and modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as "orphan drugs"). We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Risks Related to Our Common Stock

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; 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.

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 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, or the 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.

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, 2019, we had federal net operating loss carryforwards of $215.3 million and various state net operating loss carryforwards of $147.5 million. If not utilized, the federal net operating losses generated in taxable years ending 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 ending after December 31, 2017 can be carried forward indefinitely and can be utilized to offset up to 80% of taxable income in subsequent tax years. As of December 31, 2019, we had $8.3 million and $1.0 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, or the 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, or 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, the Tax Cuts and Jobs Act, or the TCJA, was enacted in 2017 and significantly reformed the Code. The TCJA, among other things, contained significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), limitation of the deduction for net operating losses from taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks generated in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), and the modification or repeal of many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as "orphan drugs"). 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.

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.

Provisions in our 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.

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.

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.

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 of 1933, as amended (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. On August 5, 2019, that decision was appealed to the Delaware Supreme Court and the appeal is pending. Unless and until the Court of Chancery's decision in *Sciabacucchi* is reversed by the Delaware Supreme Court or otherwise abrogated, we will not seek to enforce our Federal Forum Provision designating the Northern District of Illinois as the exclusive forum for Securities Act claims. In the event that the Delaware Supreme Court affirms the Court of Chancery's *Sciabacucchi* decision or otherwise determines that federal forum selection provisions are invalid, our Board intends to amend promptly our bylaws to remove our Federal Forum Provision. As a result of the Court of Chancery's *Sciabacucchi* decision or a decision by the Supreme Court of Delaware affirming the Court of Chancery's decision, we may incur additional costs associated with our Federal Forum Provision, which could have an adverse effect on our business, financial condition and results of operations.

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, as applicable. 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, as applicable, may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders.

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. Our Chicago office occupies approximately 41,000 square feet of leased space. The lease term expires on June 30, 2031. We also maintain a product development site in San Diego, California which occupies approximately 17,105 square feet of leased space under a 60-month lease term through June 2023. We currently believe that the Chicago and San Diego 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 10, 2020, there were approximately 58 stockholders of record of our common stock and the closing price of our common stock was $2.01 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, 2019.

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, 2019.

ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data are derived from the financial statements. The data presented below should be read in conjunction with the consolidated financial statements of the Company and related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this Annual Report on Form 10-K. The selected statements of operations data for the years ended December 31, 2019 and 2018 and the selected balance sheets data as of December 31, 2019 and 2018 are derived from our audited financial statements included elsewhere in this Annual Report on Form 10-K. The selected statements of operations data for the year ended December 31, 2017 and 2016 and the selected balance sheet data as of December 31, 2017 and 2016 are derived from our audited financial statements not included in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of the results that may be expected in the future.

	Years Ended December 31,			
(in thousands, except share and per share data)	2019	2018	2017	2016
Statements of Operations Data				
Net sales	$ 1,627	$ —	$ —	$ —
Grant and other income	1,095	2,423	1,552	1,067
Cost of goods sold	1,603	—	—	—
Gross profit	1,119	2,423	1,552	1,067
Operating expenses:				
Research and development	60,438	40,654	20,166	10,238
Selling, general and administrative	63,061	21,113	8,015	4,060
Total operating expenses	123,499	61,767	28,181	14,298
Loss from operations	(122,380)	(59,344)	(26,629)	(13,231)
Other income (expense):				
Interest and other income	2,813	1,613	124	5
Interest expense	(7,163)	(2,545)	(2)	(2)
Change in fair value of warrants	692	196	(46)	24
Other expense	—	—	(1)	(5)
Total other income (expense)	(3,658)	(736)	75	22
Net loss before benefit from income taxes	(126,038)	(60,080)	(26,554)	(13,209)
Benefit from income taxes	458	—	—	—
Net loss	$ (125,580)	$ (60,080)	$ (26,554)	$ (13,209)
Net loss per common share - basic and diluted [1]	$ (4.81)	$ (4.99)	$ (13.09)	$ (7.17)
Weighted average common shares outstanding - basic and diluted [1]	26,110,297	12,045,999	2,028,224	1,842,416

	As of December 31,			
(in thousands)	2019	2018	2017	2016
Balance Sheets Data				
Cash and cash equivalents	$ 19,519	$ 45,716	$ 42,045	$ 32,269
Short-term investments	56,030	66,917	—	—
Working capital [2]	60,145	107,727	39,193	30,647
Investments	13,231	—	—	—
Total assets	108,987	120,028	44,998	33,533
Long-term debt, net of unamortized deferred costs	58,305	31,890	—	—
Other liabilities	8,908	2,560	90	42
Total liabilities	94,551	44,622	4,950	2,569
Total convertible preferred stock	—	—	97,878	62,898
Total stockholders' equity (deficit)	14,436	75,406	(57,830)	(31,934)

(1) Refer to Note 14, "Net Loss Per Common Share," for an explanation of the calculations of our basic and diluted net loss per share and the shares used in computing basic and diluted net loss per share.

(2) We define working capital as current assets less current liabilities.

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 leveraging our novel non-aqueous formulation technology platforms, XeriSol and XeriJect, to develop and commercialize ready-to-use injectable and infusible drug formulations. We have developed and launched the first ready-to-use, room-temperature stable liquid glucagon formulation that, unlike the current standard of care, can be administered without any preparation or reconstitution. Our first product, Gvoke, delivers ready-to-use glucagon via a commercially available 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 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 on September 10, 2019. We began the commercial launch of Gvoke PFS in November 2019. Gvoke PFS 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. We expect Gvoke HypoPen will be commercially available in July 2020, in the same doses as the Gvoke PFS. Additionally, in November 2019, we submitted a Marketing Authorisation Application ("MAA") to the European Medicines Agency ("EMA") for our novel ready-to-use, room temperature stable liquid glucagon formulation for the treatment of severe hypoglycemia in people with diabetes. We are also applying our novel liquid glucagon formulation to the management of hypoglycemia associated with additional intermittent and chronic conditions with significant unmet medical need. Finally, 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 114 patents issued globally, including a composition of matter patent covering our ready-to-use glucagon formulation that expires in 2036.

We have built our commercial organization, including hiring individuals in commercial operations and sales and marketing, to support the commercial launch of Gvoke in the United States. Outside the United States we plan to pursue development and commercialization partnerships. 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 initiating the commercialization of our first product, Gvoke, which was approved by the FDA on September 10, 2019.

We have funded our operations to date primarily with proceeds from the sale of preferred and common stock, debt financing and grant awards. We have received gross proceeds of $104.9 million from sales of our preferred stock, $12.7 million from grant awards received from the National Institutes of Health ("NIH") and other philanthropic organizations, $98.3 million from our June 2018 initial public offering ("IPO") of our common stock, $60.0 million from the Amended Loan Agreement, and $60.0 million from our February 2019 public offering. On August 6, 2019, we filed a shelf registration statement on Form S-3 with the U.S. Securities and Exchange Commission's ("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. The Shelf was declared effective by the SEC on August 21, 2019. In December 2019, we sold an aggregate of 204,427 shares of common stock under the Shelf for gross proceeds of $1.8 million. In February 2020, we completed a public 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. Gross proceeds from the offering were $42.7 million.

For the years ended December 31, 2019 and 2018, we reported net losses of $125.6 million and $60.1 million, respectively. We have not been profitable since inception, and, as of December 31, 2019, our accumulated deficit was $246.2 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 for the commercial launch 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 do not expect to generate significant product revenue until we successfully commercialize Gvoke. We expect to 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. In addition, we may not be profitable even if we commercialize any of our product candidates.

Components of our Results of Operations

Net Sales

Net sales represent gross product sales less estimated allowances for patient co-pay assistance programs, prompt payment discounts, payor rebates, chargebacks, service fees, and product returns, all of which are recorded at the time of sale to pharmaceutical wholesalers. 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 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 available for commercial sale;
- expenses incurred under agreements with contract research organizations, or CROs, as well as investigative sites and consultants that conduct our preclinical studies and clinical trials;
- employee-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 conduct new clinical trials, prepare regulatory filings for our product candidates, and add headcount to support these efforts. In particular, we expect to continue to incur significant research and development expenses in the near term as we:

- conduct additional manufacturing scale-up for Gvoke HypoPen;
- continue the development of our additional ready-to-use glucagon programs including Post-Bariatric Hypoglycemia and Exercise-Induced Hypoglycemia;
- conduct preclinical and clinical work for our Pramlintide-Insulin program;
- continue clinical development for our ready-to-use diazepam rescue pen; and
- continue to advance other pipeline candidates.

Our research and development expenses may vary significantly over time due to uncertainties relating to the timing of regulatory approvals and results of our clinical trials.

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. We expect selling and marketing costs to increase significantly as we continue our marketing and selling efforts for the commercial launch of Gvoke in the United States.

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

Other Income (Expense)

Other income (expense) consists primarily of interest expense related to our loan agreements, interest income earned on deposits and investments, grant income and the change in fair value of our warrants.

Grant income is derived from grants that we received from the NIH and other philanthropic organizations to help bring necessary drugs to the marketplace where there are currently unmet needs. As of December 31, 2019, we are eligible to receive $0.2 million from an awarded unused grant that can be utilized to offset program costs for our diazepam program, in accordance with the grant agreement. This award will be recognized as grant income when we have performed the services outlined in the grant agreement.

In addition, other income includes service revenue from the feasibility studies we perform for third parties to determine whether our XeriSol™ and XeriJect™ technologies may enhance the formulation of such parties' proprietary drugs. Other expenses include the employees' time, materials and overhead applied to these feasibility studies.

Income Tax

We have incurred operating losses since inception and therefore do not have any taxable income. As of December 31, 2019, we had $215.3 million in federal net operating loss carryforwards, $147.5 million of various state net operating loss carryforwards, $8.3 million in federal research and orphan drug credits that begin to expire in 2025, and $1.0 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, 2019 and 2018:

(in thousands)	Years Ended December 31, 2019	2018	$ Change
Net sales	$ 1,627	$ —	$ 1,627
Grant and other income	1,095	2,423	(1,328)
Cost of goods sold	1,603	—	1,603
Gross profit	1,119	2,423	(1,304)
Operating expenses:			
Research and development	60,438	40,654	19,784
Selling, general and administrative	63,061	21,113	41,948
Total operating expenses	123,499	61,767	61,732
Loss from operations	(122,380)	(59,344)	(63,036)
Other income (expense):			
Interest and other income	2,813	1,613	1,200
Interest expense	(7,163)	(2,545)	(4,618)
Change in fair value of warrants	692	196	496
Total other income (expense)	(3,658)	(736)	(2,922)
Net loss before benefit from income taxes	(126,038)	(60,080)	(65,958)
Benefit from income taxes	458	—	458
Net loss	$ (125,580)	$ (60,080)	$ (65,500)

Net Sales

We launched Gvoke PFS for the treatment of severe hypoglycemia in people with diabetes in November 2019. Total net sales of Gvoke PFS were $1.6 million for the year ended December 31, 2019. Net sales represent gross product sales less estimated allowances for patient co-pay assistance programs, prompt payment discounts, payor rebates, chargebacks, service fees, and product returns, all of which are recorded at the time of sale to pharmaceutical wholesalers.

Grant and other income

Grant and other income decreased by $1.3 million for the year ended December 31, 2019 when compared to the year ended December 31, 2018, primarily due to a decrease in clinical work performed on grant programs during the current year, as many of these programs are nearing completion.

Cost of Goods Sold

The total cost of goods sold related to sales of Gvoke PFS was $1.6 million for the year ended December 31, 2019. Manufacturing costs for Gvoke prior to approval and commercialization were expensed as research and development expenses.

Research and Development Expenses

The following table summarizes our research and development expenses by functional area (in thousands):

	Years Ended December 31,		
	2019	2018	$ Change
Clinical and preclinical studies	$ 19,319	$ 13,295	$ 6,024
Pharmaceutical process development [(1)]	27,765	18,909	8,856
Compensation and related personnel costs	12,186	7,932	4,254
Stock-based compensation	1,168	518	650
Total research and development expenses	$ 60,438	$ 40,654	$ 19,784

(1) Includes CMC (chemistry, manufacturing and controls), product development, and regulatory expenses.

The following table summarizes our research and development expenses by program (in thousands):

	Years Ended December 31,		
	2019	2018	$ Change
Gvoke	$ 23,946	$ 20,865	$ 3,081
Other ready-to-use glucagon programs	12,411	4,741	7,670
Additional pipeline programs	7,176	2,434	4,742
Overhead (personnel, facilities and other expenses)	16,905	12,614	4,291
Total research and development expenses	$ 60,438	$ 40,654	$ 19,784

Research and development expenses increased $19.8 million for the year ended December 31, 2019 when compared to the year ended December 31, 2018. The increase was primarily driven by manufacturing costs for Gvoke prior to commercialization of $14.0 million, increased expenses associated with our clinical and preclinical trials of $6.0 million, and increases in compensation and related personnel costs of $4.9 million, partially offset by regulatory consulting fees incurred supporting the preparation of our Gvoke NDA filing in 2018.

Selling, General and Administrative Expenses

Selling, general and administrative costs increased $41.9 million for the year ended December 31, 2019 when compared to the year ended December 31, 2018. The increase was primarily driven by increases in marketing and selling expenses of $16.8 million related to the commercial launch of Gvoke, an increase in compensation and related personnel costs of $16.1 million due to additional headcount to support Gvoke commercialization efforts, and increased administrative and legal costs of $9.0 million primarily as a result of being a public company.

Other Income (Expense)

For the year ended December 31, 2019, interest expense increased $4.6 million in comparison to the year ended December 31, 2018, primarily due to a loss on extinguishment of debt of $2.3 million and increased borrowing levels. For the year ended December 31, 2019, interest and other income increased $1.2 million in comparison to the year ended December 31, 2018, as a result of an increase in cash equivalents and investments related to net proceeds from public equity offerings and debt financing. In addition, the change in fair value of warrants increased by $0.5 million for the year ended December 31, 2019 when compared to the year ended December 31, 2018.

Liquidity and Capital Resources

Our primary uses of cash are to fund marketing and selling costs related to commercialization of Gvoke, the research and development of our products, other operating expenses and working capital requirements. Historically, we have funded our operations primarily through private placements of convertible preferred stock, public offerings of common stock, issuance of debt, and grants awarded from the NIH and other philanthropic organizations. 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 public offering expenses. On February 19, 2019, we completed a public offering and 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 this public offering were $55.5 million after deducting underwriting discounts and commissions as well as other public offering expenses. On September 10, 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 on September 13, 2019. We become eligible to draw the second tranche of $15.0 million and the third tranche of $10.0 million following the Company's achievement of certain revenue targets prior to March 31, 2021 and June 30, 2021, respectively. On August 6, 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. The Shelf was declared effective by the SEC on August 21, 2019. In December 2019, we sold an aggregate of 204,427 shares of common stock under the Shelf for gross proceeds of $1.8 million. On February 14, 2020, we completed a public offering and sold 10,299,769 shares of common stock at a price of $4.15 per share, including 1,299,769 shares of common stock pursuant to the exercise of the underwriters' option to purchase additional shares. Gross proceeds from this public offering were $42.7 million.

As of December 31, 2019, we have $0.2 million in an awarded unused grant that can be utilized, in accordance with the grant agreement, to offset program costs for our diazepam program.

Capital Resources and Funding Requirements

We have incurred operating losses since inception, and we have an accumulated deficit of $246.2 million at December 31, 2019. We believe that our cash and cash equivalents and investments, funds raised in our February 2020 offering, and expected revenue from sales of Gvoke will enable us to sustain operations and capital expenditure requirements for at least the next 12 months. In addition, under the Amended Loan Agreement, we have additional borrowing capacity upon achievement of certain revenue targets prior to March 31, 2021 and June 30, 2021. We expect to incur substantial additional expenditures in the near term to support our ongoing activities and the commercial launch of Gvoke. Additionally, we expect to incur additional costs as a result of operating as a public company. 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 our planned Phase 2 and Phase 3 clinical trials, as well as commercialization of Gvoke and our product candidates 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 launch and commercialization 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 commercialize Gvoke and our product candidates, if approved. The issuance of equity securities may result in dilution to stockholders. If we raise additional funds through the issuance of 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

	Years Ended December 31,	
(**in thousands**)	**2019**	**2018**
Net cash used in operating activities	$ (104,346)	$ (56,279)
Net cash used in investing activities	(2,383)	(68,261)
Net cash provided by financing activities	80,530	128,211

The increase in cash used in operating activities for the year ended December 31, 2019 was primarily driven by increased spending in research and development and selling, general and administrative operating expenses. For a discussion regarding the increase 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, 2019 was primarily due to net sales of investments, the proceeds of which were used primarily to fund our Gvoke commercialization activities and research and development.

Cash provided by financing activities for the year ended December 31, 2019 was primarily due to the net proceeds from the public offerings of our common stock of $57.2 million and net proceeds from the issuance of long-term debt of $22.6 million. In the year ended December 31, 2018, cash provided by financing activities was primarily due to net proceeds from the initial public offering of our common stock of $88.9 million, net proceeds from the issuance of long-term debt of $34.7 million and net proceeds from the sale of Series C Preferred Stock of $4.4 million.

Off-Balance Sheet Arrangements

As of December 31, 2019, we did not have any off-balance sheet arrangements, as defined in Item 303(a)(4)(ii) of Regulation S-K promulgated by the SEC, that have, or are reasonably likely to have, a current or future material effect on our consolidated financial condition, results of operations, liquidity, capital expenditures, or capital resources.

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 products primarily to pharmaceutical wholesalers. These wholesalers then resell our products to their retail customers, such as pharmacies and mass merchandisers. In addition, we enter into arrangements with payors, group purchasing organizations, and health care providers that provide for government-mandated or privately negotiated discounts and allowances related to our products.

Revenue is recognized when our customer (e.g., a wholesaler) obtains control of promised goods or services, 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 co-pay assistance, prompt payment 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 co-pay assistance programs, prompt payment discounts, payor rebates, chargebacks, service fees, and product returns, all of which are recorded at the time of sale to pharmaceutical wholesalers. 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 Co-Pay 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 co-pay on units sold to distributors. 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 co-pay 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, accrues 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 commercial entities to provide rebates. 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 and Discounts

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

Chargebacks

Our products are subject to certain programs whereby pricing on products is discounted below wholesaler list price to participating commercial or government entities. 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 contract prices, sales data obtained from third-party information and estimated levels of inventory in the distribution channel and record the chargebacks as a reduction of revenue. Accrued chargebacks are included in accrued trade discounts and rebates on the consolidated balance sheets.

Service Fees

We record service fees paid to our 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, we maintain a return goods policy that allows customers to return product due to order or shipment errors, overstock, dating, recall or other changes in regulatory guidelines. Generally, product may be returned for a period beginning six months prior to its expiration date and up to one year after its expiration date. To determine the estimate of the provision for returns, we analyze branded product return history of comparable products and other market data. In a reporting period, we may decide to constrain revenue for product returns based on information from various sources, including channel inventory levels, inventory dating, prescription data, the expiration dates of product currently being shipped, price changes of competitive products and introductions of generic products. At December 31, 2019, we increased our returns reserve above the level indicated by the return history of comparable products due to factors related to the initial stocking of inventory for the launch of our new product. 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 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 for Gvoke prior to approval and commercial salability 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:

	Years Ended December 31,	
(in thousands)	**2019**	**2018**
Research and development	$ 1,168	$ 518
Selling, general and administrative	5,316	1,210
Total stock-based compensation expense	$ 6,484	$ 1,728

We account for our stock-based compensation awards in accordance with Accounting Standards Codification Topic 718, *Compensation-Stock Compensation*, or 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.

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 as well as the historical volatility of our own common stock since we began trading subsequent to our IPO in June 2018. 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 or similar public companies until a sufficient amount of historical information regarding the volatility of our own common stock share price becomes available, or unless circumstances change such that the identified companies are no longer similar to us, in which case more suitable companies whose share prices are publicly available would be utilized in the calculation.
- *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, or 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, 2019 would increase or decrease interest income by approximately $0.9 million on an annual basis.

Amended Loan Agreement—Our interest rate risk relates primarily to U.S. dollar LIBOR-indexed borrowings. Based on our outstanding borrowings at December 31, 2019, a one-percentage point increase or decrease in interest rates would have a $0.6 million effect on interest expense on an annual basis.

Foreign Exchange Risk

Foreign Exchange—In 2019, we began to 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, 2019, we had immaterial liabilities denominated in the Euro and 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, 2019.

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, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the years in the two-year period ended December 31, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2019, 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.

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

/s/ KPMG LLP

Chicago, Illinois
March 11, 2020

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

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 19,519	$ 45,716
Short-term investments	56,030	66,917
Trade accounts receivable, net	4,693	—
Other accounts receivable, net	946	2,869
Inventory	2,176	—
Prepaid expenses and other current assets	4,119	2,397
Total current assets	87,483	117,899
Investments	13,231	—
Property and equipment, net	7,853	2,034
Other assets	420	95
Total assets	$ 108,987	$ 120,028
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 5,603	$ 866
Other accrued liabilities	18,119	8,214
Accrued trade discounts and rebates	1,375	—
Accrued returns reserve	1,957	—
Other current liabilities	284	1,092
Total current liabilities	27,338	10,172
Long-term debt, net of unamortized deferred costs	58,305	31,890
Other liabilities	8,908	2,560
Total liabilities	94,551	44,622
Commitments and contingencies (Note 10)		
Stockholders' Equity:		
Preferred stock—par value $0.0001, 10,000,000 shares authorized and no shares issued and outstanding as of December 31, 2019 and December 31, 2018, respectively	—	—
Common stock—par value $0.0001, 150,000,000 shares authorized as of December 31, 2019 and 2018, respectively; 27,214,523 and 20,808,366 shares issued and outstanding as of December 31, 2019 and 2018, respectively	3	2
Additional paid in capital	260,635	196,121
Accumulated deficit	(246,245)	(120,665)
Accumulated other comprehensive gain (loss)	43	(52)
Total stockholders' equity	14,436	75,406
Total liabilities and stockholders' equity	$ 108,987	$ 120,028

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,	
	2019	2018
Net sales	$ 1,627	$ —
Grant and other income	1,095	2,423
Cost of goods sold	1,603	—
Gross profit	1,119	2,423
Operating expenses:		
Research and development	60,438	40,654
Selling, general and administrative	63,061	21,113
Total operating expenses	123,499	61,767
Loss from operations	(122,380)	(59,344)
Other income (expense):		
Interest and other income	2,813	1,613
Interest expense	(7,163)	(2,545)
Change in fair value of warrants	692	196
Total other income (expense)	(3,658)	(736)
Net loss before benefit from income taxes	(126,038)	(60,080)
Benefit from income taxes	458	—
Net loss	$ (125,580)	$ (60,080)
Other comprehensive gain (loss), net of tax:		
Unrealized gains (losses) on investments	93	(52)
Foreign currency translation adjustments	2	—
Comprehensive loss	$ (125,485)	$ (60,132)
Net loss per common share - basic and diluted	$ (4.81)	$ (4.99)
Weighted average common shares outstanding - basic and diluted	26,110,297	12,045,999

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

XERIS PHARMACEUTICALS, INC.

Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(in thousands, except share data)

	CONVERTIBLE PREFERRED STOCK						STOCKHOLDERS' EQUITY (DEFICIT)					
	SERIES A		SERIES B		SERIES C		COMMON STOCK		ADDITIONAL PAID IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE GAIN (LOSS)	ACCUMULATED DEFICIT	TOTAL
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT				
Balance, December 31, 2017	1,843,965	$ 1,945	5,696,834	$ 18,536	12,834,912	$ 77,397	2,159,068	$ 1	$ 2,754	$ —	$ (60,585)	$ (57,830)
Net loss	—	—	—	—	—	—	—	—	—	—	(60,080)	(60,080)
Issuance of common stock upon Initial Public Offering	—	—	—	—	—	—	6,555,000	—	88,903	—	—	88,903
Issuance of Series C Preferred Stock	—	—	—	—	707,680	4,414	—	—	—	—	—	—
Conversion of convertible preferred stock into common stock	(1,843,965)	(1,945)	(5,696,834)	(18,536)	(13,542,592)	(81,811)	11,837,073	1	102,292	—	—	102,293
Exercise and vesting of stock-based awards	—	—	—	—	—	—	248,978	—	395	—	—	395
Exercise of warrants	—	—	—	—	—	—	8,247	—	49	—	—	49
Stock-based compensation	—	—	—	—	—	—	—	—	1,728	—	—	1,728
Other comprehensive loss	—	—	—	—	—	—	—	—	—	(52)	—	(52)
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 public offerings	—	—	—	—	—	—	6,201,202	1	57,226	—	—	57,227
Exercise and vesting of stock-based awards	—	—	—	—	—	—	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 gain	—	—	—	—	—	—	—	—	—	95	—	95
Balance, December 31, 2019	—	$ —	—	$ —	—	$ —	27,214,523	$ 3	$ 260,635	$ 43	$ (246,245)	$ 14,436

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,	
	2019	2018
Cash flows from operating activities:		
Net loss	$ (125,580)	$ (60,080)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,078	320
Amortization of investments	(686)	(218)
Amortization of debt issuance costs	948	560
Stock-based compensation	6,484	1,728
Loss on extinguishment of debt	2,324	—
Change in fair value of warrants	(692)	(196)
Changes in operating assets and liabilities:		
Trade accounts receivable	(4,693)	—
Other accounts receivable	1,634	(1,670)
Prepaid expenses and other current assets	(960)	(1,588)
Inventory	(2,176)	—
Other assets	(247)	62
Accounts payable	4,737	(1,110)
Other accrued liabilities	8,912	5,630
Accrued trade discounts and rebates	1,375	—
Accrued returns reserve	1,957	—
Other liabilities	1,239	283
Net cash used in operating activities	(104,346)	(56,279)
Cash flows from investing activities:		
Capital expenditures	(1,107)	(1,510)
Purchases of investments	(102,472)	(68,851)
Sales and maturities of investments	101,196	2,100
Net cash used in investing activities	(2,383)	(68,261)
Cash flows from financing activities:		
Proceeds from Initial Public Offering	—	98,325
Payments for Initial Public Offering costs	—	(9,422)
Proceeds from public offerings	61,692	—
Payments of public offering costs	(4,465)	—
Proceeds from sale of Series C Preferred Stock	—	4,438
Payments of Series C Preferred Stock offering costs	—	(24)
Proceeds from issuance of debt	60,000	35,000
Repayment of debt	(35,000)	—
Payments of debt issuance costs	(2,381)	(333)
Proceeds from employee stock purchase plan	532	—
Proceeds from exercise of stock awards	152	227
Net cash provided by financing activities	80,530	128,211
Effect of exchange rate changes on cash and cash equivalents	2	—
Increase (decrease) in cash and cash equivalents	(26,197)	3,671
Cash and cash equivalents, beginning of period	45,716	42,045
Cash and cash equivalents, end of period	$ 19,519	$ 45,716
Supplemental schedule of cash flow information:		
Cash paid for interest	$ 3,717	$ 1,711
Supplemental schedule of non-cash investing and financing activities:		
Tenant improvement allowance	$ 5,658	$ —
Accrued debt issuance costs	$ 1,800	$ 2,325
Allocation of debt costs to warrants	$ —	$ 1,012

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 our inception in 2005, the Company has 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 initiating the commercialization of our first product, Gvoke, which was approved by the FDA on September 10, 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. The Company has financed its operations through the issuance of its common stock, convertible preferred stock and other equity instruments, debt financing and grant funding from the National Institutes of Health ("NIH") and other philanthropic organizations.

The Company has generated $1.6 million in revenue from product sales as of December 31, 2019. The Company has incurred operating losses since inception and has an accumulated deficit of $246.2 million as of December 31, 2019. 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, 2019, in addition to the funds raised in its February 2020 equity offering, the Company believes 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 development and commercialization of its drug candidates, the development of new technological innovations by its competitors, protection of intellectual property and market acceptance of the Company's products.

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 Updates ("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 products primarily to pharmaceutical wholesalers. These wholesalers then resell the Company's products to their retail customers, such as pharmacies and mass merchandisers. In addition, the Company enters into arrangements with payors, group purchasing organizations, and health care providers that provide for government-mandated or privately-negotiated discounts and allowances related to the Company's products.

Revenue is recognized when the Company's customer (e.g., a wholesaler) obtains control of promised goods or services, 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 co-pay assistance, prompt payment 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 co-pay assistance programs, prompt payment discounts, payor rebates, chargebacks, service fees, and product returns, all of which are recorded at the time of sale to pharmaceutical wholesalers. 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 Co-Pay 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 co-pay on units sold to distributors. 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 co-pay 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, accrues the discount on all eligible sales. The Company records the discount as an allowance against trade accounts receivable on the consolidated balance sheets and as a reduction of revenue.

Commercial Rebates

The Company contracts with certain commercial entities to provide rebates. 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 and Discounts

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 Coverage Gap Discount Program. The Company accrues estimated rebates and discounts based on estimated percentages of product sold to qualified patients, estimated rebate or discount percentages and estimated levels of inventory in the distribution channel that will be prescribed to qualified patients and records the rebates or discounts as a reduction of revenue. Accrued government rebates and discounts are included in accrued trade discounts and rebates on the consolidated balance sheets.

Chargebacks

The Company's products are subject to certain programs whereby pricing on products is discounted below wholesaler list price to participating commercial or government entities. 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 contract prices, sales data obtained from third-party information and estimated levels of inventory in the distribution channel and records the chargebacks as a reduction of revenue. Accrued chargebacks are included in accrued trade discounts and rebates on the consolidated balance sheets.

Service Fees

The Company records service fees paid to its 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 maintains a return goods policy that allows customers to return product due to order or shipment errors, overstock, dating, recall or other changes in regulatory guidelines. Generally, product may be returned for a period beginning six months prior to its expiration date and up to one year after its expiration date. To determine the estimate of the provision for returns, the Company analyzes branded product return history of comparable products and other market data. In a reporting period, the Company may decide to constrain revenue for product returns based on information from various sources, including channel inventory levels, inventory dating, prescription data, the expiration dates of product currently being shipped, price changes of competitive products and introductions of generic products. At December 31, 2019, the Company increased its returns reserve above the level indicated by the return history of comparable products due to factors related to the initial stocking of inventory for the launch of our new product. 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 year ended December 31, 2019, three customers accounted for 94% of the Company’s gross sales. These same three customers accounted for 97% of the trade accounts receivable at December 31, 2019.

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 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 conducting certain clinical trials 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 research 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 agency securities, 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 accumulated other comprehensive loss on the Company's balance sheets. 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, 2019 and 2018, 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 $4.5 million of direct costs associated with the public equity offerings in additional paid in capital for the year ended December 31, 2019 and $9.4 million of direct costs associated with the IPO in additional paid in capital for the year ended December 31, 2018. 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, 2019 and 2018, $0.4 million and $0, respectively, of deferred costs related to equity financings are included in other assets on the 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 commercial salability 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*, or 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.

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 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, 2019 and 2018, the Company did not accrue any interest or penalties on uncertain tax positions.

Grant income

The Company has received several grants from the NIH and other philanthropic organizations for certain research and development projects the Company has and is currently performing. Grant income is recognized when these research and development activities are performed and the Company has met criteria for reimbursement per the grant agreements. The Company has also received grants that were funded upfront. The Company defers the recognition of these awards until the related research and development expenses are incurred.

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 gain (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 debt securities classified as available-for-sale investments and foreign currency translation adjustments.

Reclassifications

In the fourth quarter of 2019, in conjunction with the recognition of product sales and related cost of sales, the Company reclassified grant income, service revenue and the related cost of revenue to other income (expense) on the Company's consolidated statements of operations and comprehensive loss. There was no impact to net loss. Prior periods have been revised to conform to the current year presentation.

New accounting pronouncements

Recently issued accounting pronouncements

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, 2020 and interim periods within fiscal years beginning after December 15, 2021. 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, 2019	December 31, 2018
Raw materials	$ 1,321	$ —
Work in process	662	—
Finished goods	193	—
Inventory	$ 2,176	$ —

Note 4. Property and Equipment

Property and equipment consisted of the following:

(in thousands)	December 31, 2019	December 31, 2018
Lab equipment	$ 2,528	$ 1,658
Furniture and fixtures	1,611	541
Computer equipment	232	87
Office equipment	80	109
Software	347	110
Leasehold improvements	4,543	180
	9,341	2,685
Less: accumulated depreciation and amortization	(1,488)	(651)
Property and equipment, net	$ 7,853	$ 2,034

Depreciation and amortization expense relating to property and equipment was $1.1 million and $0.3 million for the years ended December 31, 2019 and 2018, respectively.

Note 5. Other Accrued Liabilities

Other accrued liabilities consisted of the following:

(in thousands)	December 31, 2019	December 31, 2018
Accrued research and development costs	$ 7,062	$ 2,221
Accrued employee costs	6,818	4,326
Accrued marketing and selling costs	1,973	—
Accrued interest expense	449	274
Accrued other costs	1,817	1,393
Other accrued liabilities	$ 18,119	$ 8,214

Note 6. Long-term Debt

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 "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 was $20.0 million and was drawn down in February 2018 (the "2018 Term A Loan"). The second tranche was $15.0 million and was drawn down in September 2018 (the "2018 Term B Loan"). The interest rate under the Loan Agreement was the thirty-day U.S. LIBOR rate plus 6.75%, which was 8.84% as of September 13, 2019, the date of repayment of the amounts outstanding under the Loan Agreement. Payments on the Loan Agreement were interest only for the first 24 months. The Company also issued warrants to the Lenders to purchase common stock, which is further discussed in Note 9, "Warrants."

On September 10, 2019, the Company entered into an Amended Loan Agreement with the Lenders which amended and restated the Loan Agreement. Under the Amended Loan Agreement, the Lenders will 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 on September 13, 2019. The second tranche of $15.0 million (the "Term B Loan") and the third tranche of $10.0 million (the "Term C Loan") will become available to the Company upon the achievement of certain revenue targets prior to March 31, 2021 and June 30, 2021, respectively. The 2018 Term A Loan and 2018 Term B Loan and the related final payment fee of $2.3 million were repaid in conjunction with the execution of the Amended Loan Agreement.

The Amended Loan Agreement provides for interest-only payments through March 31, 2021, after which the principal will be payable in 27 equal monthly installments. However, if the Term B Loan is funded, then the period for interest-only payments is extended through December 31, 2021, after which the principal will be payable in 30 equal monthly installments. If the Term C Loan is funded, then the period for interest-only payments is further extended through September 30, 2022, after which the principal will be payable in 21 equal monthly installments. The maturity date is June 1, 2023, provided that if the Term B Loan is funded, then the maturity date will be extended to June 1, 2024. After repayment, no loans may be reborrowed. For the period from the funding date of the Term A Loan through and including December 31, 2019, the loans incurred interest at a rate of 8.68%. Following such time, the loans shall 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. The Company incurred total debt issuance costs of $1.9 million related to the Amended Loan Agreement, which are reflected as a direct reduction to the term loan balance and are being amortized into interest expense over the life of the loan using the effective interest method.

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

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. Prior to April 1, 2021, the Company is subject to a prepayment fee equal to 1.50% of the principal amount being prepaid. In the event the Company draws down the second or third tranche, the period subject to the 1.50%

prepayment fee is extended to January 1, 2022 and October 1, 2022, respectively. A final payment fee of 3.0% multiplied by the original principal amount of each tranche drawn is due upon the earlier to occur of the maturity date of the Amended Loan Agreement, the acceleration of 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.

The components of debt are as follows:

(in thousands)	December 31, 2019	December 31, 2018
2018 Term A Loan	$ —	$ 20,000
2018 Term B Loan	—	15,000
Term A Loan	60,000	—
Principal amount of long-term debt	60,000	35,000
Less: Unamortized deferred costs	(1,695)	(3,110)
Long-term debt	$ 58,305	$ 31,890

The following table sets forth the Company's future minimum principal payments (in thousands):

2019	$ 0
2020	0
2021	20,000
2022	26,700
2023	13,300
	$ 60,000

For the year-to-date period 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 Loan Agreement. For the year ended December 31, 2018, the Company recognized interest expense of $2.5 million, of which $0.6 million was related to the amortization of debt issuance costs.

Note 7. Public Stock Offerings

On June 25, 2018, the Company closed the Initial Public Offering ("IPO") of its common stock pursuant to a registration statement on Form S-1, as amended. The Company sold an aggregate of 6,555,000 shares of common stock under the registration statement at an IPO price of $15.00 per share, including 855,000 shares of common stock pursuant to the exercise of the underwriters' option to purchase additional shares. Net proceeds from the IPO were $88.9 million after deducting underwriting discounts and commissions as well as other IPO expenses. Upon closing the IPO, all outstanding shares of the Company's Series A, B and C convertible preferred stock were converted into 11,837,073 shares of common stock.

On February 19, 2019, the Company completed a public 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 public 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.

Note 8. Convertible Preferred Stock

In February 2018, the Company issued an additional 707,680 shares of Series C convertible preferred stock for net proceeds of $4.4 million.

During the second quarter of 2018, a majority of the holders of the Company's convertible preferred stock elected to have their shares converted into common stock; therefore, all outstanding shares of preferred stock were converted into 11,837,073 shares of common stock at a conversion rate of 1:1.78112 upon the closing of the Company's IPO on June 25, 2018.

Prior to the conversion of the convertible preferred stock into common stock, the holders of the Company’s convertible preferred stock were entitled to receive non-cumulative dividends at the rate of 8% of the purchase price per annum in preference to any dividends to the holders of the common stock, payable as and if when declared by the Board of Directors. The holders of the convertible preferred stock also were entitled to participate pro rata in any dividends paid to the holders of the common stock on an as-converted basis. No dividends were declared by the Company’s Board of Directors.

Note 9. 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. There have been 18,512 2014 Warrants exercised, and 1,419 warrants remain outstanding as of December 31, 2019.

As part of the 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 initial 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 Term A Warrants or Term B Warrants, and as such all 53,720 warrants and 40,292 warrants were outstanding as of December 31, 2019, respectively.

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 a gain (loss) 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 Term A Warrants and the Term B Warrants, respectively. The Company recognized a gain (loss) of $(56,000), $(108,000) and $360,000 upon the change in fair value of the warrants during the year ended December 31, 2018 related to the 2014 Warrants, the Term A Warrants and the Term B Warrants, respectively.

As of December 31, 2019, the following warrants were outstanding:

	Outstanding Warrants	Exercise Price per Warrant	Expiration Date
2014 Warrants	1,419	$5.912	August 2020
Term A Warrants	53,720	$11.169	February 2025
Term B Warrants	40,292	$11.169	September 2025
	95,431		

Note 10. Commitments and Contingencies

Commitments

The Company has non-cancellable operating leases for office space, which expire at various times through 2031. The non-cancellable office lease agreements provide for monthly lease payments, which increase during the term of each lease agreement.

In the first quarter of 2018, the Company signed a lease for office space in Chicago, Illinois. In the fourth quarter of 2018, the Company signed an amendment to this lease to occupy new space and relocated to this new space in March 2019.

Future minimum lease payments under operating leases at December 31, 2019 are as follows (in thousands):

2020	$	1,575
2021		2,208
2022		2,263
2023		1,745
2024		1,278
Thereafter		8,476
Total minimum lease payments	$	17,545

Total rent expense under these operating leases was approximately $2.2 million and $1.3 million for the years ended December 31, 2019 and 2018, respectively.

As of December 31, 2019, we had unused letters of credit of $1,083,000 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, 2019 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 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 determined 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).

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, 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 in the Company's capitalization. On January 1, 2019, the number of shares of common stock available for issuance under the 2018 Plan was automatically increased by 835,728 shares. As of December 31, 2019, there were approximately 809,000 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, 2019, the number of shares of common stock available for issuance under the ESPP increased by 208,932 shares. The number of shares reserved under the ESPP is subject to adjustment in the event of a stock split, stock dividend or other change in capitalization. The Company issued 73,607 shares at a weighted average price of $7.22 per share during the year ended December 31, 2019. As of December 31, 2019, there were approximately 328,000 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 in our capitalization. As of December 31, 2019, there were approximately 340,000 shares of common stock available for future issuance under the Inducement Plan.

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 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 Company uses historical data to estimate employee terminations within the valuation model.

The fair value of stock options granted was estimated with the following weighted average assumptions:

	Years Ended December 31,	
	2019	**2018**
Expected term (years)	6.0	6.0
Risk-free interest rate	2.14%	2.48%
Expected volatility	60.27%	56.84%
Expected dividends	—	—

Stock option activity under the 2011 Plan, 2018 Plan and Inducement Plan for the year ended December 31, 2019 was as follows:

	OPTIONS	WEIGHTED AVERAGE EXERCISE PRICE	WEIGHTED AVERAGE CONTRACTUAL LIFE (YEARS)
Outstanding - January 1, 2019	3,130,700	$ 8.06	8.69
Granted	1,600,650	12.21	
Exercised and vested	(128,307)	1.99	
Forfeited	(172,655)	16.33	
Expired	(1,403)	19.77	
Outstanding - December 31, 2019	4,428,985	$ 9.40	8.19
Exercisable - December 31, 2019	1,647,911	$ 6.07	7.31
Vested and expected to vest at December 31, 2019	4,202,205	$ 9.32	8.16

The weighted average fair value of awards granted during the year ended December 31, 2019 was $6.97 per share. The total intrinsic value of options exercised during the year ended December 31, 2019 was $1.0 million. The aggregate intrinsic value of awards vested and expected to vest as of December 31, 2019 was $7.8 million.

At December 31, 2019, there was a total of $14.1 million of unrecognized stock-based compensation expense related to stock options that is expected to be recognized over a weighted average period of 2.3 years.

Restricted stock unit ("RSU") awards for the year ended December 31, 2019 were as follows:

	Units
Unvested balance - January 1, 2019	0
Granted	125,000
Unvested balance - December 31, 2019	125,000

Restricted stock unit awards are measured based on the fair market value of the underlying stock on the date of grant and recognized as expense on a straight-line basis over the employee's requisite service period (generally the vesting period). As of December 31, 2019, there was $1.3 million of unrecognized stock-based compensation expense related to RSUs, which is expected to be recognized over the weighted-average remaining vesting period of 3.1 years.

The fair value of the ESPP Plan shares was estimated using the Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year Ended December 31, 2019
Expected term (years)	0.5
Risk-free interest rate	1.85%
Expected volatility	70.70%
Expected dividends	—

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

	Years Ended December 31,	
	2019	2018
Research and development	$ 1,168	$ 518
Selling, general and administrative	5,316	1,210
Total stock-based compensation expense	$ 6,484	$ 1,728

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, 2019 and 2018 (in thousands):

	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

	Total as of December 31, 2018	Level 1	Level 2	Level 3
Assets				
Cash and cash equivalents:				
Cash and money market funds	$ 45,716	$ 45,716	$ —	$ —
Investments:				
U.S. government securities	38,737	38,737	—	—
Corporate securities	15,066	—	15,066	—
Agency securities	11,931	—	11,931	—
Commercial paper	1,183	1,183	—	—
Total investments	$ 66,917	$ 39,920	$ 26,997	$ —
Liabilities				
Warrant liabilities	$ 860	$ —	$ —	$ 860

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 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 changes in the warrant liabilities (in thousands):

Balance at December 31, 2018	$ 860
Exercise of warrants	(18)
Change in fair value of warrants	(692)
Balance at December 31, 2019	$ 150

There were no transfers between any of the levels of the fair value hierarchy during the years ended December 31, 2019 and 2018.

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, 2019, 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 two years at the date of purchase. Debt securities as of December 31, 2019 had an average remaining maturity of 0.70 years. The debt securities are reported at fair value with unrealized gains or losses recorded in accumulated other comprehensive gain (loss) in the consolidated balance sheets. 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, 2019 and 2018 (in thousands):

	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

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Total Fair Value
Investments:				
Agency securities	$ 11,944	$ —	$ (13)	$ 11,931
Commercial paper	1,183	—	—	1,183
Corporate securities	15,081	—	(15)	15,066
U.S. government securities	38,761	—	(24)	38,737
Total available-for-sale investments	$ 66,969	$ —	$ (52)	$ 66,917

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, 2019 and 2018, 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 is determined by dividing net loss applicable to common stockholders by the weighted average common shares outstanding during the period. For all periods presented, the outstanding shares of preferred stock, warrants, stock option awards and restricted stock units 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 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,	
	2019	2018
Vested and unvested stock options	4,428,985	3,130,700
Restricted stock units	125,000	—
Warrants	95,431	102,647
	4,649,416	3,233,347

Note 15. 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 year ended December 31, 2019, the Company made $0.4 million of matching contributions to the plan.

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:

	Years Ended December 31,	
(in thousands)	**2019**	**2018**
Federal tax benefit at statutory rate	$ (26,468)	$ (12,617)
State tax benefit, net of federal benefit	(5,570)	(1,842)
Research and development and orphan drug credits	(2,912)	(2,279)
Uncertain tax positions	342	603
Permanent adjustments to expenses	169	45
Stock-based compensation	683	76
Return to provision adjustment	(3,278)	(2,470)
Rate impact of deferred tax balance	—	(63)
Statutory rate differential	(51)	—
Other	339	9
Changes in valuation allowance	36,288	18,538
Total income tax benefit	$ (458)	$ —

The benefit for income taxes for 2019 is attributable to an Australian research and development tax incentive that will be refunded to the Company after the 2019 income tax filing. During the years ended December 31, 2019 and 2018, the Company had no interest and penalties related to income taxes.

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, 2019, 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:

	December 31,	
(in thousands)	**2019**	**2018**
Deferred tax assets:		
Net operating losses	$ 55,110	$ 25,372
Federal research and orphan drug credits	8,309	5,426
Stock-based compensation	1,092	267
Other temporary differences	4,648	1,679
Valuation allowance	(68,950)	(32,662)
Total assets	209	82
Deferred tax liabilities:		
Fixed and intangible assets	(155)	(82)
Other deferred tax liabilities	(54)	—
Total liabilities	(209)	(82)
Net deferred tax assets	$ —	$ —

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. As of December 31, 2018, the Company had federal net operating loss carryforwards of $108.8 million and various state net operating loss carryforwards of $35.6 million. Net operating loss carryforwards for U.S. federal income tax purposes that were generated prior to January 1, 2018 have a twenty-year carryforward life and the earliest layers will begin to expire in 2025. Under the Tax Act, federal net operating losses incurred in 2018 and in future 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, 2019, the Company had $8.3 million and $1.0 million of federal and state income tax credits, respectively, to reduce future tax liabilities. As of December 31, 2018, the Company had $5.8 million and $2.0 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 the 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, 2019 and 2018 is as follows (in thousands):

Valuation allowance at December 31, 2017	$ (14,124)
Increase for 2018 activity	(18,538)
Valuation allowance at December 31, 2018	(32,662)
Increase for 2019 activity	(36,288)
Valuation allowance at December 31, 2019	$ (68,950)

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, 2019 and 2018, excluding interest and penalties, consisted of the following (in thousands):

	December 31,	
	2019	2018
Beginning balance - uncertain tax positions	$ 603	$ —
Increases related to tax positions taken during the current year	246	228
Increases related to tax positions taken during the prior year	96	375
Ending balance - uncertain tax positions	$ 945	$ 603

For the year ended December 31, 2019, the increase in uncertain tax positions was attributable primarily to the U.S. federal orphan drug credits and research and development credits. In the Company’s balance sheet, uncertain tax positions of $0.9 million were offset against deferred tax assets.

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. The Company did not accrue any interest or penalties for the years ended December 31, 2019 and 2018.

Note 17. Subsequent Event

On February 14, 2020, the Company completed a public offering of its common stock pursuant to a shelf registration statement on Form S-3, which was filed on August 6, 2019 and declared effective by the SEC on August 21, 2019. The Company sold 10,299,769 shares of common stock at a price of $4.15 per share, including 1,299,769 shares of common stock pursuant to the partial exercise of the underwriters' option to purchase up to an additional 1,350,000 shares of common stock. Gross proceeds from the offering were $42.7 million.

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, 2019 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, 2019 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, 2019.

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, 2019 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, 2019 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, 2019 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, 2019 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, 2019 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, 2019 and is incorporated in this Annual Report on Form 10-K by reference.

PART IV

ITEM 15. EXHIBITS, 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)
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
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	Lease Agreement, dated as of September 29, 2017, by and between Are-SD Region No. 30, LLC and the Registrant (Incorporated by reference to Exhibit 10.6 to our Registration Statement on Form S-1 filed with the SEC on May 24, 2018)
10.7#	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)
10.8#	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)
10.9#	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)
10.10#	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)
10.11#	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)
10.12#	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)

Exhibit No.	Description
10.13#	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)
10.14+	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)
10.15+	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)
10.16+	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)
10.17+	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)
10.18	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)
10.19+	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)
10.20#	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)
10.21+	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)
10.22#	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)
10.23	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)
10.24	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 the Company's Current Report on Form 8-K filed with the SEC on September 10, 2019)
10.25	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 the Company's Quarterly Report on Form 10-Q filed with the SEC on August 6, 2019)
10.26#	Consulting Agreement between the Registrant and Jonathan Rigby, dated March 26, 2019 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on May 9, 2019)
23.1*	Consent of Independent Registered Public Accounting Firm
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended
32.1*	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

32.2*	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* 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 hereunto duly authorized.

Xeris Pharmaceuticals, Inc.

By /s/ Paul R. Edick

Paul R. Edick

President, Chief Executive Officer and Chairman

Date March 11, 2020

Pursuant to the requirements of the Securities Act of 1933, as amended, this Report has been signed by the following persons on behalf of the registrant in the capacities indicated on the 11th day of March, 2020.

SIGNATURE	**TITLE**
/s/ Paul R. Edick Paul R. Edick	President, 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
/s/ Mark Thierer Mark Thierer	Director