

**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 period ended December 31, 2018

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

(State or Other Jurisdiction of
Incorporation or Organization)

20-3352427

(I.R.S. Employer
Identification Number)

180 N. LaSalle Street, Suite 1810

Chicago, Illinois 60601

(Address of Principal Executive Offices)

(844) 445-5704

(Registrant's Telephone Number, Including Area Code)

Securities Registered Pursuant to Section 12(b) of the Exchange Act:

Title of Each Class

Name of Each Exchange on Which Registered

Common Stock, \$0.0001 par value per share

The Nasdaq Global Select Market

Securities Registered Pursuant to Section 12(g) of the Exchange 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 Securities 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 during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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 Exchange Act). Yes No

As of June 30, 2018, the aggregate market value of the Registrant's common stock held by non-affiliates of the Registrant was approximately \$281.9 million based on the closing sales price as reported on the Nasdaq Exchange. As of February 28, 2019, 26,809,851 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 2019 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, 2018.

XERIS PHARMACEUTICALS, INC.

Index to Annual Report on Form 10-K Year Ended December 31, 2018

	Page
Cautionary Statements for Forward-Looking Information	3
Part I.	
Item 1. Business	4
Item 1A. Risk Factors	49
Item 1B. Unresolved Staff Comments	87
Item 2. Properties	87
Item 3. Legal Proceedings	87
Item 4. Mine Safety Disclosures	87
Part II.	
Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	87
Item 6. Selected Financial Data	89
Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations	90
Item 7A. Quantitative and Qualitative Disclosures About Market Risk	97
Item 8. Financial Statements and Supplementary Data	98
Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	119
Item 9A. Controls and Procedures	119
Item 9B. Other Information	119
Part III.	
Item 10. Directors, Executive Officers and Corporate Governance	119
Item 11. Executive Compensation	119
Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	119
Item 13. Certain Relationships and Related Transactions, and Director Independence	119
Item 14. Principal Accountant Fees and Services	119
Part IV.	
Item 15. Exhibits, Financial Statement Schedules	120
Index to Exhibits	121
Signatures	123

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 timing or likelihood of approval by the U.S. Food & Drug Administration of our New Drug Application for our Gvoke HypoPen;
- our estimates regarding the market opportunities for our product candidates;
- the commercialization, marketing and manufacturing of our product candidates, if approved;
- the pricing and reimbursement of our Gvoke HypoPen or any other of our product candidates, if approved;
- the rate and degree of market acceptance and clinical utility of our Gvoke HypoPen or any other of our product candidates for which we receive marketing approval;
- 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 initial public offering in ways that increase the value of your investment;
- our expectations related to the use of proceeds from our initial public offering, or any subsequent public equity offerings, and estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to manufacture, or the ability of third parties to deliver, sufficient quantities of components and drug product for commercialization of our Gvoke HypoPen or any other of our product candidates;
- 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;
- our ability to avoid any findings of material weakness or significant deficiencies by our independent registered public accounting firm in the future; and
- other risks and uncertainties, including those listed under the caption “Risk Factors.”

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” (refer to Part I, Item 1A, of this Annual Report on Form 10-K). 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 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 a ready-to-use, room-temperature stable liquid glucagon formulation that, unlike any currently available products, can be administered without any preparation or reconstitution. Our lead product candidate, Gvoke HypoPen, delivers ready-to-use glucagon via a commercially-available auto-injector for the treatment of severe hypoglycemia, a potentially life-threatening condition, in people with diabetes. We have completed three Phase 3 clinical trials for our Gvoke HypoPen and submitted a New Drug Application, or NDA, to the U.S. Food & Drug Administration, or the FDA, in August 2018. The FDA set June 10, 2019 as the Prescription Drug User Fee Act, or PDUFA, action goal date for our NDA. If our NDA is approved at that time, we believe we will have the first ready-to-use, room-temperature stable liquid glucagon formulation that can be administered without any preparation or reconstitution. Additionally, through our interactions with the European Medicines Agency, or EMA, regarding our development path in Europe, we have finalized our regulatory plan and initiated a requisite Phase 3 pivotal trial to support our European Marketing Authority Application, or MAA. We also are applying our novel ready-to-use, room-temperature stable liquid glucagon formulation for the management of hypoglycemia associated with additional intermittent and chronic conditions with significant unmet medical need. In addition, we are applying our technology platforms to convert other commercially-available drugs into ready-to-use, room-temperature stable liquid formulations to address the needs in multiple therapeutic areas and conditions, including epilepsy and diabetes. We own the worldwide rights to our proprietary formulation technology platforms and our product candidates, with 74 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 technologies allow for the subcutaneous, or SC, and intramuscular, or IM, delivery of highly-concentrated, ready-to-use formulations of peptides, small molecules, proteins, and 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 care providers, including multi-step reconstitution, refrigeration requirements, large injection volumes and intravenous, or IV, administration over several hours. Our broadly-applicable platforms offer the opportunity to eliminate 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 these existing aqueous formulations. 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 developing and commercializing our lead product candidate, the Gvoke HypoPen, for the treatment of severe hypoglycemia in people with diabetes to address limitations of currently marketed emergency glucagon kits. Hypoglycemia, a key concern of people with both Type 1 Diabetes, or T1D, and Type 2 Diabetes, or 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. Currently marketed emergency 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 currently marketed 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 currently marketed 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 our Gvoke HypoPen addresses the administration challenges of currently marketed products, and, if approved, has the potential to be the preferred emergency glucagon product. Our ready-to-use Gvoke HypoPen does not require reconstitution or refrigeration and features two-year room-temperature stable liquid glucagon delivered in an auto-injecting device with no visible needle. In our human factors study, 99% of users were able to successfully administer the full dose with our ready-to-use Gvoke HypoPen.

Our goal is to establish our Gvoke HypoPen, if approved, 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 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 at increased risk of clinically significant hypoglycemia. There are an estimated 1.3 million people with T1D who are treated with insulin because their bodies do not naturally produce insulin, all of whom are clinically appropriate for glucagon. Approximately 4.3 million additional people with T2D 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 3.5 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 activate demand through targeted direct-to-patient promotion. We also plan to use our medical affairs team to actively drive market access and obtain payor coverage for our Gvoke HypoPen.

Due to the limitations of currently marketed products, only approximately 662,000 total prescriptions for emergency glucagon kits were written in 2018 in the United States, resulting in the purchase of approximately 978,000 single-dose kits. Based on our market research, we intend to market two Gvoke HypoPens per package and to target all 3.5 million people that we believe are clinically appropriate for glucagon. In 2018, U.S. sales for emergency glucagon kits were approximately \$246 million, but we believe that increasing penetration, including by new entrants that address unmet patient and caregiver needs such as our Gvoke HypoPen, may result in a potential sales opportunity totaling up to \$2.0 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. Following the receipt of EMA scientific advice, we initiated a requisite Phase 3 pivotal trial of our glucagon auto-injector to support our European MAA. We expect top-line results from this trial in the first half of 2019 and plan to seek MAA approval in the second half of 2020. We plan to pursue development and commercialization collaborations for all the non-U.S. markets we seek to enter.

We are also applying our glucagon formulation to five intermittent and chronic use conditions with significant unmet medical need. In 2018, all five development programs either produced positive clinical trial results or advanced into clinical trials. We plan to continue to advance all five of these programs going forward. These additional applications are:

- < Post-Bariatric Hypoglycemia, or 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.
- < Congenital Hyperinsulinism, or CHI, a condition caused by several genetic defects that result in severe, persistent hypoglycemia in infants and children, which can lead to brain damage and death.
- < Hypoglycemia-Associated Autonomic Failure, or HAAF, 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.
- < Exercise-Induced Hypoglycemia, or 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 also are applying our technology platforms to develop additional product candidates, such as ready-to-use, liquid-stable diazepam delivered via a commercially-available auto-injector for the emergency treatment of epileptic seizures and a fixed-dose co-formulation of pramlintide and insulin, or Pram-Insulin, for the management of diabetes. 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 four indications for our product candidates, which are 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 for the EMA for CH and Noninsulinoma Pancreatogenous Hypoglycaemia Syndrome, or 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 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, or the 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. Similarly, in the EU, we intend to submit an MAA through the Centralised Procedure via Article 8(3) - Full Mixed Dossier, which offers data protection and market exclusivity for up to 11 years.

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, Amylin Pharmaceuticals, PowderJect Technologies and Alharma.

Our Pipeline

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

Product Candidate	Indication	Development Stage					Next Milestone	
		Preclinical	Phase 1	Phase 2	Phase 3	Under Review	Event	Expected Date
Glucagon Pen	Severe Hypoglycemia	Under Review					FDA decision	6.10.19
Glucagon Pen - EU	Severe Hypoglycemia	Phase 3					Ph 3 Results	1H '19
Self-Administered Glucagon	Post-Bariatric Hypoglycemia*	Phase 2					Ph 2 Results (Vial/Syringe)	1H '19
Continuous Glucagon	Congenital Hyperinsulinism*	Phase 2					Initiate Ph 3	1H '19
Continuous Glucagon	Hypoglycemia-Associated Autonomic Failure	Phase 2					Ph 2 Results	2H '19
Self-Administered Glucagon	Exercise-Induced Hypoglycemia	Phase 2					Ph 2 Results	2H '19
Diazepam	Acute Repetitive Seizures* Dravet Syndrome*	Phase 1					Ph 1 Results	1H '19
Pramlintide-Insulin	T1D / T2D Blood Sugar Control	Preclinical					Initiate Ph 2	2H '19

* Orphan drug designation

Additionally, we are providing ready-to-use glucagon to Oregon Health & Science University, or OHSU, in their ongoing Phase 1 closed-loop dual-hormone artificial pancreas study and expect OHSU to report top-line results in the first half 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, epilepsy and diabetes. 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:

- < **Rapidly secure regulatory approval for our lead product candidate, Gvoke HypoPen for severe hypoglycemia.** We have completed three Phase 3 clinical trials for our Gvoke HypoPen and submitted an NDA to the FDA early in August 2018 utilizing the 505(b)(2) regulatory pathway, which has been accepted for review by the FDA with a PDUFA action goal date of June 10, 2019. Additionally, through our interactions with the European Medicines Agency, or EMA, regarding our development path in Europe, we have finalized our clinical study plan and initiated a Phase 3 pivotal trial to support EMA registration of an MAA.
- < **Maximize the commercial potential for Gvoke HypoPen.** If approved, we plan to commercially launch our Gvoke HypoPen in the United States in the second half of 2019. We expect to initially target approximately 8,000 healthcare professionals who are high prescribers of current glucagon kits and/or mealtime insulin products, using an expected initial sales force of 60-70 individuals, and activate demand through targeted direct-to-patient promotion. We have accelerated our build of our commercial organization and critical infrastructure, including individuals in operations, supply chain, medical affairs, pharmacovigilance, compliance, regulatory, marketing, sales leadership, market access and sales operations, as well as our medical affairs organization. Outside of the United States, we plan to pursue development and commercialization partnerships.
- < **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 and CHI as well as in diabetes for HAAF and EIH. We are also evaluating our liquid-stable glucagon as the glucagon component of a fully-integrated, bi-hormonal artificial pancreas. During 2018, all five of these programs either produced positive clinical trial results or advanced into clinical trials. 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 are developing an improved formulation of diazepam for the treatment of ARS in patients with epilepsy as well as patients with Dravet syndrome, to be administered through a ready-to-use auto-injector. We have completed formulation development and preclinical pharmacokinetic studies. 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 evaluating the pharmacokinetics and pharmacodynamics of our ready-to-use, room-temperature stable liquid diazepam formulation in normal volunteers. We initiated this trial in December 2018 and expect top-line results in the first half of 2019. If results are positive, we plan to initiate a Phase 2 clinical trial in the second half of 2019. In addition, we formulated and completed several preclinical studies of a fixed-ratio pramlintide-insulin coformulation combination product for the treatment of diabetes and plan to begin a Phase 2 clinical trial in the second half of 2019. Finally, we have advanced several additional formulation programs in the past year and plan to continue to advance these programs to clinical trials.
- < ***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 several companies on feasibility programs to evaluate the formulation of their proprietary therapeutics with, depending on the type of molecule, XeriSol or XeriJect. Active programs include feasibility evaluations with Regeneron Pharmaceuticals, Inc., Asahi Kasei Pharma Corporation, Hawaii Biotech, Inc. and Islet Sciences, Inc. on XeriJect monoclonal antibody formulations, a XeriJect biologic product formulation, a XeriJect vaccine formulation, and a XeriSol co-formulation of a peptide and small molecule for insulin-dependent diabetes, respectively. 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 the current 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 or prevention of hypoglycemic conditions and improve the lives of people who experience hypoglycemia.

Our Product Candidates

Gvoke HypoPen

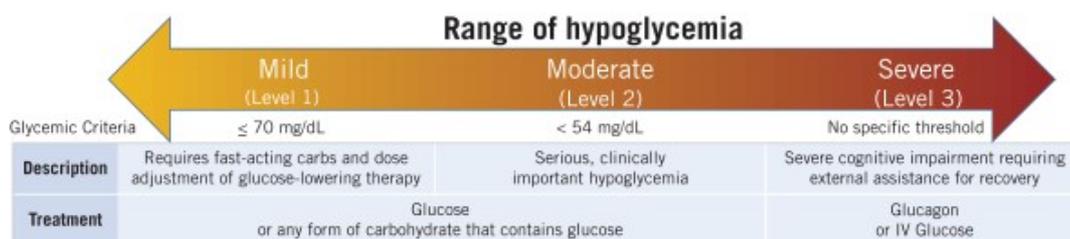
Our Gvoke HypoPen offers a ready-to-use, room-temperature stable glucagon that is designed to be administered subcutaneously in a simple two-step process. In our human factors study, 99% of users were able to successfully administer the full dose with our Gvoke HypoPen. Conversely, in published human factors studies of currently marketed emergency glucagon kits, only 6% to 31% of users were able to successfully administer the full dose. If approved, we believe we can establish our Gvoke HypoPen as the preferred emergency glucagon product and drive greater adoption and penetration of emergency glucagon therapy for patients and caregivers. We have completed three Phase 3 clinical trials for our Gvoke HypoPen and submitted an NDA to the FDA in August 2018, which the FDA has accepted for review and issued a PDUFA action goal date of June 10, 2019. If our NDA is approved at that time, we believe we will have the first ready-to-use, room-temperature stable liquid glucagon formulation that can be administered without any preparation or reconstitution.

Additionally, through our interactions with the EMA regarding our development path in Europe, we have finalized our regulatory plan and initiated a requisite Phase 3 pivotal trial to support our European MAA. We have no current plans to submit our Gvoke HypoPen for regulatory approval in Canada, but we have submitted a clinical trial applications to Health Canada to allow the inclusion of Canadian clinical research sites in XSGP-301, XSGP-303, XSGP-304, and XSMP-204 clinical trials.

Hypoglycemia Background

Diabetes is a widespread condition that affects an estimated 425 million people worldwide with an estimated 20.2 million drug-treated people in the United States. Among people with diabetes in the United States, all of the approximately 1.3 million people with T1D and 4.3 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 American Diabetes Association, or 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, or 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 is 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 Products

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. Two emergency glucagon products are currently available to treat severe hypoglycemia: Eli Lilly's Glucagon Emergency Kit, or GEK, which represents approximately 78% of U.S. sales, and Novo Nordisk's GlucaGen, which represents approximately 22% of U.S. sales. Each product 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 current glucagon kits outlined below 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.

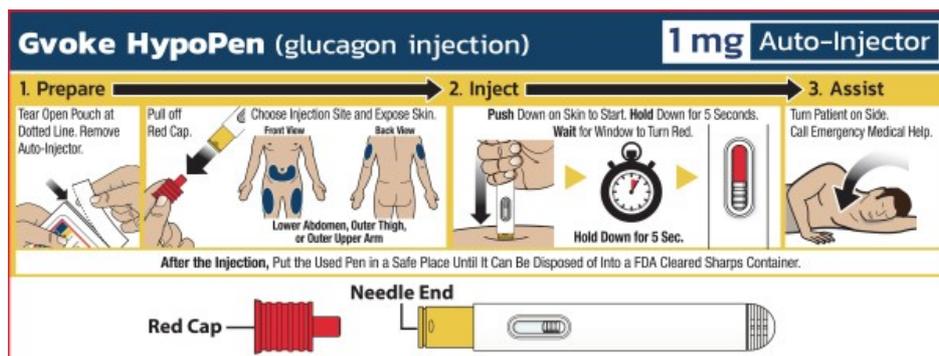
Step-by-Step Instructions for GEK

1. Flip off the seal from the vial of Glucagon powder.
2. Remove the needle cover from the syringe. **DO NOT REMOVE THE PLASTIC CLIP FROM THE SYRINGE**, as this may allow the push rod to come out of the syringe.
3. Insert the needle into the rubber stopper on the vial, then inject the entire contents of the syringe into the vial of Glucagon powder.
4. Remove the syringe from the vial, then swirl the vial until the liquid becomes clear. Glucagon should not be used unless the solution is clear and of a water-like consistency.
5. Insert the same syringe into the vial and slowly withdraw all the liquid. To use on children weighing less than 44 pounds, withdraw half of the liquid (0.5 mark on the syringe).
6. Cleanse site on buttock, arm or thigh and inject Glucagon immediately after mixing, and then withdraw the needle. Apply light pressure against the injection site.
7. Turn the person on his/her side. When an unconscious person awakens, he/she may vomit. **Call 911 immediately after administering Glucagon. If the person does not awaken within 15 minutes, you may administer a second dose of Glucagon, if previously instructed to do so by a healthcare professional.**
8. As soon as the person is awake and able to swallow, give him/her a fast-acting source of sugar (such as fruit juice), followed by a snack or meal containing both protein and carbohydrates (such as cheese and crackers, or a peanut butter sandwich).
9. Discard any unused reconstituted Glucagon. Remember to notify your healthcare professional that an episode of severe hypoglycemia has occurred. These are not the complete instructions. Go to "Information for the User" for complete instructions on how to administer Glucagon.

In 2018, we conducted a quantitative study with 700 caregivers and people with diabetes evaluating the market perceptions of current 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 current kits and only half were confident that a glucagon kit user would be able to correctly administer the current emergency glucagon products. Furthermore, in three published comparative human factors studies with currently marketed 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.

Xeris Gvoke HypoPen Key Features and Benefits

Leveraging our patented XeriSol technology, we believe our Gvoke HypoPen offers an important advancement in the treatment of severe hypoglycemia. We are developing the Gvoke HypoPen as a ready-to-use, room-temperature stable liquid glucagon delivered via auto-injector available in 1 mg and 0.5 mg pre-measured doses for adult and pediatric use, respectively. We have designed the Gvoke HypoPen to be easy to administer, as depicted in the figure below.



The key features of our Gvoke HypoPen are:

- < **Ready-to-use:** With its easy two-step administration process, the user simply pulls off the red cap and pushes the Gvoke HypoPen down on the skin for five seconds, until the window turns red. There is no reconstitution required at the time of emergency.
- < **Easy-to-use:** In our human factors study, 99% of users were able to successfully administer the full dose with our Gvoke HypoPen.
- < **No dose calibration required:** The Gvoke HypoPen will be offered in two pre-measured doses, 0.5 mg for pediatric administration and 1 mg for adolescents and adults.
- < **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.
- < **Two-year room-temperature stability:** No refrigeration is required at any time.



We also intend to offer our ready-to-use glucagon in a pre-filled syringe presentation, Gvoke PFS, which may be preferred by some healthcare professionals.



In contrast to currently marketed emergency glucagon kits, our Gvoke HypoPen features the following benefits:

	GEK	Xeris Gvoke HypoPen
No Reconstitution in Emergency	X	✓
Auto-Injection	X	✓
Needle Auto-Retraction and Needle Guard	X	✓
Dose Volume Pre-measured for Pediatrics	X	✓
Room-Temperature Stable as a Liquid	X	✓
Rate of Successful Full Dose Delivery in Human Factors Studies	6 - 31%	99%
Route of Administration	SC or IM	SC

In our Caregiver and Patient Perceptions Study, more than 75% responded that they would prefer our Gvoke HypoPen over currently available glucagon kits. 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 our Gvoke HypoPen was available. Based on this market research, we believe that the glucagon market will become more penetrated and that our Gvoke HypoPen will become the preferred emergency glucagon delivery solution.

Xeris Gvoke HypoPen Market Potential

Based on current market data as well as our Caregiver and Patient and Healthcare Professional Perceptions Studies, we believe that our Gvoke HypoPen, if approved, 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 products they have on hand.

There are approximately 20.2 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 1.3 million people with T1D who are treated with insulin because their bodies do not naturally produce insulin and approximately 4.3 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 3.5 million people in the United States. We intend to sell our Gvoke HypoPen in a package of two, based on responses from our market research indicating that potential buyers would purchase, on average, two 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 currently marketed kits, the annual U.S. potential sales opportunity may total up to \$2.0 billion.

Despite the risk of experiencing a severe hypoglycemic event, we believe that emergency glucagon therapy is underappreciated, under-evaluated and under-taught, resulting in a market that is under-penetrated. 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 currently marketed products and the lack of conversations regarding glucagon limit their adoption. Two of the top reasons given by people with diabetes for nonrenewal of glucagon prescriptions were that they were not confident that a caregiver or other person would be able to correctly administer the currently available kit, and their healthcare professional did not discuss the need for a new one with them. In the United States, approximately 662,000 total prescriptions for emergency glucagon kits were written in 2018 in the United States, resulting in the purchase of approximately 978,000 single-dose kits. In 2018, U.S. sales for emergency glucagon kits totaled approximately \$246 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 was 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 our 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 our Gvoke HypoPen, if approved, to shift the site of care from the emergency room or hospital to less costly settings such as the home.

We believe that a relevant market analogue for our Gvoke HypoPen is the epinephrine auto-injector, including EpiPen, for life-threatening allergic reactions. The table below provides a comparison of the severe allergy and hypoglycemia markets.

	SEVERE ALLERGIC REACTION (EPINEPHRINE)	SEVERE HYPOGLYCEMIA (GLUCAGON)
Clinically Appropriate Patient Population in the United States	5.2 million patients	3.5 million patients
No. of Units Sold in the United States (2018)	~8.2 million auto-injectors	~978,000 kits*

* Single-dose units of Eli Lilly's Glucagon Emergency Kits and Novo Nordisk's GlucaGen

We believe this comparison of the allergy and hypoglycemia markets supports the potential of our Gvoke HypoPen, if approved, to increase both the number of clinically appropriate people who have glucagon, as well as the number of glucagon products they have on hand.

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, 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 under-penetrated in those regions.

Commercial Strategy

If approved, we will seek to replace currently marketed emergency glucagon kits with our Gvoke HypoPen, 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 our Gvoke HypoPen 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 are preparing to launch our Gvoke HypoPen product as soon as practicable following approval, with our PDUFA action goal date of June 10, 2019. In July 2018, Eli Lilly announced its NDA submission for its intranasal glucagon product candidate. We believe this competing product candidate could receive FDA approval and launch at least two months ahead of our Gvoke HypoPen. Therefore, we plan to accelerate our commercial launch activities. Our plan to execute on our go-to-market strategy for our Gvoke HypoPen includes the following:

- < **Create awareness and anticipation prior to launch.** We plan to use the FDA's NDA review period to both better understand the market and create excitement and anticipation for our company and our technology. We expect to hire ten regional medical affairs directors prior to commercial launch to establish additional relationships with key opinion leaders and gain insight into current practice patterns and burdens. We also plan to begin to raise awareness in the market on the incidence, prevalence and impact of severe hypoglycemic events.
- < **Drive awareness and adoption of our Gvoke HypoPen.** If approved by the FDA, we plan to drive awareness and adoption of our Gvoke HypoPen to replace current emergency glucagon kits in the market.
 - o **Healthcare Professionals:** At launch, our targets will consist of high glucagon prescribing healthcare professionals. Approximately 3,000 healthcare professionals issue 50% of current glucagon prescriptions. We plan to hire 60-70 sales representatives initially to reach these professionals.
 - o **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 anticipate having the first product to market in a competitive landscape, we plan to increase our spend on direct-to-consumer tactics. Because of our earlier than expected action date, we plan to accelerate these activities into late 2019. 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 HypoPen market is currently significantly underpenetrated due to the lack of, and limitations in, current treatment options. We are designing our Gvoke HypoPen 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:
 - o **Healthcare Professionals:** In addition to the 3,000 healthcare professionals who issue about half of the current glucagon prescriptions, we will target approximately 5,000 healthcare professionals who are high meal time insulin prescribers but who are under-indexed in prescribing glucagon. We intend to reach these professionals using our initial sales representatives.
 - o **Patients and Caregivers:** We believe there is an opportunity to activate patient and caregiver demand for our Gvoke HypoPen. Our Gvoke HypoPen is designed as an easy-to-use solution for a segment of patients and caregivers who currently lack the confidence in administering current emergency glucagon kits and would rather rely on emergency responders for treatment.
- < **Promote access:** Current 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 94% 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 Medicare and approximately 15% are covered by Medicaid. 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 our Gvoke HypoPen. We plan to engage with payors to more fully understand their drivers and barriers and convey the health and pharmacoeconomic value of our Gvoke HypoPen prior to launch.

We plan to establish a distribution channel in the United States for the commercialization of our Gvoke HypoPen. We expect to sell our Gvoke HypoPen to wholesale pharmaceutical distributors, who, in turn, will sell our Gvoke HypoPen to pharmacies and other customers. We expect to 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.

Clinical Experience

We have completed three Phase 3 clinical trials for our Gvoke HypoPen and submitted an NDA to the FDA in August 2018. The FDA set June 10, 2019 as the PDUFA action goal date for our NDA. In addition, we have evaluated our Gvoke HypoPen in six preclinical studies, one Phase 1 pharmacokinetic (PK) and pharmacodynamic (PD) study and two Phase 2 clinical trials. Additionally, through our interactions with the EMA regarding our development path in Europe, we have finalized our regulatory plan and initiated a requisite Phase 3 pivotal trial to support our European MAA for severe hypoglycemia. We expect top-line results from this trial in the first half of 2019. The following table summarizes the completed clinical trials for our Gvoke HypoPen.

PROTOCOL NO./TITLE	PHASE OF DEVELOPMENT	DESIGN/OBJECTIVES	STUDY POPULATION AND DEMOGRAPHICS	DOSE (NO. EXPOSED EACH TREATMENT) AND DOSAGE FORM/ PRODUCT CONFIGURATION
<p>Completed</p> <p>XSGP-302 A Phase 3 Study to Evaluate the Glucose Response of Glucagon Rescue Pen (Glucagon Injection) In Pediatric Patients With Type 1 Diabetes</p>	Phase 3a	Non-randomized, open-label, single dose/Efficacy, PD, PK, safety and tolerability	Children (2<6, 6<12 and 12<18 years) with T1D n=31	Ages 2<6 years (n=7), single dose of 0.5mg Glucagon Rescue Pen; ages 6<12 years (n=13), single dose of 0.5mg Glucagon Rescue Pen; ages 12<18 years (n=11), single dose of 1mg Glucagon Rescue Pen followed by single dose of 0.5mg Glucagon Rescue Pen 7 to 28 days later/ Rescue Pen
<p>XSGP-301 Glucagon Rescue Pen (Glucagon Injection) Compared To Eli Lilly Glucagon (Glucagon For Injection [rDNA Origin]) For Induced Hypoglycemia Rescue In Adult Patients With T1D: A Phase 3, Randomized, Blinded, 2-Way Crossover Study To Evaluate Efficacy and Safety</p>	Phase 3a	Double-blind, randomized, two-way crossover/Efficacy (return to plasma glucose >70.0 mg/dL) of Glucagon Rescue Pen 1 mg to be non-inferior to Eli Lilly's glucagon; compare the PD characteristics of Glucagon Rescue Pen versus Eli Lilly's glucagon; safety and tolerability; PK.	Adult patients with T1D n=80	Glucagon Rescue Pen 1mg (n=78), Eli Lilly's glucagon 1mg (n=79)/Rescue Pen

PROTOCOL NO./TITLE	PHASE OF DEVELOPMENT	DESIGN/OBJECTIVES	STUDY POPULATION AND DEMOGRAPHICS	DOSE (NO. EXPOSED EACH TREATMENT) AND DOSAGE FORM/PRODUCT CONFIGURATION
XSGP-303 Glucagon Rescue Pen (Glucagon Injection) Compared To Eli Lilly Glucagon (Glucagon For Injection [rDNA Origin]) For Induced Hypoglycemia Rescue In Adults With T1D: A Phase 3B Multi-Centered, Randomized, Controlled, Single-Blind, 2-Way Crossover Study To Evaluate Efficacy And Safety	Phase 3b	Non-inferiority, multi-centered, randomized, controlled, single-blind, two-period, two-way crossover/ Efficacy and safety	T1D adult male/female patients 18-75 years of age n=81	Glucagon Rescue Pen 1 mg, Eli Lilly's glucagon 1 mg/ Rescue Pen
XSGP-202 Glucagon Rescue Pen (Glucagon Injection) For Induced Hypoglycemia Rescue In Adult Patients With T1D: A Phase 2A Pilot Study To Evaluate Protocol Design Issues For An Upcoming Phase 3 Clinical Study	Phase 2	Open-label 2-way crossover Explore safety efficacy in treatment of insulin-induced hypoglycemia	T1D adult male/female patients 18-65 years of age n=7	Glucagon Rescue Pen 0.5 mg (n=6) and 1 mg (n=7), subcutaneous injections given one week apart/Pre-Filled Syringe
XSGP-201 A Randomized, Phase 2, Double-Blind, 3-Way Crossover Study With Glucagon Rescue Pen (Glucagon For Injection) To Evaluate Safety, Tolerability and Comparative Pharmacokinetics and Pharmacodynamics To Eli Lilly Glucagon (Glucagon For Injection [rDNA Origin]) In Healthy Volunteers	Phase 2	Double-blind, randomized, 3-way crossover/Safety, tolerability, PK and efficacy vs. marketed comparator	Healthy male/female volunteers 18-60 years of age n=28	Subcutaneous injection of: Glucagon Rescue Pen 0.5 mg (n=29) and 1 mg (n=28) and Eli Lilly's glucagon (rDNA origin) 1 mg/ Pre-Filled Syringe
XSGP-101 A Two-Way Crossover Comparative PD/PK Study Of Glucagon Rescue Pen (Glucagon Injection) Administered By Auto-Injector And Pre-Filled Syringe	Phase 1	Two-way crossover comparative bioequivalence, safety, tolerability and PD/PK of Glucagon Rescue Pen administered via auto-injector vs. pre-filled syringe	Healthy male/female volunteers 18-64 years of age n=32	Glucagon Rescue Pen 1 mg/Pre-Filled Syringe 1 mg

Completed Phase 3 Clinical Trials

XSGP-302: A Phase 3 Study to Evaluate the Glucose Response of Glucagon Rescue Pen (Glucagon Injection) In Pediatric Patients With Type 1 Diabetes

In 2017, we conducted a sequential non-randomized, open-label, single dose efficacy and safety Phase 3 clinical trial in pediatric subjects with T1D. This clinical trial included a total of 31 subjects (seven subjects 2 to <6 years, 13 subjects 6 to <12 years and eleven subjects 12 to <18 years). In this clinical trial, we induced hypoglycemia, defined as plasma glucose <80 mg/dL, with administration of insulin and then treated subjects with our Gvoke HypoPen. The primary endpoint of this clinical trial was to assess the increase in plasma glucose of subjects from baseline to 30 minutes after injection of an age-appropriate dose of our Gvoke HypoPen, defined as 0.5 mg dose for subjects 2 to <12 years and in separate visits both a 0.5 mg and 1.0 mg dose for subjects 12 to <18 years.

All three age groups met the primary endpoint of non-zero glucose response at 30 minutes post-administration of our Gvoke HypoPen. All evaluable subjects achieved a target glucose increase of at least 25 mg/dL. Following administration, plasma glucose levels over time showed similar glucose responses for subjects in each age group and in each dose in the 12 to <18 years age group. Further, in each age group the observed effect was statistically significant with increases from baseline in mean plasma glucose at 30 minutes following administration of an age-appropriate dose of our Gvoke HypoPen. Administration of 0.5 mg of our Gvoke HypoPen in the 12 to <18 years age resulted in a glucose response that was similar to the age-appropriate dose of 1 mg of our Gvoke HypoPen.

Overall, our Gvoke HypoPen was observed to be well-tolerated. All auto-injectors, or AIs, delivered a full dose. There were no discontinuations due to adverse events, or AEs, no severe AEs, no device-related AEs and no serious adverse events, or SAEs. The majority of treatment-emergent AEs observed were gastrointestinal disorders.

The following table summarizes additional trial design parameters and clinical results that we observed from XSGP-302:

GLUCAGON DOSE	0.5 MG DOSE			1 MG DOSE
	2 TO < 6 YEARS	6 TO < 12 YEARS	12 TO < 18 YEARS	12 TO < 18 YEARS
n	7	13	11	11
% with >25 mg/dL rise in glucose within 30 minutes	100	100	100	100
Glucose C _{max} (mg/dL) Mean (SD)	207.8 (35.9)	206.9 (49.6)	212.1 (40.6)	198.9 (60.0)
Glucose T _{max} (minutes) Mean (SD)	67.7 (11.1)	66.4 (15.7)	78.2 (11.5)	81.8 (15.6)
% with nausea	42.9	53.8	36.4	36.4
% with emesis	14.3	23.1	0	18.2

XSGP-301: Glucagon Rescue Pen (Glucagon Injection) Compared To Eli Lilly Glucagon (Glucagon For Injection [rDNA Origin]) For Induced Hypoglycemia Rescue In Adult Patients With T1D: A Phase 3, Randomized, Blinded, 2-Way Crossover Study To Evaluate Efficacy and Safety

In 2017, we completed a non-inferiority, prospective, randomized, controlled, double-blinded, two-period, two-way crossover, comparative efficacy and safety Phase 3 pivotal clinical trial in male and female patients aged 18 to 75 years with T1D in an inpatient setting. The trial was conducted across seven locations in the United States and enrolled 80 subjects. The objectives of this clinical trial were to compare the safety, tolerability and efficacy of our Gvoke HypoPen and Eli Lilly's glucagon, as determined by an increase in plasma glucose concentration from below 50 mg/dL to greater than 70 mg/dL within 30 minutes after receiving glucagon. We also evaluated an additional primary endpoint of plasma glucose > 70 mg/dL or increase by > 20 mg/dL within 30 minutes. This additional primary endpoint was defined and pre-specified for analysis prior to unblinding the study. Additional endpoints of interest included plasma glucose of >70 mg/dL or resolution of all induced neuroglycopenic symptoms within 30 minutes of glucagon, relief of hypoglycemia symptoms, global feeling of hypoglycemia and glucose elevation 0-90 minutes post-injection.

In this clinical trial, we induced severe hypoglycemia by an IV infusion of regular insulin followed by initial and subsequent bolus doses if plasma glucose after 30 minutes was > 60 mg/dL. Subjects were also administered an IV infusion of regular insulin based on a subject's historical use of basal insulin. The investigator adjusted the IV insulin infusion rate if the rate of glucose change after 30 minutes was < 1 mg/dL/minute. Investigators were instructed to avoid any bolus doses or basal infusion rate increases within 20 minutes of blinded study drug administration. Once the initial plasma glucose measurement < 50 mg/dL was achieved, the IV insulin infusion was stopped. Once the confirmatory plasma glucose reading < 50 mg/dL was achieved, subjects were administered blinded study drug via the subcutaneous route in the upper arm, leg or abdomen.

Subjects were randomized to receive glucagon in one of two sequence groups: our Gvoke HypoPen followed by Eli Lilly’s glucagon, or Eli Lilly’s glucagon followed by our Gvoke HypoPen. Following glucagon dosing, plasma glucose was monitored every five minutes until 90 minutes post-dosing. Additional blood samples were collected at regular intervals. Subjects also completed a questionnaire regarding hypoglycemia symptoms at the start of the hypoglycemia induction period and periodically until 45 minutes post-treatment with glucagon. Tolerability was assessed by comparing adverse event reports between the groups. In addition, subjects completed questionnaires concerning injection site discomfort. After a wash-out period of seven to 28 days, subjects returned to the clinic and the study procedures were repeated with each subject crossing over to the other treatment group.

Analyses of the primary endpoints were performed according to pre-specified intent-to-treat, or ITT, modified intent-to-treat, or mITT, and per-protocol methods. The ITT cohort was defined as all subjects randomized to one of the two sequence groups. The mITT cohort was defined as the ITT cohort minus one subject that mistakenly received two doses of Eli Lilly’s glucagon. The per-protocol cohort was defined as the mITT cohort minus any subjects adjudicated for at least one major protocol violation. Criteria for major protocol violations were defined and pre-specified prior to unblinding of the trial. Following adjudication of major protocol violations, two subjects, one in each study arm, who received a clinically significant (20%) increase in basal IV insulin rate during the final 20 minutes of the induction procedure were censored to establish the per-protocol cohort.

For the ITT and mITT analysis, three or fewer response failures were defined as the pre-specified threshold demonstrating non-inferiority of our Gvoke HypoPen. For the primary endpoint of glucose increase > 70 mg/dL within 30 minutes, the total difference in response failures was four, representing one more than the pre-specified threshold of three response failures. For the additional primary endpoint of plasma glucose > 70 mg/dL or increase by > 20 mg/dL within 30 minutes, the total difference in response failures was two and, therefore, ITT analysis of this additional primary endpoint demonstrated that our Gvoke HypoPen was non-inferior to Eli Lilly’s glucagon. The per-protocol analysis of both primary endpoints met the pre-specified threshold. Certain of our analyses may be viewed as post-hoc analyses, and although post-hoc analyses can result in the introduction of bias and may be given less weight by the FDA, we believe that this retrospective analysis can provide additional information regarding results from this trial.

We believe the clinical trial results support the potential of our Gvoke HypoPen to reverse severe hypoglycemia in a reliable manner. In accordance with FDA and International Council for Harmonisation guidance for evaluation of non-inferiority studies, we presented a series of analyses implementing ITT, mITT and per-protocol cohorts for this clinical trial to the FDA at a pre-NDA meeting held in December 2017. In that meeting, the FDA agreed overall that the totality of data for our Gvoke HypoPen is sufficient to support NDA review.

Additionally, a single dose of our Gvoke HypoPen increased plasma glucose and improved clinical symptoms such as cognitive impairment and other neuroglycopenic/neurogenic symptoms that are associated with severe hypoglycemia in 100% of subjects. We also observed comparable increases in plasma glucose concentration from below 50 mg/dL to greater than 70 mg/dL within 30 minutes after receiving our Gvoke HypoPen and comparable resolution of clinical symptoms to Eli Lilly’s glucagon, such as cognitive impairment and other neuroglycopenic/neurogenic symptoms that are associated with severe hypoglycemia, as well as comparable pharmacodynamics.

The following table summarizes the efficacy outcomes for XSGP-301.

CLINICAL COMPARISON	mITT RESPONSE RATE	
	GVOKE HYPOPEN	ELI LILLY GLUCAGON
Subjects successfully rescued from induced hypoglycemia without other rescue therapy (e.g., intravenous dextrose)	100% (78/78)	100% (79/79)
Plasma glucose >70 mg/dL within 30 minutes of glucagon (primary endpoint)	Intent-to-treat†	Intent-to-treat
	94.9% (74/78)	100% (79/79)
Plasma glucose of >70 mg/dL or ≥ 20 mg/dL increase within 30 minutes of glucagon (additional primary endpoint)	Per-protocol	Per-protocol
	96.1% (74/77)	100% (78/78)
Plasma glucose of >70 mg/dL or resolution of all induced neuroglycopenic symptoms within 30 minutes of glucagon	Intent-to-treat	Intent-to-treat
	97.4% (76/78)	100% (79/79)
Plasma glucose of >70 mg/dL or resolution of all induced neuroglycopenic symptoms within 30 minutes of glucagon	Per-protocol	Per-protocol
	97.4% (75/77)	100% (78/78)
Resolution of hypoglycemia symptoms	100% (78/78)	100% (79/79)
Global feeling of hypoglycemia improvement pre/post injection	100% (77/77)	100% (79/79)
Sustained glucose elevation from 0-90 minutes post-injection	100% (78/78)	100% (79/79)

† one (1) additional endpoint failure exceeded the non-inferiority threshold of N=3; all other comparisons demonstrate non-inferiority vs. Eli Lilly’s glucagon.

Overall, all treatment regimens were well-tolerated. One SAE of hypoglycemia was reported for a participant treated with Eli Lilly's glucagon. The SAE was determined by the study investigator not to be related to the study drug and resolved during the trial. The incidence of AEs was low in both groups, and the most commonly reported AE was nausea: 20.5% for our Gvoke HypoPen and 12.7% for Eli Lilly's glucagon (p=not significant), followed by vomiting and headache. AEs were generally mild or moderate in severity, transient and resolved with no treatment.

XSGP-303: Glucagon Rescue Pen (Glucagon Injection) Compared to Eli Lilly Glucagon (Glucagon For Injection [rDNA Origin]) For Induced Hypoglycemia Rescue in Adult Patients With T1D: A Phase 3b Multi-Centered, Randomized, Controlled, Single Blind, 2-Way Crossover Study To Evaluate Efficacy and Safety.

In the second quarter of 2018, we completed a non-inferiority, prospective, randomized, controlled, single-blinded, two-period, two-way crossover, comparative efficacy and safety Phase 3b clinical trial in male and female patients aged 18 to 75 years with T1D in an inpatient setting. The trial was conducted across six locations in the United States and Canada and enrolled 81 subjects. The objectives of this clinical trial were to compare the safety, tolerability and efficacy of our Gvoke HypoPen and Eli Lilly's glucagon, as determined by an increase in plasma glucose concentration from below 50 mg/dL to greater than 70 mg/dL within 30 minutes after receiving glucagon. We also evaluated an additional endpoint of plasma glucose > 70 mg/dL or increase by ≥ 20 mg/dL within 30 minutes. Additional endpoints of interest also included plasma glucose of >70 mg/dL or resolution of all induced neuroglycopenic symptoms within 30 minutes of glucagon, relief of hypoglycemia symptoms, global feeling of hypoglycemia and total elapsed time required from decision to dose and actual time of injection (e.g. preparation time).

Consistent with our XSGP-301 trial, in XSGP-303 we induced severe hypoglycemia by an IV infusion of regular insulin followed by initial and subsequent bolus doses if plasma glucose after 30 minutes was > 60 mg/dL. The subjects' IV infusion of regular insulin was based upon their historical use of basal insulin. The investigator adjusted the IV insulin infusion rate if the rate of glucose change after 30 minutes was < 1 mg/dL/minute. Investigators were instructed to avoid any bolus doses when a subject's plasma glucose was < 60 mg/dL. Once the initial plasma glucose measurement < 50 mg/dL was achieved, the IV insulin infusion was stopped. Once the confirmatory plasma glucose reading < 50 mg/dL was achieved, subjects were administered blinded study drug via the subcutaneous route in the abdomen.

Subjects were randomized to receive glucagon in one of two sequence groups: our Gvoke HypoPen followed by Eli Lilly's glucagon, or Eli Lilly's glucagon followed by our Gvoke HypoPen. Following glucagon dosing, plasma glucose was monitored every five minutes until 90 minutes post-dosing. Additional blood samples were collected at regular intervals. Subjects also completed a questionnaire regarding hypoglycemia symptoms at the start of the hypoglycemia induction period and periodically until 180 minutes post-treatment with glucagon. Tolerability was assessed by comparing adverse event reports between the groups. In addition, subjects completed questionnaires concerning injection site discomfort. After a wash-out period of seven to 28 days, subjects returned to the clinic and the study procedures were repeated with each subject crossing over to the other treatment group.

Analyses of the primary endpoints were performed according to pre-specified intent-to-treat, or ITT, and per-protocol methods. The ITT cohort was defined as all subjects randomized to one of the two sequence groups. The per-protocol cohort was defined as the ITT cohort minus any subjects adjudicated for at least one major protocol violation.

For the ITT analysis, three or fewer response failures were defined as the pre-specified threshold demonstrating non-inferiority of our Gvoke HypoPen. For the primary endpoint of glucose increase from below 50 mg/dL to >70 mg/dL within 30 minutes, all subjects who received a study drug experienced successful plasma glucose recovery. As there were no treatment failures observed, the ITT analysis of the primary endpoints demonstrated that our Gvoke HypoPen was non-inferior to Eli Lilly's glucagon.

Criteria for major protocol violations were defined and pre-specified prior to starting the trial. Following adjudication of major protocol violations, two subjects in the Gvoke HypoPen arm were identified who were administered study drug despite not being within a steady state of hypoglycemia. In addition, subjects who did not receive a study drug were considered major protocol violations. These subjects were censored to establish the per-protocol cohort. Despite the major protocol violation in the subjects who received Gvoke HypoPen, plasma glucose recovery was achieved within 30 minutes and the subjects successfully met the study primary endpoint.

We believe the results of XSGP-303 corroborate the outcomes observed in XSGP-301 and further support the potential of our Gvoke HypoPen to reverse severe hypoglycemia in a reliable manner. We incorporated the results of this study into the NDA submission.

The following table summarizes the efficacy outcomes for XSGP-303.

Clinical Comparison	RESPONSE RATE	
	GVOKE HYOPEN	ELI LILLY GLUCAGON
Subjects successfully rescued from induced hypoglycemia without other rescue therapy (e.g., D50).	100% (76/76)	100% (78/78)
Plasma glucose >70 mg/dl in 30 minutes. (primary endpoint)	Intent-to-treat 100% (76/76)	Intent-to-treat 100% (78/78)
	Per-protocol 100% (73/73)	Per-protocol 100% (73/73)
Plasma glucose of >70 mg/dl or \geq 20 mg/dl increase within 30 minutes of glucagon.	Intent-to-treat 100% (76/76)	Intent-to-treat 100% (78/78)
	Per-protocol 100% (73/73)	Per-protocol 100% (73/73)
Plasma glucose of >70 mg/dl or resolution of all induced neuroglycopenic symptoms within 30 minutes of glucagon.	100% (76/76)	100% (78/78)
Resolution of hypoglycemia symptoms	100% (76/76)	100% (78/78)
Global feeling of hypoglycemia improvement pre/post injection†	100% (73/73)	100% (76/76)
Sustained glucose elevation from 0-90 minutes post-injection	100% (76/76)	100% (78/78)

† Population of subjects only includes those reporting hypoglycemic symptoms at baseline.

Overall, all treatment regimens were well-tolerated. There were no reported SAEs. The incidence of AEs was low in both groups and the most commonly reported AE was nausea, followed by vomiting and headache. AEs were generally mild or moderate in severity, transient and resolved with no treatment.

XSGP-101: A Two-Way Crossover Comparative PD/PK Study Of Glucagon Rescue Pen (Glucagon Injection) Administered By Auto-Injector And Pre-Filled Syringe

At our pre-NDA meeting in December 2017, the FDA recommended to us that we address three areas of inquiry regarding our Gvoke PFS: the characterization of PD/PK data to compare changes in serum plasma glucose levels and serum hormone levels when glucagon is administered by an auto-injector versus hand injection, a human factors validation study for this presentation and device reliability testing for this presentation. As a result of this meeting, with respect to the Gvoke PFS, we initiated our XSGP-101 clinical trial in the first quarter of 2018. Based on the results of this trial, combined with the human factors studies and device reliability testing, we included the Gvoke PFS in our Gvoke HypoPen NDA submission to the FDA.

In the second quarter of 2018, we completed a Phase 1 two-way crossover comparative PD/PK study of glucagon administered by auto-injector versus pre-filled syringe to demonstrate bioequivalence in fasted healthy subjects with low to normal plasma glucose levels. We enrolled 32 healthy male and female subjects, ranging from 19 to 63 years old, with a median age of 46.5 years. Subjects were randomly assigned to a treatment sequence and each received a 1 mg dose of glucagon via auto-injector and another 1 mg dose via pre-filled syringe. Both treatments were administered subcutaneously to the abdomen.

Analysis of the primary PK endpoints of plasma glucagon $AUC_{(0-240min)}$ and C_{max} indicated bioequivalence of glucagon whether administered by auto-injector or pre-filled syringe. The PD endpoints of plasma glucose $AUC_{(0-240min)}$, C_{max} , and T_{max} also demonstrated bioequivalence and PD equivalence between the two devices.

Overall, auto-injector and pre-filled syringe treatments were generally well tolerated and similar AEs were observed between the two treatment groups. The most commonly experienced AEs were nausea, vomiting and headache. All of the AEs were mild or moderate in severity. There were no SAEs or discontinuations due to an AE.

Other Completed Supporting Trials

Phase 2 Clinical Trials

XSGP-201: A Randomized, Phase 2, Double-Blind, 3-Way Crossover Study with Glucagon Rescue Pen (Glucagon For Injection) To Evaluate Safety, Tolerability and Comparative Pharmacokinetics and Pharmacodynamics To Eli Lilly Glucagon (Glucagon For Injection [rDNA Origin]) In Healthy Volunteers

In 2014, we completed a double-blind, randomized, three-way crossover Phase 2 clinical trial of glucagon in 28 healthy male and female subjects 18 to 60 years of age to evaluate the safety, tolerability, PK and efficacy versus Eli Lilly's glucagon. Subjects were subcutaneously injected with glucagon via a pre-filled syringe in doses of 0.5 and 1 mg and with Eli Lilly's glucagon for injection in a dose of 1 mg.

Plasma glucose concentration-time curves showed little separation between treatment groups, and there were no substantial differences between our glucagon 1 mg and Eli Lilly's glucagon for injection 1 mg in terms of glucose area under the curve, maximum concentration, or C_{max} , and time to reach maximum concentration, or T_{max} .

Results showed that all treatments were well-tolerated and demonstrated a comparable safety profile. No SAEs were observed, and all AEs were transient and consistent with rescue injections of glucagon.

XSGP-202: Glucagon Rescue Pen (Glucagon Injection) For Induced Hypoglycemia Rescue In Adult Patients With T1D: A Phase 2a Pilot Study To Evaluate Protocol Design Issues For An Upcoming Phase 3 Clinical Study

In 2015, we completed an open-label two-way crossover Phase 2 clinical trial to explore the safety and efficacy of glucagon for the treatment of insulin-induced hypoglycemia in seven adult males and females with T1D 18 to 65 years of age. Subjects were given our glucagon injection via the pre-filled syringe 0.5 mg (n=6) and 1 mg (n=7) as subcutaneous injections given one week apart.

All subjects in a state of insulin-induced hypoglycemia experienced objective and subjective response to rescue doses of glucagon with return of glucose to > 70 mg/dL and resolution of all hypoglycemia symptoms within 30 minutes of injection.

Results showed AEs were generally mild and corresponded to known effects of rescue doses of glucagon. Vasovagal syncope, or fainting, was observed in one patient, which met the definition of an SAE as an important medical event but was attributed by the investigator to study procedures.

Ongoing Clinical Trials

XSGP-304: G-Pen Compared to GlucaGen HypoKit for Induced Severe Hypoglycemia Rescue in Adults With Type 1 Diabetes: A Phase 3 Multi-Center Randomized, Controlled, Single Blind, 2-Way Crossover Study to Evaluate Efficacy and Safety

The objectives of this clinical trial were developed following scientific advice from the EMA in support of our planned European MAA. We are comparing the safety, tolerability and efficacy of our glucagon pen and GlucaGen HypoKit (Novo Nordisk), as determined by an increase in plasma glucose concentration from below 54 mg/dL to greater than 70 mg/dL within 30 minutes after receiving glucagon or increase by 20 mg/dL within 30 minutes. Additional endpoints of interest include relief of hypoglycemia symptoms, global feeling of hypoglycemia and total elapsed time required from decision to dose and actual time of injection (e.g., preparation time). The trial involves two daytime clinical research center, or CRC, visits with random assignment to receive glucagon pen 1 mg during one period and GlucaGen HypoKit 1 mg during the other. Each daytime visit is preceded by an overnight stay in the CRC. In the morning of the inpatient study visit, the subject is brought into a state of severe hypoglycemia through IV administration of regular insulin diluted in normal saline. After a hypoglycemic state with plasma glucose < 54 mg/dL (3 mmol/L) is verified, the subject is administered a dose of glucagon pen or GlucaGen HypoKit via subcutaneous injection. Plasma glucose levels are monitored for up to 180 minutes post-dosing, with a value of >70.0 mg/dL (3.89 mmol/L) or an increase of > 20 mg/dL (>1.11 mmol/L) within 30 minutes of glucagon administration indicating a positive response. After 3 hours, the subject is given a meal and discharged when medically stable. After a wash-out period of 7 to 28 days, subjects return to the CRC, and the procedures are repeated with each subject crossed over to the other treatment. A follow-up visit as a safety check is conducted 2-7 days following administration of the final dose of study drug. We initiated this trial in the second half of 2018 to be conducted at six sites in North America and three sites in Europe. We have a target enrollment of 122 subjects and expect top-line results in the first half of 2019.

Preclinical Studies

Six preclinical studies, consisting of five studies in rats and one study in rabbits, demonstrated that our concentrated, non-aqueous solution of glucagon was safe in animal models. Studies included PK and PD studies, toxicity and potential impurities studies, toxicokinetic evaluations and local tolerance assessment. We conducted these studies during 2010 to 2018. These studies administered glucagon to a total of 206 rats and 8 rabbits.

Human Factors Summative Validation Study

In 2017, we conducted a human factors summative validation study in users, which confirmed that our Gvoke HypoPen can be correctly, safely and effectively used. Of the 75 injections, 74 (99%) were successful. There was a single failure that occurred when an untrained subject prematurely lifted the pen from the injection site within approximately 1.5 seconds of activation, resulting in a partial dose. The subject admitted to not reading the label guide. No mitigation response was needed as the failure was attributed to the participant's noncompliance with reading the label guide while performing the procedure. After reviewing the label guide, the subject successfully administered the injection during an unaided second attempt. The study concluded that the Gvoke HypoPen dose label, packaging, device and injection procedure, label guide and instructions for use had been successfully validated.

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 five intermittent and chronic conditions with significant unmet medical need. In particular, our formulation may be applied to conditions requiring continuous doses or smaller or 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 our Gvoke HypoPen. Aspects include:

- < Chemistry, manufacturing and controls, or 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 two toxicology studies in rats, one toxicology study in pigs, one tolerability study in rabbits, two PK studies in rats and one toxicology and PK study in rats (320 rats, 54 pigs and 8 rabbits). These preclinical studies demonstrated the safety of the ready-to-use glucagon and supported further clinical development. A number of additional toxicology studies are ongoing to support long-term chronic use of ready-to-use glucagon in additional hypoglycemic conditions.

For commercialization in our 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 HAAF and EIH. Furthermore, because there are few CHI patients and they are primarily treated at a handful of centers of excellence in the United States, we believe we can engage these clinicians with a small group of regional medical affairs directors.

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 HAAF 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 Noninsulinoma Pancreatogenous Hypoglycaemia Syndrome, or 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 from an estimated 158,000 procedures per year in 2011 to 228,000 in

2017, growing nearly 45% in just six years. 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, or 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. 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 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, 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 at the time of 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 meal time 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 NIH, or National Institute of Diabetes and Digestive and Kidney Diseases, awarded us \$1.78 million in Fast-Track Small Business Innovation Research, or SBIR, grants to demonstrate the potential benefits of ready-to-use glucagon in these patients. Collaborators on this grant include endocrinologists at the Joslin Diabetes Center and device engineers at the Harvard University John R. Paulson School of Engineering and Applied Science.

Clinical Experience

We have completed seven preclinical studies in multiple species a proof-of-concept clinical trial and a randomized controlled Phase 2a clinical trial for our ready-to-use glucagon for 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 a new Phase 2 trial evaluating our ready-to-use, room-temperature stable liquid glucagon formulation for patients who experience hyperinsulinemic hypoglycemia after bariatric surgery.

We commenced this clinical trial in the second half of 2018. We expect the results from this trial will help enable the evaluation of ready-to-use glucagon in a future Phase 3 clinical trial using a vial/syringe in an outpatient setting.

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

In 2017, 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 the inpatient setting, subjects received a mixed-meal tolerance test, 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 this product candidate.

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 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 SAEs.

Since this was the first implementation of the ready-to-use glucagon formulation in mini-doses in PBH, the dosage 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 dosage 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 our closed-loop glucagon pump for PBH measured by real-time continuous glucose monitoring, or CGM. Secondary objectives included safety and tolerability. Following a mixed-meal tolerance test, or MMT, 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 MMT was employed, and then subjects were treated based on CGM based measurements of subject blood glucose. The subject was treated with the study drug (Ready-to-use glucagon or placebo) at a dose of 300 mcg followed by 150 mcg if needed. Of 12 subjects that completed the trial, seven experienced severe hypoglycemia in response to MMT. 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 treatments were well tolerated with no reported SAEs. An abstract of these study results has been submitted to a clinical diabetes meeting for presentation in the first half of 2019.

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 authorization in October, we initiated a new Phase 2 clinical trial at six clinical research centers in North America. This study is a randomized, placebo-controlled, double-blind, two-treatment, two-period, crossover comparison in a 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, or Glucagon RTU, via vial/syringe to treat symptomatic postprandial hypoglycemia in subjects with PBH. It will also collect safety and efficacy information to help inform a future Phase 3 clinical trial.

During the CRC stage, subjects will undergo two high-carbohydrate, solid/liquid-meal tests. After each meal, subjects will self-administer blinded study drug (Glucagon RTU 300 mcg or placebo) when any postprandial autonomic symptom is experienced or hypoglycemia is confirmed with a blood glucose measurement < 70 mg/dL by blood glucose meter. After CRC study-related procedures are completed, subjects will enter the 12-week outpatient stage. The subjects will be discharged home with their assigned study drug: Glucagon RTU 300 mcg or placebo. Subjects also will be trained to self-administer their assigned study treatment, i.e., dose study drug with the presence

of any postprandial autonomic symptoms or a blood glucose measurement < 70 mg/dL. During postprandial hyperinsulinemic hypoglycemia episodes, the trial will evaluate plasma glucose recovery (i.e., blood glucose (BG) \geq 70 mg/dL) at 15 minutes after dosing with Glucagon RTU and placebo. Safety, tolerability and quality-of-life will also be assessed. The trial will comprise 12 evaluable subjects. We expect top-line results from the CRC stage of this trial in the first half of 2019.

Ready-to-Use Glucagon for Congenital Hyperinsulinism

We are evaluating our ready-to-use glucagon formulation for chronic management of congenital hyperinsulinism, for which there are currently no approved therapies. In the United States, 80 to 160 infants are born with CHI on an annual basis. We estimate that there are approximately 6,200 patients with CHI in the United States. In September 2014, we received orphan drug designation from the FDA for ready-to-use glucagon for the prevention of chronic, severe hypoglycemia in patients with CHI. In October 2014, we also received orphan drug designation from the EMA for ready-to-use glucagon for the treatment of CHI. We recently concluded a Phase 2 proof-of-concept trial and anticipate initiating a Phase 3 outpatient study in the first half of 2019.

Congenital Hyperinsulinism Market

CHI is the result of several genetic defects that present as dysregulated increased insulin secretion, causing severe, persistent hypoglycemia in infants and children. CHI often responds poorly or not at all to current medical approaches and can sometimes lead to surgical removal of the pancreas, or near-total pancreatectomy. In CHI, microscopic abnormalities in the pancreas can result in prolonged severe hypoglycemia which, if untreated, can cause death. Repeated episodes of severe and prolonged hypoglycemia, even if not fatal, can result in permanent neurologic damage, including developmental delay, mental retardation and focal central nervous system deficits.

Management of CHI is aimed at preventing morbidity associated with repeated hypoglycemic episodes, including permanent brain damage, as well as mortality. Currently, there are no approved drugs for CHI. While limited treatment options are available, they have marginal efficacy, are poorly tolerated by patients and negatively impact quality of life. Often, severe cases of CHI are resistant to diazoxide due to the type of genetic mutation. Other drugs, such as octreotide, have been used to reduce insulin secretion but may be ineffective in maintaining normal blood sugar and may cause substantial side effects.

Pancreatectomy is an option if a solitary focal lesion in the pancreas can be identified and surgically removed, typically resulting in a cure without the need for medication or continuous feedings. However, if the disease is not localized, near-total pancreatectomy would be required. Patients who undergo near-total pancreatectomy are at high risk for developing insulin-dependent diabetes later in life. This risk increases with the extent of pancreatic removal, but the risk is significant even with conservative surgical procedures. The use of pancreatectomy oftentimes addresses CHI but creates another chronic condition, insulin-dependent diabetes.

Xeris Offering—Continuous Subcutaneous Infusion of Ready-to-Use Glucagon

If approved, we believe our ready-to-use glucagon would enable safe, continuous administration of glucagon from a pump to manage CHI. IV glucagon is routinely used in the hospital and in conjunction with IV glucose to stabilize blood glucose levels in affected infants, but the IV must be changed every 24 hours or less due to the instability of glucagon in aqueous solution. The use of glucagon has historically been limited due to the lack of a stable formulation and convenient delivery system for long-term administration, especially in the home setting where a central catheter is impractical and a gastrostomy-tube is cumbersome.

We believe that the continuous subcutaneous infusion of ready-to-use glucagon, if approved, is superior to the use of off-label drugs because ready-to-use glucagon:

- < Offers a direct effect of increasing glucose levels compared to indirect mechanisms of glucose control.
- < Enables release of patient's excess glycogen stores.
- < Avoids the side effects related to octreotide, nifedipine and diazoxide.

In addition, we believe that the continuous subcutaneous infusion of ready-to-use glucagon, if approved, is superior to the use of infused glucose because ready-to-use glucagon:

- < Provides an approach to wean the patient off a central glucose line, such as an IV, to enable discharge from the hospital.
- < Eliminates bloating observed with the high-volume glucose infusions often required to maintain normal blood glucose levels.

Finally, we believe that the continuous subcutaneous infusion of ready-to-use glucagon, if approved, is superior to pancreatectomy, because patients may be able to avoid the development of insulin-resistant diabetes as a lifetime condition. CHI patients who progress to adolescence typically normalize or at least no longer require intensive medical management. We believe that avoiding pancreatectomy is likely the most impactful result of management of CHI with ready-to-use glucagon.

In the short-term inpatient setting, we believe our ready-to-use formulation may enable administration of glucagon from a small, wearable, infusion pump. In the long term, we believe the glucagon pump system may enable outpatient administration of glucagon for prevention of hypoglycemia. We expect most patients that are candidates for ready-to-use glucagon would use the product until mid-adolescence and transition out of the standing patient pool.

There are currently no therapeutic options indicated for treatment of CHI, and current standard of care involves near-total pancreatectomy or use of multiple off-label therapeutics. We believe payors will include our ready-to-use glucagon on their formularies because CHI is a rare pediatric disease and ready-to-use glucagon has the potential to reduce time spent in the NICU, avoid expensive pancreatectomies, as well as avoid the long-term costs associated with diabetes treatment resulting from pancreatectomy. We intend to conduct additional payor research as product development progresses.

From 2015 to 2017, we were awarded \$2.1 million in SBIR grants from the NIH National Institute of Diabetes and Digestive and Kidney Diseases to initiate clinical studies in infant patients with CHI.

Clinical Experience

We recently concluded enrollment in a Phase 2 proof-of-concept randomized controlled clinical trial and previously completed a number of preclinical studies in multiple species that we are leveraging for all of our intermittent and chronic glucagon programs.

XSGO-CH01: A Phase 2 Proof-of-Concept Study of CSI Glucagon (Continuous Subcutaneous Glucagon Infusion) to Prevent Hypoglycemia with Lower Intravenous Glucose Infusion Rates in Children up to One Year of Age with Congenital Hyperinsulinism

XSGO-CH01 was a Phase 2, multi-center, randomized, placebo-controlled, double-blind trial with open-label follow up designed to assess the efficacy of CSI Glucagon delivered with a patch pump as a subcutaneous continuous infusion to prevent hypoglycemia with lower IV glucose infusion rates, or GIRs, in patients less than one year of age with congenital hyperinsulinism. The trial had a target enrollment of 24 subjects, with a built-in interim analysis after 12 subjects. However, only five subjects were enrolled over 23 months. In consultation with the lead study investigator at Cook Children’s Medical Center, we concluded enrollment in September 2018 and analyzed available results. A total of five subjects were screened for inclusion and enrolled in the study (intent-to-treat). Subjects began in a baseline phase to stabilize GIR. Subjects were then randomized into a 2-day blinded treatment period, followed by an open label treatment period for up to 28 days. All subjects completed all three study periods with no adverse events observed. In this trial, CSI Glucagon within the tested dose range was observed to directly reduce GIR to a large and clinically meaningful extent (44%-66%) when used as a sole therapy. A summary of these results is provided in the following table:

Glucose Infusion Rate Response in Study XSGO-CH01

PER PROTOCOL (4 SUBJECTS)	BASELINE STABILIZATION	RANDOMIZED BLINDED TREATMENT (PLACEBO)	RANDOMIZED BLINDED TREATMENT (CSI GLUCAGON)	OPEN-LABEL CSI-GLUCAGON (CSI GLUCAGON)
Stable GIR	5/5 ^a	0/2	2/2	4/4
GIR Response (reduction ≥ 20% at 24 hrs.)	N/A	1/2	2/2	N/A
GIR Response (reduction ≥ 33% at 48 hrs.)	N/A	0/2	2/2	4/4 ^b
GIR change (range)	N/A	31% reduction, to 34% increase	53%-65% reduction	44%-66% reduction

a: The first enrolled subject, 01-01, was not deemed evaluable for responsive to glucagon based upon prior history of glucagon resistance, per investigator. Selection criteria were changed after this first patient enrollment to exclude glucagon resistance.

b: Treatment time varied from 4-52 hours.

CSI glucagon was well tolerated in this trial. There were no reported AEs, no skin reactions and no other negative treatment effects associated with study drug administration. CSI glucagon was well tolerated within the dose range of 5-20 µg/kg/hr. Furthermore, there were no reports of occlusions, leakage or other pump issues in the trial, or any instances of severe hypoglycemia during pump change-out.

Based on the results generated in this study, we believe CSI Glucagon has the potential to be used in an outpatient setting by caregivers following adequate training, if approved. In XSGO-CH01 CSI Glucagon within the tested dose range was observed to directly reduce GIR to a large and clinically meaningful extent (44%-66%) when used as a sole therapy. Given the distinct mechanism of action from other treatments for CHI, CSI Glucagon has the potential to serve as a complementary therapy with other available therapies. We believe the short-term positive treatment effects observed in the Phase 2 study support our efforts to evaluate CSI Glucagon in the context of a Phase 3 outpatient study, which we anticipate initiating in the first half of 2019.

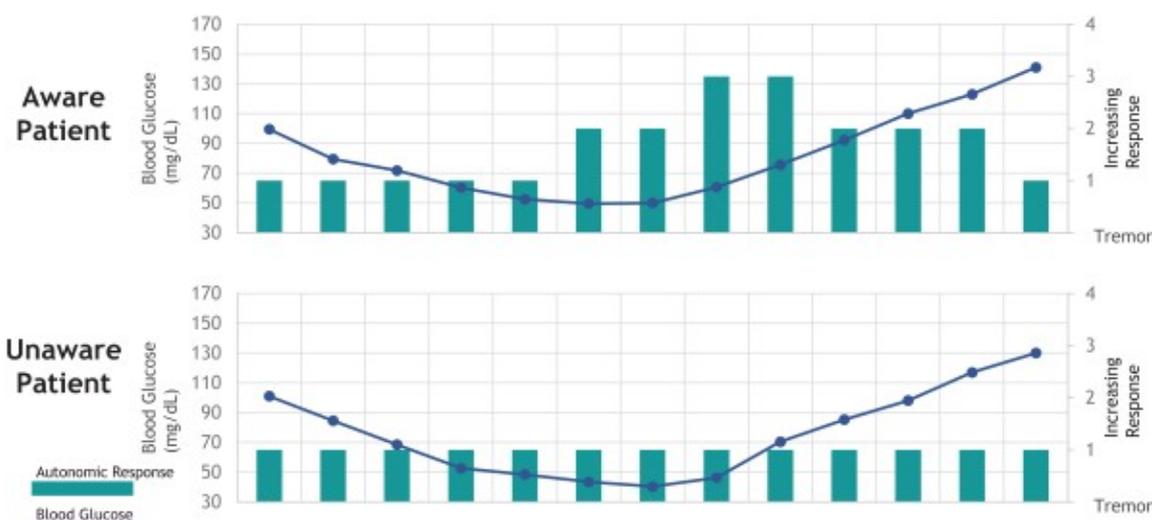
Ready-to-Use Glucagon for Hypoglycemia-Associated Autonomic Failure

We are evaluating our ready-to-use glucagon for HAAF, a condition for which there are currently no therapeutic options. We have initiated a Phase 2a clinical trial from which we expect to obtain top-line results in the second half of 2019. If clinical development is successful, we expect to submit an NDA under the 505(b)(2) pathway for FDA review.

Hypoglycemia-Associated Autonomic Failure Market

Typically, a decrease in plasma glucose below the normal range triggers defensive counter-regulatory responses that restore blood sugars. However, individuals with HAAF have defects in that counter-regulatory response. These individuals do not experience the physiological symptoms of worsening hypoglycemia and are at risk of being unaware of an impending severe hypoglycemic event. Chronic hypoglycemia is thought to lead to this defective glucose counter-regulation and hypoglycemia unawareness. The lack of awareness of an oncoming hypoglycemic event may result in the inability to treat or prevent it, creating a vicious cycle of recurrent hypoglycemia and possibly leading to the sudden onset of severe hypoglycemia, putting patients at risk for severe hypoglycemia, neuroglycopenia, seizure, coma and, if left untreated, death. As such, hypoglycemia unawareness is a major concern for this subset of people with T1D and T2D and their caregivers.

The figures below depict the effect of hypoglycemic unawareness where symptoms do not signal corresponding blood glucose.



It has been shown that the autonomic response and awareness of hypoglycemia can be restored with scrupulous avoidance of hypoglycemia for two to three weeks. However, this restoration can currently only be achieved with intensive diet and behavior modification, which we believe results in low participation and success rates.

Based on our research, we estimate that approximately 20% of people with T1D and 14% of people with T2D (primarily those on insulin) have HAAF. In primary market research, physicians indicated approximately half of patients with some form of HAAF are moderately to severely affected. However due to the need for better diagnosis procedures and guidelines for HAAF, the physicians surveyed also reported that they currently expect approximately 40% and 50% under-diagnosis rates of HAAF in people with T1D and T2D, respectively. We believe there is a critical unmet need for a therapeutic treatment for insulin deficient diabetes patients with HAAF.

Xeris Offering—Continuous Subcutaneous Infusion of Ready-to-Use Glucagon

We are developing a novel continuous subcutaneous glucagon infusion system incorporating our ready-to-use, liquid-stable glucagon formulation with an infusion pump. Continuous subcutaneous infusion of ready-to-use glucagon could be used to avoid hypoglycemia during a three- to four-week period to restore autonomic response and hypoglycemia awareness. Combined with patient training, the treatment may result in a significant long-term reduction in hypoglycemia rates post-intervention, particularly of severe hypoglycemia. If approved, we believe our ready-to-use glucagon has the potential to be the first product designed to prevent hypoglycemia for extended periods of time to enable re-establishment of hypoglycemia awareness and treat HAAF. We believe our ready-to-use glucagon, if approved, could provide substantial therapeutic benefit to patients who suffer from severe hypoglycemic events and are taken to the emergency room multiple times per year.

The use of glucagon to treat this condition has been hampered due to the lack of a room-temperature stable liquid glucagon formulation and a convenient delivery system for continuous administration. Attempts at off-label treatment with current emergency glucagon products require reconstitution of freeze-dried glucagon powder, and the drug chamber and infusion set would likely require replacement at least every 24 hours due to the instability of glucagon in aqueous solution.

There are currently no therapeutic treatment options for HAAF. However, since at least some payors currently cover diabetes coaching and training services conducted by certified diabetes educators, which are often used to help treat or manage HAAF, we believe payors will cover ready-to-use glucagon if we can demonstrate reversal of hypoglycemia unawareness. We intend to conduct additional payor research as product development progresses.

Clinical Experience

We have initiated a Phase 2a proof-of-concept randomized controlled clinical trial and have successfully completed a number of preclinical studies in multiple species that we are leveraging in our intermittent and chronic glucagon programs.

Ongoing Phase 2 Clinical Trial

XSGO-AF01: Fixed Rate Continuous Subcutaneous Glucagon Infusion (CSGI) vs Placebo in Type 1 Diabetes Mellitus Patients with Recurrent Severe Hypoglycemia: Effects On Counter Regulatory Responses to Insulin Induced Hypoglycemia

XSGO-AF01 is a prospective, randomized, controlled, double-blind, parallel four-group trial with the primary analysis after four weeks of treatment with continuous subcutaneous glucagon infusion, or CSGI, or placebo. After a one-week qualification on CGM, subjects will have their baseline hypoglycemia counter-regulatory response hormones quantified using a step-wise hypoglycemia induction procedure. Subjects meeting eligibility requirements will be randomized to one of four treatment groups, two glucagon, two placebo. Subjects will receive blinded study drug for four weeks, and they will be followed for an additional 26 weeks post-treatment. Subjects' counter-regulatory hormone response will be measured at baseline, the end of treatment (four weeks), and 13 and 26 weeks after treatment ends. We are conducting the trial at six sites in the United States and expect top-line results from 48 subjects in the second half of 2019. We expect data from this Phase 2a clinical trial to help outline pivotal study endpoints and inform a discussion with the FDA.

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

We are evaluating our ready-to-use glucagon and plan to initiate an additional Phase 2 clinical study in the first half of 2019 for EIH, for which there are currently no approved therapies. Based on these results and previous data, we intend to discuss our registration pathway with FDA in the second half of 2019. In November 2013, we filed an IND application for the use of mini-dose ready-to-use glucagon for EIH. We are the sponsor of this IND, which is active as of the date of this Annual Report on Form 10-K.

Exercise-Induced Hypoglycemia in Diabetes Market

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 is frustrating and may lead to minimized or complete omission of exercise for many patients. People with diabetes who use insulin 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, and who could potentially use a mini-dose of ready-to-use glucagon each time they exercised. If approved, our ready-to-use glucagon would represent a significant market opportunity in the treatment for 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. Our previous proof-of-concept study demonstrated that 150 µg of this mini-dose glucagon corrected non-severe hypoglycemia to a substantially similar degree as oral glucose tablets that are commonly used during exercise in correcting non-severe hypoglycemia in adults with T1D, while enabling avoidance of unnecessary caloric intake.

Modestly increasing glucagon levels at the start of exercise has previously not been possible, since current commercially available glucagon preparations are unstable in aqueous solution. They 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 of the current glucagon kits.

We have been awarded over \$3.1 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 three Phase 2 safety and efficacy clinical trials in subjects with T1D.

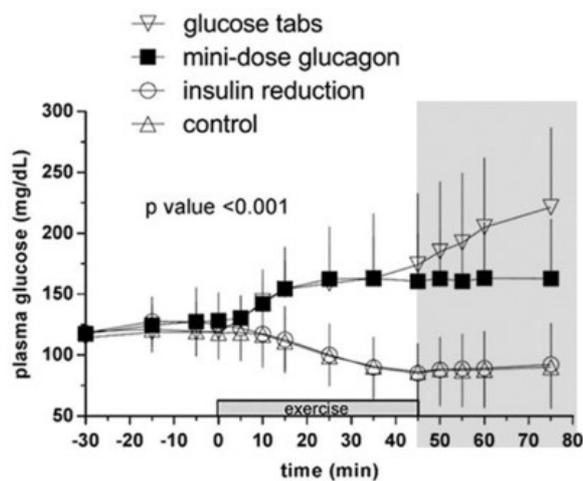
Phase 2 Clinical Trials

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

Based on our previous dose-finding trials (XSMP-201 and XSMP-202), we initiated 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 that 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 single center randomized, placebo-controlled, double-blind, two-treatment, two-period, crossover comparison in a CRC setting followed by a randomized, placebo-controlled, double-blind, two arm parallel comparison with a third open-label arm in the outpatient setting. The purpose of the trial is to evaluate the preliminary efficacy of Glucagon RTU to prevent exercise-induced hypoglycemia 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 in an inpatient setting and at least 30 minutes duration in the outpatient setting and will be monitored for hypoglycemia in the exercise recovery period. The trial will examine if the subcutaneous administration of Glucagon RTU 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; 3.89 mmol/L) measured by blood glucose meter during and after moderate-to-high intensity aerobic exercise by adult subjects with T1D in an outpatient setting. The trial has a target enrollment of 48 subjects and we expect top-line results in the second half of 2019.

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-2018, OHSU initiated a Phase 1 proof-of-concept randomized three-way crossover clinical trial to evaluate the utility of such a system. We expect OHSU to report top-line results from this trial in the first half of 2019. Based on these results, we expect to move forward with a clinical program for a bi-hormonal artificial pancreas closed-loop system. 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, or 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 continuous glucose monitoring, or CGM, 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, 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 1.3 million people with T1D as well as approximately 500,000 people with T2D. Of this combined population, approximately one-third is 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 JDRE.

Clinical Experience

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

Ongoing 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 is a single center, randomized, three-way, crossover investigation-initiated trial conducted by OHSU using our ready-to-use glucagon in a vial. Subjects undergo the 76-hour study with 9 hours inpatient and 67 hours outpatient using the closed-loop artificial pancreas controller. The trial initiated in mid-2018 and is designed to compare the glucose control resulting from the use of a bi- and single-hormone closed-loop system as compared to a predictive low glucose suspend system, 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 after exercise, as compared to an insulin only closed-loop system and a predictive low glucose suspend system. This clinical trial has a planned enrollment of 19 subjects and we expect OHSU to report results in the first half of 2019.

Additional Programs

Ready-to-Use Diazepam

Leveraging our XeriSol formulation technology, we are developing a ready-to-use diazepam formulation for the treatment of ARS in patients with epilepsy. Approximately 160,000 people in the United States experience ARS.

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 2017, these diazepam formulations generated total U.S. sales of approximately \$127 million, of which Diastat Rectal Gel and its generic formulations comprised \$83 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 rescue pen 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 \$1.5 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 evaluating the pharmacokinetics and pharmacodynamics of our ready-to-use, room-temperature stable liquid diazepam formulation in normal volunteers. We initiated this trial in December 2018 and expect top-line results in the first half of 2019. If results are positive, we plan to initiate a Phase 2 clinical trial in the second half of 2019.

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

This trial is a Phase 1, open-label, single-center, single-dose, three-way crossover study in 24 healthy adult subjects which will evaluate the bioavailability of ready-to-use diazepam (10 mg) administered subcutaneously to the abdomen and intramuscularly to the deltoid, as compared to the rectal administration of Diastat (10 mg) when each is administered under fasted conditions. The sequence of treatments will be randomly assigned and there will be a fixed 21-day washout period between treatments. This trial will also assess the safety and tolerability of ready-to-use diazepam administered subcutaneously and intramuscularly, as compared to rectal administration of the marketed gel formulation of diazepam (Diastat). A final safety visit will be completed 22 to 36 days after the last treatment.

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 type 1 diabetes. 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 diabetics for use at all major meals for which patients are already administering four injections of a basal-bolus insulin per day. The addition of a pramlintide regimen would add three or more separate injections daily which could be a challenging proposition in this patient population. Thus, a daily pramlintide injection burden made it unattractive to pump users who often chose pumps to avoid repeated injections. 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 shelf stable XeriSol 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 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 properties from a patient use perspective: potential two-year shelf life stability when refrigerated and up to 90 days at temperatures up to room temperature. This stability profile is comparable to current vial-based insulin products and would not likely introduce a new regiment of storage and use for existing insulin patients.

In preclinical studies, we characterized the pharmacokinetics and pharmacodynamics (glycemic changes are presented for clarity) of pramlintide and various insulin formulations in normal and streptozotocin induced diabetic rats (mimicking T1DM) 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 SC 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 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 commercial product combinations (mimicking human SC administration) that begin to lose glucose control after approximately two hours.

We are preparing to study our novel XeriSol pramlintide-insulin co-formulation in a clinical trial in T1D in the third quarter of 2019. This study will compare 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 Symlin®/Humulin® Co-Injection

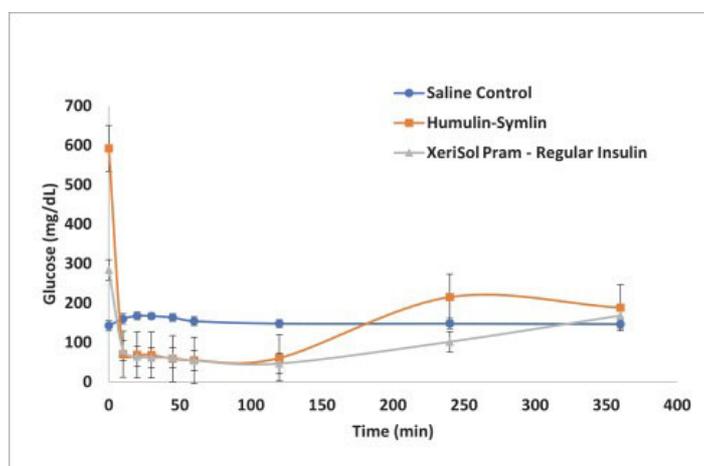
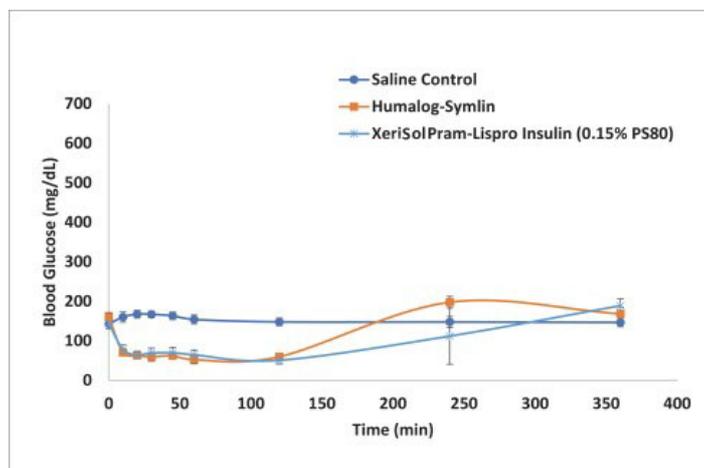


Figure 2 Glucose Levels after Injection of XeriSol™ Pramlintide-Lispro and Symlin®/Humalog® Co-Injection



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, or 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, or API, used in our Gvoke HypoPen and our intermittent and chronic hypoglycemia products in development that utilize ready-to-use glucagon. We intend to use Bachem Americas, Inc., or Bachem, as 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 our Gvoke HypoPen and other pipeline products utilizing ready-to-use glucagon, we are actively engaged in developing a second API source.

Manufacturing drug product for our Gvoke HypoPen requires an aseptic fill/finish facility capable of handling solvents and a cyclic olefinic polymer syringe. Pyramid Laboratories, Inc., or Pyramid, has been actively involved in the development of our product candidates, and we intend to use its facility in California to be 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 our Gvoke HypoPen is a proprietary multi-product device platform developed by SHL Medical AG, SHL Pharma LLC, SHL Pharma, or SHL. We entered into a joint development agreement in January 2016 to develop an auto-injector suitable for our Gvoke HypoPen. 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 our Gvoke HypoPen, and we intend to enter into one or more commercial supply agreements. A number of third-party logistic providers can provide commercial order processing and finished good distribution services to U.S. wholesale customers, and we expect to enter into one or more commercial distribution agreements 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 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 products are currently available to treat severe hypoglycemia: Eli Lilly's GEK and Novo Nordisk's GlucaGen. 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 inactive and potentially toxic. We believe that the drawbacks of currently marketed products and the lack of conversations regarding glucagon limit their adoption. In addition to the currently marketed GEK from Eli Lilly and Novo Nordisk's GlucaGen, we are currently aware of several product candidates that are expected to compete with our Gvoke HypoPen, if approved. Eli Lilly is developing an intranasal glucagon dry powder and submitted an NDA two months ahead of our NDA submission. While healthcare professionals as well as patients and caregivers believe both our Gvoke HypoPen and the intranasal dry powder are easy to use, they have expressed concern that the full dose of glucagon may not be delivered via intranasal absorption. Of note, in a Phase 1 clinical trial, a pediatric subject failed to achieve a >25 mg/dL rise in glucose because he blew his nose immediately after a 2 mg intranasal dose administration.

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 needleless attribute. In our market research, caregivers and people with diabetes associated our 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 our Gvoke HypoPen is the greater likelihood of successful dose delivery.

In addition, Zealand Pharma is developing an SC dasiglucagon, a stable analog of human glucagon, in an auto-injector. Based on its public filings, Zealand has stated it intends to file an NDA in the second half of 2019. Zealand's dasiglucagon is currently in Phase 3 development and is being studied in adults and children. Data released to date indicate that Zealand's dasiglucagon will have a room-temperature stable shelf-life up to 12 months.

While there are currently no FDA approved products indicated for treatment of PBH, we are aware of a number of product candidates in development. For example, Eiger Biopharma is developing its product candidate exendin 9-39, a glucagon-like peptide-1 receptor antagonist, to be administered subcutaneously, which is currently in Phase 2 development.

Currently, there are no approved drugs for CHI and limited treatment options are available, but we are aware of several product candidates in development. For example, Rezolute is developing RZ358, an IV administered fully human antibody that inhibits the effects of elevated insulin via allosteric modulation of the insulin receptor, which is currently in Phase 2 development. In addition, Zealand Pharma is developing an SC infusion of dasiglucagon, which is currently in Phase 3 clinical development.

There are currently no approved products for the treatment of HAAF. Many other therapeutic compounds have been investigated in academic clinical research for the indirect prevention of hypoglycemia. While none of these interventions have been successful to date, this research shows there is considerable interest in restoring hypoglycemia awareness and HAAF.

Currently, the first-line emergency treatment of epileptic seizures in the outpatient setting is the administration of diazepam in a non-sterile rectal gel marketed by Valeant Pharmaceuticals as Diastat. We also are aware of a product candidate for which an NDA has been recently submitted for the treatment of ARS in patients with epilepsy. Neurelis announced that they submitted an NDA for VALTOCO, which is an NRL-1, an intranasal formulation of diazepam in August 2018. In addition, Aquestive is developing AQST-203, a buccal soluble formulation of diazepam, which is currently in Phase 3 development.

Intellectual Property

Proprietary Protection

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our drug candidates, manufacturing and process discoveries and other know-how, to operate without infringing the proprietary rights of others, and to prevent others from infringing on 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, 2018, we owned 74 issued patents globally, of which 13 are issued U.S. patents. As of December 31, 2018, we owned 75 patent applications pending globally, of which 13 are patent applications pending in the United States. As of December 31, 2018, 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 shall own all inventions conceived by the individual in the course of 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 registered trademark for the mark Xeris Pharmaceuticals. We also own pending trademark applications for XERISOL, XERIJECT, 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 as well as 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 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, 2018, we have received \$0.8 million out of an expected \$0.9 million in grant proceeds for the development of a stable liquid glucagon for use in an artificial pancreas. Under the terms of the agreement, we will be required to pay up to four times the 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, 2018, we received \$0.9 million in grant proceeds to help fund our EIH program. Under terms of this agreement, we will be required to pay up to two times the 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, 2018, 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 the Loan and Security Agreement that provides 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. The third tranche is \$10.0 million and is available beginning upon approval of our Gvoke HypoPen NDA by the FDA until the earlier of September 30, 2019 or the 30th day following NDA approval by the FDA. 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 federal Food, Drug, and Cosmetic Act, or FDCA, and its 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, and biologics under the FDCA, the Public Health Service Act, PHSA, and their implementing regulations 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 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 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 of our product candidates. Accordingly, we plan to investigate our products through the IND framework and seek approval through the NDA or BLA pathway. Based on our discussions with the FDA to date, we do not anticipate that the FDA will require a separate medical device authorization for the device, but this could change during the course of its review of any marketing application that we may submit. The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- < completion of extensive preclinical laboratory tests, animal studies and formulation studies in accordance with applicable regulations, including the FDA’s Good Laboratory Practice, or 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, or 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, or 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, or cGMP;
- < potential FDA audit of the clinical trial sites that generated the data in support of the NDA or BLA and 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, or 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. Pre-clinical 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 institutional review board, or 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 2019 is \$2,588,478 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 2019 is \$309,915. 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, or 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 risk evaluation and mitigation strategy, or 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 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, or 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, or 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, or 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, or 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 challenge 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, or 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, or 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, or QS, regulations applicable to medical devices.

Drug-device combination products present unique challenges for competitors seeking approval of Abbreviated New Drug Applications, or 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, or PDMA, a part of the FDCA, as well as the Drug Supply Chain Security Act, or 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 their 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 typically may not market or promote such off-label uses.

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

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

Other Regulatory Matters

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

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, voluntary recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, exclusion from federal healthcare programs, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or effectiveness of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

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

Orphan Designation and Exclusivity

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States. Alternatively, orphan drug designation may be available if the disease or 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, or 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 European Union, or 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 European Medicines Authority, or EMA, for a marketing authorization application, or 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 European Union, the EMA's Committee for Orphan Medicinal Products, or 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 European Union Community, or when, without incentives, it is unlikely that sales of such products in the European Union 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 European Union, 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. Our activities are also subject to regulation by numerous regulatory authorities include the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, or DHHS, the Department of Justice, or DOJ, the Drug Enforcement Administration, or DEA, the Consumer Product Safety Commission, or CPSC, the Federal Trade Commission, or FTC, the Occupational Safety & Health Administration, or OSHA, the Environmental Protection Agency, or 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:

- < the federal Anti-Kickback Statute, or AKS, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, receive or pay any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in exchange for, or intended to induce or reward, including arranging for or recommending, either the referral of an individual, or the purchase, lease, order, prescription or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs; a person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (see below) 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;
- < federal civil and criminal false claims laws and civil monetary penalties laws, such as the federal False Claims Act, which impose criminal and civil penalties and authorizes 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 that are false or fraudulent; 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. 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 supplier of items or services reimbursable by a federal or state governmental program;
- < 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, which imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program (including private payors) 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. 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 HITECH, and their respective implementing regulations, which impose specified 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 associate with pursuing 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 requires 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 U.S. Department of Health and Human Services information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- < federal government price reporting laws, which require us 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, or 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, or the 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 commonly the requirement that all individuals maintain health insurance coverage or pay a penalty, referred to as the "individual mandate. 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. While Congress has not passed repeal legislation to date, the 2017 Tax Reform Act includes a provision repealing 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. 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. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. 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 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, 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 2027. 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. 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 inseparable feature of the ACA, and therefore because the mandate was repealed 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. 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. 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 2027 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.

The Centers for Medicare & Medicaid Services, or CMS, has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization, or PA, and step therapy, or ST, for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs, and change the definition of “negotiated prices,” and add a definition of “price concession” to the regulations. It is unclear whether these proposed changes will be accepted, and if so, what effect such changes will have on our business.

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, but the manufacturer must develop an internal policy 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, 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 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 medical product or service does not ensure that other payors will also provide coverage for the medical 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 medical 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 rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for 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, or AMP, to 23.1% of AMP, and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, creating a new methodology by which rebates owed by manufacturers are calculated for drugs that are inhaled, infused, instilled, implanted or injected, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. 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 (phased-in by 2014). 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, or the 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. Unlike Medicare Parts A and B, Part D coverage is not standardized. 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. 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. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we obtain marketing approval. 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 AMP and Medicaid 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 orphan drugs. As 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition 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 reimbursement formula change instituted by CMS under the 340B program. For the 2018 and 2019 fiscal years, CMS altered the reimbursement formula from Average Sale Price, or ASP, plus 6% to ASP minus 22.5% on specified covered outpatient drugs, or 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. The court has not determined whether reimbursement rates should be retroactively returned to the ASP plus 6% rate and the difference in such reimbursement made to the covered facilities, or if some other remedy is more appropriate. It is unclear how the invalidation of the formula could affect pharmaceutical manufacturers and hospitals who prescribe their products. 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 the Department of Health and Human Services, 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 drug candidates, 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 drug candidate. 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.

In recent years, additional laws have resulted in direct or indirect reimbursement reductions for certain Medicare providers, including:

- < The Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2027 unless additional Congressional action is taken.
- < The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

These 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 product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate 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 products 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 and 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, once approved, or put pressure on our product pricing.

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 European Union, 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, 2018, we had 90 employees, 42 of whom were primarily engaged in product development and research, 42 of whom were primarily engaged in administration and finance, and six of whom were primarily engaged in sales and marketing.

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 1810, 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 no history of 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 are a clinical-stage pharmaceutical company with a limited operating history. Pharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have not generated any product revenues and have financed our operations primarily through private placements of our preferred stock, borrowings under the Loan and Security 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 offering in February 2019. We do not expect to generate any product revenues unless one or more of our product candidates receives regulatory approval and is commercialized. We have not yet demonstrated an ability to obtain marketing approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies prior to regulatory approval 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 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, 2018 and 2017, we reported a net loss of \$60.1 million and \$26.6 million, respectively. In addition, our accumulated deficit as of December 31, 2018 was \$120.7 million. Substantially all our operating losses have resulted from costs incurred in connection with research and development of our product candidates and clinical and regulatory initiatives to obtain approvals for our product candidates.

We expect that our operating expenses will continue to increase 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 our expenses will increase substantially as we:

- < continue our research and development efforts;
- < seek regulatory approval for new product candidates and product enhancements;
- < build commercial infrastructure to support sales and marketing for our product candidates;
- < hire and retain additional personnel and add operational, financial and management information systems; and
- < continue to operate as a public company.

All of our product candidates are still in development and none have been approved for sale. We submitted a New Drug Application, or NDA, for our Gvoke HypoPen to the U.S. Food and Drug Administration, or FDA, in August 2018. The FDA has set June 10, 2019 as the Prescription Drug User Fee Act, or PDUFA, action goal date for our NDA. However, the FDA may not approve our Gvoke HypoPen. Our ability to generate revenue from our product candidates and to transition to profitability and generate positive cash flows is uncertain and depends on the successful development and commercialization of our product candidates. Successful development and commercialization will require achievement of key milestones, including completing clinical trials of our product candidates that are under clinical development, 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.

We have not generated any revenue from our product candidates, including our Gvoke HypoPen, and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from any of our product candidates. We do not expect to generate significant revenue unless or until we obtain marketing approval of, and begin to sell, our product candidates. We do not expect to commercialize any of our product candidates before the second quarter of 2019, if ever. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- < obtain marketing approval for our product candidates, including our Gvoke HypoPen;
- < obtain commercial quantities of our product candidates, if approved, at acceptable cost levels;
- < commercialize our product candidates, if approved, by developing our own sales force for commercialization in the United States or in other key territories by entering into partnership or co-promotion arrangements with third parties;
- < set an acceptable price for our product candidates, if approved;
- < obtain and maintain third-party coverage and adequate reimbursement for our product candidates, if approved; and
- < achieve an adequate level of market acceptance of our product candidates, if approved, 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.

If any of our product candidates are approved for commercial sale, we expect to incur significant sales and marketing costs as we prepare for its commercialization. Even if we receive marketing approval and expend these costs, our product candidates 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. In addition, if any of our product candidates are approved, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. 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 our Gvoke HypoPen, as well as any of our other product candidates that receive marketing approval.

We may be required 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 Loan and Security Agreement is secured by substantially

all of our existing property and assets other than our intellectual property assets, subject to certain exceptions. Our Loan and Security Agreement also contains a negative pledge on intellectual property owned by us, pursuant to which we have agreed not to encumber any of our intellectual property.

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 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 Loan and Security Agreement provides for term loans of up to an aggregate of \$45.0 million, of which \$20.0 million was borrowed upon signing. Following submission of an NDA for our Gvoke HypoPen, we drew down an additional \$15.0 million in September 2018. We become eligible to draw the remaining \$10.0 million if we receive approval of our Gvoke HypoPen NDA by the FDA before September 30, 2019, and then only available to be drawn until the earlier of September 30, 2019 or the 30th day following NDA approval by the FDA.

All obligations under our Loan and Security Agreement are secured by substantially all of our existing property and assets other than our intellectual property assets, subject to certain 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 Loan and Security Agreement could result in an event of default and, as a result, our lenders could accelerate all of the amounts due. Events of default include our failure to comply with customary affirmative covenants as well as our breach of customary negative covenants in the Loan and Security Agreement. Affirmative covenants include the maintenance of a \$5.0 million minimum cash balance 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 the occurrence of material adverse changes in the company's business or its prospect of repayment of its obligations. In the event of an acceleration of amounts due under our Loan and Security 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 Product Development and Regulatory Approval of Our Product Candidates

We are dependent on the success of our glucagon product candidates, particularly our Gvoke HypoPen. We cannot be certain that our Gvoke HypoPen or any of our other product candidates will receive marketing approval. Without marketing approval, we will not be able to commercialize our product candidates or generate product revenues.

We have devoted a significant portion of our financial resources and business efforts to the development of the Gvoke HypoPen. We submitted an NDA for the Gvoke HypoPen in the third quarter of 2018; however, we have not received approval from regulatory authorities to market the Gvoke HypoPen or any other product candidate in any jurisdiction, and it is possible that neither our Gvoke HypoPen nor any other product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us to commence product sales. The FDA's decision to accept the NDA for filing and set a PDUFA date does not indicate that it has made any decision regarding approval nor does it guarantee approval by June 10, 2019, if at all. We cannot be certain that our Gvoke HypoPen or any of our other 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 an NDA 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.

NDA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. NDAs must also include significant information regarding the chemistry, manufacturing and controls for the product. Obtaining approval of an NDA is a lengthy, expensive and uncertain process, and we may not be successful in obtaining approval. Our Gvoke HypoPen is considered to be a drug-device combination product by the FDA, and its NDA will require review and coordination by the FDA's drug and device centers prior to approval. We cannot predict whether we will obtain regulatory approval to commercialize our Gvoke HypoPen or any of our other product candidates, and we cannot, therefore, predict the timing of any future revenues from these product candidates, if any. Any delay or setback in the regulatory approval or commercialization of any of these 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 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 Gvoke HypoPen or any 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 there are unacceptable risks associated with the device component of our Gvoke HypoPen or that there are deficiencies with the information submitted to demonstrate the safety, effectiveness and reliability of the device component;
- < may determine that we have identified the wrong listed drug or drugs or that approval of our Section 505(b)(2) application for our Gvoke HypoPen or any of our other 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 those of our Gvoke HypoPen or any of our other 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.

At our pre-NDA meeting with the FDA in December 2017, we presented the results from our two Phase 3 Gvoke HypoPen clinical trials that had been completed as of that meeting. Our first Phase 3 clinical trial was a non-inferiority comparison of the Gvoke HypoPen against Eli Lilly's glucagon determined by an increase in plasma glucose concentration from below 50.0 mg/dL to greater than 70.0 mg/dL within 30 minutes after receiving glucagon. In this trial, our Gvoke HypoPen did not meet a primary endpoint for noninferiority in the intent-to-treat, or ITT, population due to one response failure in excess of the pre-specified threshold of three response failures. In the same trial, two subjects were censored from the modified ITT, or mITT, population because of a clinically significant protocol violation, and the remaining subjects were used for the per-protocol analysis. In accordance with FDA and International Council for Harmonisation guidance for evaluation of non-inferiority studies, we presented a series of analyses implementing ITT, mITT, and per-protocol cohorts for all the endpoints for this clinical trial to the FDA at this pre-NDA meeting. In that meeting, the FDA agreed overall that the totality of data for our Gvoke HypoPen is sufficient to support NDA review. However, certain of our analyses may be viewed as post-hoc analyses, and although we believe that post-hoc analyses can provide additional information regarding results from this trial, retrospective analyses can result in the introduction of bias and may be given less weight by the FDA, including for purposes of determining whether to approve our NDA.

The FDA provided additional comments to address prior to NDA submission related to the pre-filled syringe presentation of our ready-to-use glucagon, or Gvoke PFS. Based on these comments, we conducted additional studies, the results from which were included in our Gvoke HypoPen submission to the FDA.

In order to generate additional information regarding the entire treatment episode, we completed an additional non-inferiority Phase 3b clinical trial in the second quarter of 2018 comparing our Gvoke HypoPen to Eli Lilly's glucagon, the results of which were included in our NDA submission. Even though we completed this Phase 3b clinical trial, the FDA or other regulatory authorities may require us to conduct additional clinical trials prior to approval.

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, including our Gvoke HypoPen. If the FDA does not conclude that the Gvoke HypoPen or such other 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 Federal Food, Drug and Cosmetic Act, or FDCA, for the approval of certain of our product candidates, including our Gvoke HypoPen, 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 Gvoke HypoPen or our other 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 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 exclusivities 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 recently 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 new 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 other product candidates. Any delay in, or termination of, our clinical trials will delay the submission of the applicable NDA 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 our product candidates because they are combination products.

Certain of our product candidates, including our Gvoke HypoPen, 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 contract research organizations, or 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 Internal Review Boards, or 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.

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 other 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 any of our product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by such products:

- < regulatory authorities may require the addition of labeling statements, including "black box" warnings, contraindications or dissemination of field alerts to physicians and pharmacies;
- < we may be required to change instructions regarding the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- < we may be subject to limitations on how we may promote the product;
- < sales of the product may decrease significantly;
- < regulatory authorities may require us to take our approved product off the market;
- < we may be subject to litigation or 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 Post-Bariatric Hypoglycemia, or PBH, and congenital hyperinsulinism, or 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 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 a medically plausible basis for its use. 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 and our ready-to-use glucagon for PBH product candidates, 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. While we identified several potential applications of our ready-to-use glucagon, including our Gvoke HypoPen and 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 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 the Commercialization and Marketing of our Product Candidates

Our business depends entirely on the success of our 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 going forward will be focused on seeking marketing approval for and planning for potential commercialization of our lead product candidate, our Gvoke HypoPen, in the United States. Our business and future success are substantially dependent on our ability to successfully and timely obtain regulatory approval for and commercialize our Gvoke HypoPen. Our other product candidates are in earlier stages of development and subject to the risks of failure inherent in developing drug products. Accordingly, our ability to generate product revenues in the immediate term will depend on our ability to successfully obtain marketing approval for and commercialize our Gvoke HypoPen. Any delay or setback in the regulatory approval or commercialization of any of our product candidates will adversely affect our business.

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

- < the scope of regulatory approvals, including limitations or warnings contained in a product candidate's regulatory-approved labeling;
- < our ability to produce, through a validated process, sufficiently large quantities of our product candidates 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 product candidates;
- < the acceptance in the medical community of the potential advantages of the product candidate, including with respect to our efforts to increase adoption of our product candidates such as our Gvoke HypoPen by patients and healthcare providers;
- < the incidence, prevalence and severity of adverse side effects of our product candidates;
- < the willingness of physicians to prescribe our product candidates and of the target patient population to try these therapies;
- < the price and cost-effectiveness of our product candidates;
- < 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 the product candidate 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 the Gvoke HypoPen or any of our other product candidates receives marketing approval and 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 products, 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 our product candidates may be smaller than we estimate.

The potential market opportunity for our product candidates is difficult to precisely estimate. Our estimates of the potential market opportunity for our product candidates include several key assumptions of the current market size and current pricing for commercially available products and are based on industry and market data obtained from industry publications, studies conducted by us, our industry knowledge, third-party research reports and other surveys. Industry publications and third-party research generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. For example, our projections for the potential size of the market for our Gvoke HypoPen 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, then the actual market for our product candidates, including our Gvoke HypoPen, could be smaller than our estimates of our potential market opportunity. If the actual market for 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 is currently developing an internal sales organization. If we are unable to establish marketing, sales and distribution capabilities or enter into agreements with third parties to market, sell and distribute our product candidates, we may not be able to generate product revenues.

We currently do not have sufficient infrastructure for the sales, marketing or distribution of our product candidates, and the cost of establishing and maintaining such an organization may exceed the benefits of doing so. In order to commercialize our product candidates, we must expand our marketing, sales, distribution, managerial and other non-technical capabilities and/or make arrangements with third parties to perform these services. We intend to establish a sales force to market our Gvoke HypoPen in the United States, if we obtain FDA approval. 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 the development of our internal sales, marketing and distribution capabilities could delay any product launch, which would adversely impact

the commercialization of our product candidates, including our Gvoke HypoPen. We are building out our commercial organization in anticipation of receiving marketing approval of our Gvoke HypoPen. If the expected commercial launch of our Gvoke HypoPen is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

We cannot be sure that we will be able to hire a sufficient number of sales representatives or that they will be effective at promoting our products that receive regulatory approval, if any. 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 and train 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 creating an independent sales and marketing organization.

In the event that we are unable to effectively implement our sales organization or distribution strategy on a timely and effective 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 establish for our Gvoke HypoPen 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.

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 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 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, and 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. 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, if approved, and if we are unable to obtain adequate coverage and reimbursement by third-party payors for our products, our ability to successfully commercialize our 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 Glucagon Emergency Kit, or GEK, is covered at or above 94% 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.

Even if we successfully obtain approval for, produce and distribute our Gvoke HypoPen, its success will be dependent on its proper use by patients, healthcare practitioners and caregivers.

While we have designed our Gvoke HypoPen to be operable by patients, caregivers and healthcare practitioners, we cannot control the successful use of the product by patients, caregivers and healthcare practitioners. Even though our Gvoke HypoPen was used correctly by individuals in our human factors study, there is no guarantee that these results will be replicated by users in the future. If we are not successful in promoting the proper use of our Gvoke HypoPen, if approved, by patients, healthcare practitioners and caregivers, we may not be able to achieve market acceptance or effectively commercialize our Gvoke HypoPen. In addition, even in the event of proper use

of our Gvoke HypoPen, 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 product candidates that receive approval, result in negative press coverage, or increase the risk that we may be sued.

Guidelines and recommendations can reduce the use of our product candidates.

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

Risks Related to our Industry and the Ongoing Legal and Regulatory Requirements to which our Product Candidates are Subject

Even if our product candidates receive regulatory approval, 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 safety data arise, we could lose our marketing approvals and our business would be seriously harmed.

Our 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. In addition, 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 current Good Manufacturing Practices, or cGMPs, and applicable Quality System Regulations, or 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 others with whom we work 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, if any, 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. 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 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 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 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 Glucagon Emergency Kit and Novo Nordisk's GlucaGen, and in the future may include a subcutaneous dasiglucagon auto-injector, being developed by Zealand Pharma, and an intranasal glucagon dry powder, being developed by Eli Lilly. 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 our Gvoke HypoPen, if approved. For example, based on its public disclosure of its submission of an NDA to the FDA for its intranasal glucagon in 2018, we believe Eli Lilly's product candidate could receive marketing approval prior to our PDUFA target action date. 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, 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 our product candidates even if commercialized. For example, emergency glucagon products are currently available for hypoglycemia and are widely accepted in the medical community and have a long history of use. These treatments will compete with our Gvoke HypoPen, if approved, and may limit the potential for our Gvoke HypoPen to receive widespread acceptance if commercialized.

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 our Gvoke HypoPen 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 any grant of exclusivity to us.

If the FDA or other applicable regulatory authorities approve generic products that compete with any of our 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 product candidate, 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 product candidate. In some cases, even this limited bioequivalence testing can be waived by the FDA. Competition from generic equivalents to our product candidates could substantially limit our ability to generate revenues and therefore to obtain a return on the investments we have made in our product candidates.

Even if we obtain FDA approval of our lead product candidate, Gvoke HypoPen, or our other 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 approved for sale in any jurisdiction, including in 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 Gvoke HypoPen, we are engaged in ongoing interactions with European regulatory authorities regarding our development path in Europe. For our Gvoke HypoPen, because Eli Lilly's Glucagon Emergency Kit is not approved in Europe, we are conducting an additional clinical trial comparing our Gvoke HypoPen to Novo Nordisk's GlucaGen, in addition to our existing clinical trials involving Eli Lilly's Glucagon Emergency Kit. Such requirements may increase our development expenses and delay our regulatory development plans for potential European approval of our Gvoke HypoPen. There can be no assurance that the results that we observed from our prior clinical trials for our Gvoke HypoPen will be replicated in our ongoing and any future clinical trials that we undertake, or that any such results 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 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, including our Gvoke HypoPen, restrict or regulate post-approval activities and affect our ability to profitably sell any 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 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 70% 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 "individual mandate." However, as a result of tax reform legislation passed in December 2017, the individual mandate has been eliminated effective January 1, 2019. 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 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, the Centers for Medicare & Medicaid Services, or CMS, has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization, or PA, and step therapy, or ST, for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" while a definition of "price concession" in the regulations. It is unclear whether these proposed changes will be accepted, and if so, 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 2027. 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. 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 inseparable feature of the ACA, and therefore because the mandate was repealed 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. 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. 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 proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other 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. 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 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.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications. Notably, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and Budget on February 2, 2017, the Trump administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. Further, on

February 24, 2017, President Trump issued an Executive Order requiring each agency to designate a regulatory reform officer and create a regulatory reform task force to evaluate existing regulations and make recommendations regarding their repeal, replacement or modification. It is difficult to predict how these requirements will be implemented and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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 false claims and civil monetary penalties laws, including the federal civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or knowingly avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties.
- < **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 covered entities and their business associates, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information.
- < **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 the CMS information related to payments or transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as information regarding ownership and investment interests held by the physicians described above and their immediate family members.
- < **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.

In the event we decide to conduct clinical trials in the European Union, or EU, we may be subject 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 of 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 product candidates. The 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 of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with laws and regulations in each new jurisdiction in which we plan to operate, and these laws may preclude us from developing, manufacturing, or selling certain drugs and product candidates outside of 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, is 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 European Union, 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 Dependence on Third Parties

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

We depend on independent clinical investigators, CROs, academic institutions and other third-party service providers to conduct clinical trials with and for our product candidates. Although we rely heavily on these parties for successful execution of our clinical trials, we

are ultimately responsible for the results of their activities and many aspects of their activities are beyond our control. For example, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial, but the independent clinical investigators may prioritize other projects over ours or may fail to timely communicate issues regarding our products to us. Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory requirements or our stated protocols. The delay or early termination of any of our clinical trial arrangements, the failure of third parties to comply with the regulations and requirements governing clinical trials, or our reliance on results of trials that we have not directly conducted or monitored could hinder or delay the development, approval and commercialization of our product candidates and would adversely affect our business, results of operations and financial condition.

We maintain compliance programs related to our clinical trials through our clinical operations and development personnel working with our finance and legal groups' support. Our clinical trial vendors are required to monitor and report to us the possible remedial action required for the conduct of clinical studies, and we are obliged to take the appropriate action. We also monitor clinical trial vendors through our regulatory and quality assurance staff and service providers. However, we cannot assure you that our programs and personnel will timely and fully discover any fraud or abuse that may occur in connection with our clinical trials. Such fraud or abuse, if it occurs, could have a material adverse effect on our research, development, and commercialization activities and results.

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

We do not currently own or operate manufacturing facilities for the production of any of our product candidates, including our Gvoke HypoPen. 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 supply agreements with Bachem, Pyramid and SHL Pharma. 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 key materials or products in the future, which could have a material adverse effect on our business.

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.

Our product candidates, including Gvoke HypoPen, are drug-device combination products that will be regulated under the drug regulations of the FDCA based on its primary mode of action as a drug. Third-party manufacturers may not be able to comply with the 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 QSR 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 product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs and QSRs. 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 the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor 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 clinical research activities and our ability to develop our product candidates and market our products following approval.

The FDA and other foreign regulatory authorities require manufacturers to register manufacturing facilities. The FDA and corresponding foreign regulators also inspect these facilities to confirm compliance with applicable 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. Any failure to comply

with cGMP or QSR requirements or other FDA, EMA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our 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 European Union, 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 by suppliers due to terms within long-term supply arrangements 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 or geo-political events, 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 a necessary raw material or components becomes 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 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.

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

In order to produce sufficient quantities to meet the demand for clinical trials and subsequent commercialization of our Gvoke HypoPen or any of our other 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 our Gvoke HypoPen and other components of our product candidates, or if they are unable to produce increased amounts of 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.

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 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.

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. 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 patent applications filed 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, is 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 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 product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our 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 preissuance 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 stop others from using or commercializing similar or identical technology and products, or 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 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 have taken 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 patents or patent applications, 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 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 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 of 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 involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. New 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 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 of 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 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 claims, 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 stop the other party from using 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 stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. 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 candidate.

We submitted our NDA for our Gvoke HypoPen in August 2018 under Section 505(b)(2) of the FDCA, and we expect to submit NDAs for our other product candidates, to the FDA for approval under this section. 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, 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 our Gvoke HypoPen, 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 product candidates and, if approved, our products. These claims may be expensive to defend and may result in large judgments against us. During the course of treatment, patients using our product candidates could suffer adverse medical effects for reasons that may or may not be related to our product candidates. We will face even greater risks upon any commercialization by us of our product candidates. Any of these events could result in a claim of liability. Any such claims against us, regardless of their merit, could result in significant costs to defend or awards against us that could materially harm our business, financial condition or results of operations. In addition, any such claims against us could result in a distraction to management, decreased demand for our products, an adverse effect on our public reputation, and/or difficulties in commercializing our products. To date, we have not received notice of any product liability claims against us. We maintain total product liability insurance coverage of \$5.0 million.

Although we maintain product liability insurance for claims arising from the use of our product candidates in clinical trials prior to FDA approval and for claims arising from the use of our products after 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 product candidates and products 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, 2018, we had 90 employees. As our product candidates continue to progress toward potential approval and commercialization, 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-time to develop alternate third-party sources, we intend 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 will be required to devote significant resources to complete the assessment and documentation of our internal control system and financial process under Section 404 of the Sarbanes-Oxley Act, including an assessment of the design of our information systems associated with our internal controls.

We have never conducted a review of our internal control for the purpose of providing the reports required by these rules. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal control over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to timely file accurate quarterly and annual reports with the SEC under the Securities Exchange Act of 1934, or the Exchange Act, as amended. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The Nasdaq Global Select Market or other adverse consequences. We will incur significant costs to remediate any material weaknesses we identify through these efforts. We also expect these rules and regulations to make it more expensive for us to maintain directors' and officers' liability insurance and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified persons to serve on our board of directors or our board committees or as executive officers. 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 our Annual Report on Form 10-K for the year ended December 31, 2019. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company's annual and interim financial statements will not be detected or prevented on a timely basis.

We may further enhance the computer systems processes and related documentation necessary to perform the evaluation needed to comply with Section 404. We may not be able to complete our evaluation, testing and any required remediation in a timely fashion. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will

be unable to assert 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 financial control.

For example, for the year ended December 31, 2017, we identified a material weakness in our internal control over financial reporting due to a lack of proper segregation of duties within our finance and accounting function. This weakness was due to our inability to implement the appropriate segregation of duties within our historical enterprise resource planning, or ERP, system. Since August 2017, we have re-mediated this material weakness by implementing a new ERP system in December 2017 and adding additional personnel in order to develop an effective segregation of duties process. If, in the future, we are unable to conclude that our internal control over financial reporting is effective or take effective remedial measures to improve our internal control, we could lose investor confidence in the accuracy and completeness of our financial reports, which would likely cause the price of our common stock to decline.

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 would 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 as a result of the current implementation 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 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 will be materially adversely affected.

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

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. 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.

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 of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of 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 of 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 recently passed comprehensive tax reform bill 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 continue to examine the impact this tax reform legislation may have on our business. The overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. 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 may be highly volatile and could be subject to large fluctuations in response to the risk factors discussed in this section, and others beyond our control, including:

- < the timing and results of applications for FDA review and approval of our Gvoke HypoPen and other regulatory actions with respect to our 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 our Gvoke HypoPen, if approved, and of other 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 are an “emerging growth company” and the reduced disclosure requirements applicable to “emerging growth 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 nonaffiliates 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, or (ii) 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.

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, 2018, the Company had federal net operating loss carryforwards of \$108.8 million and various state net operating loss carryforwards of \$35.6 million. As of December 31, 2017, the Company had federal net operating loss carryforwards of \$55.8 million. If not utilized, the federal net operating losses produced on or before December 31, 2017 will expire at various dates between 2025 and 2037. Federal net operating losses produced on or after December 31, 2018, will be carried forward indefinitely. At December 31, 2018, the Company had \$5.8 million and \$0.2 million of federal and state income tax credits, respectively, to reduce future tax liabilities. As of December 31, 2017, the Company had \$2.0 million of federal income tax credits. If not utilized, these carryforwards will expire at various dates between 2025 and 2038. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain how various states will respond to the newly enacted federal tax law. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, 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 an ownership change, our ability to utilize our net operating losses or credits could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, many of which may be outside of our control, could result in an ownership change under 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.

We do not anticipate paying any cash dividends in the foreseeable future, and accordingly, your ability to achieve a return on your 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 Loan and Security 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;
- < 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;
- < provide that the Court of Chancery of the State of Delaware will be the exclusive forum for any 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 your 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. 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 foregoing provision.

This choice of 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. Stockholders who do bring a claim in this court could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near Delaware. The Delaware Court of Chancery 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. 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 and 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

foregoing 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. However, on December 19, 2018, the Delaware Court of Chancery issued a decision declaring that such 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 January 17, 2019, that decision was appealed to the Delaware Supreme Court. While the Delaware Supreme Court recently dismissed the appeal on jurisdictional grounds, we expect that the appeal will be re-filed after the Court of Chancery issues a final judgment. Unless and until the Court of Chancery's decision is reversed by the Delaware Supreme Court or otherwise abrogated, we will not seek to enforce our federal forum selection 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 decision or otherwise determines that federal forum selection provisions are invalid, our Board intends to amend promptly our amended and restated bylaws to remove our federal forum selection bylaw provision. As a result of the Court of Chancery's 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 selection bylaw provision, which could have an adverse effect on our business, financial condition or results of operations.

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 16,045 square feet of leased and sub-leased space, which we refer to as the existing premises. In November 2018, we signed an amendment to this lease to occupy an additional 40,850 square feet of space and expect to relocate from our existing premises to this additional space in March 2019. The lease term expires on June 30, 2031. As part of this amendment, upon completing our relocation, we will return 8,899 square feet of the existing premises back to our landlord. We intend to sublease the remaining 7,146 square feet of existing premises by the end of 2019. We also maintain a product development site in San Diego, California. Our San Diego office occupies approximately 17,105 square feet of leased space under a 60-month lease term through June 2023. We believe that the Chicago office coupled with our San Diego office will be suitable and adequate to meet our current 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 4, 2019, there were approximately 86 stockholders of record of our common stock and the closing price of our common stock was \$10.50 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 three months ended December 31, 2018.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not purchase any of our registered equity securities during the three months ended December 31, 2018.

Use of Proceeds from Initial Public Offering of Common Stock

Shares of our common stock began trading on The Nasdaq Global Select Market on June 21, 2018. The shares were registered under the Securities Act of 1933, as amended, pursuant to our registration statement on Form S-1 (Registration No. 333-2225191) relating to our initial public offering ("IPO") of common stock, which was declared effective by the U.S. Securities and Exchange Commission ("SEC") on June 20, 2018.

There has been no material change in our planned use of the net proceeds from the IPO as described in the final prospectus filed with the SEC to Rule 424(b)(4) on June 21, 2018 under the Securities Act of 1933, as amended.

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 financial statements of the Company, the notes to financial statements, 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, 2018 and 2017 and the selected balance sheets data as of December 31, 2018 and 2017 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, 2016 and the selected balance sheet data as of December 31, 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,		
	2018	2017	2016
(in thousands, except share and per share data)			
Statements of Operations Data			
Grant income	\$ 2,365	\$ 1,540	\$ 1,022
Service revenue	100	16	53
Cost of revenue	42	4	8
Gross profit	<u>2,423</u>	<u>1,552</u>	<u>1,067</u>
Operating expenses:			
Research and development	40,654	20,166	10,238
Selling, general and administrative	21,113	8,015	4,060
Expense from operations	<u>61,767</u>	<u>28,181</u>	<u>14,298</u>
Loss from operations	<u>(59,344)</u>	<u>(26,629)</u>	<u>(13,231)</u>
Other income (expense):			
Interest income	1,613	124	5
Interest expense	(2,545)	(2)	(2)
Change in fair value of warrants	196	(46)	24
Other expense	—	(1)	(5)
Total other income (expense)	<u>(736)</u>	<u>75</u>	<u>22</u>
Net loss	<u>\$ (60,080)</u>	<u>\$ (26,554)</u>	<u>\$ (13,209)</u>
Net loss per share - basic and diluted ⁽¹⁾	<u>\$ (4.99)</u>	<u>\$ (13.09)</u>	<u>\$ (7.17)</u>
Weighted average number of common shares outstanding, basic and diluted ⁽¹⁾	<u>12,045,999</u>	<u>2,028,224</u>	<u>1,842,416</u>

	As of December 31,		
	2018	2017	2016
(in thousands)			
Balance Sheets Data			
Cash and cash equivalents	\$ 45,716	\$ 42,045	\$ 32,269
Short-term investments	66,917	—	—
Working capital ⁽²⁾	107,727	39,193	30,647
Total assets	120,028	44,998	33,533
Long-term debt, net of deferred costs	31,890	—	—
Other long-term liabilities	2,560	90	42
Total liabilities	44,622	4,950	2,569
Total convertible preferred stock	—	97,878	62,898
Total stockholders' equity (deficit)	75,406	(57,830)	(31,934)

(1) Refer to Note 2, "Summary of Significant Accounting Policies", of the notes to financial statements 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 financial statements and the notes to those financial statements appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve significant risks and uncertainties. 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 technology platforms, XeriSol and XeriJect, to develop and commercialize ready-to-use, non-aqueous formulation injectable and infusible drug formulations. We have developed a ready-to-use, room-temperature stable liquid glucagon formulation that, unlike any currently available products, can be administered without any preparation or reconstitution. Our lead product candidate, Gvoke HypoPen, delivers ready-to-use glucagon via a commercially-available auto-injector for the treatment in people with diabetes of severe hypoglycemia, a potentially life-threatening condition. We have completed three Phase 3 clinical trials for our Gvoke HypoPen and submitted a New Drug Application, or NDA, to the U.S. Food & Drug Administration, or the FDA, in August 2018. The FDA has set June 10, 2019 as the Prescription Drug User Fee Act, or PDUFA, action goal date for our NDA. If our NDA is approved at that time, we believe we will have the first ready-to-use, room-temperature stable liquid glucagon formulation that can be administered without any preparation or reconstitution. Additionally, through our interactions with the European Medicines Agency, or EMA, regarding our development path in Europe, we have finalized our regulatory plan and initiated a requisite Phase 3 pivotal trial to support our European Marketing Authority Application, or MAA. We also are applying our novel ready-to-use, room-temperature stable liquid glucagon formulation for the management of hypoglycemia associated with additional intermittent and chronic conditions with significant unmet medical need. In addition, we are applying our technology platforms to convert other commercially-available drugs into ready-to-use, room-temperature stable liquid formulations to address the needs in multiple therapeutic areas and conditions, including epilepsy and diabetes.

We have begun building out our commercial organization, including individuals in operations and marketing as well as medical affairs, in preparation for a commercial launch of the Gvoke HypoPen in the United States in the second half of 2019. 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 and raising capital. We do not have any products approved for sale and have not generated any revenue from product sales.

We have funded our operations to date primarily with proceeds from the sale of preferred and common stock, bank financings and grant awards received from the National Institutes of Health, or NIH, and other philanthropic organizations. In particular, we have received cash proceeds of \$104.9 million from sales of our preferred stock, \$35.0 million from drawdowns of the Loan and Security Agreement, \$10.6 million from grant awards from the NIH and other philanthropic organizations, and \$98.3 million from our June 2018 initial public offering, or IPO, of our common stock pursuant to a registration statement on Form S-1, as amended. In the IPO, we sold an aggregate of 6,555,000 shares of our common stock under the registration statement at a public offering price of \$15.00 per share, including 855,000 shares of our common stock pursuant to the exercise of the underwriters' option to purchase additional shares. Net proceeds were \$88.9 million after deducting underwriting discounts and commissions as well as other offering expenses. The Loan and Security Agreement includes an additional \$10.0 million that will be available beginning upon approval of our Gvoke HypoPen NDA by the FDA until the earlier of September 30, 2019 or the 30th day following NDA approval by the FDA.

For the years ended December 31, 2018 and 2017, our net loss was \$60.1 million and \$26.6 million, respectively. We have not been profitable since inception, and, as of December 31, 2018, our accumulated deficit was \$120.7 million. In the near term, we expect to continue to incur significant expenses, operating losses and net losses as we:

- < prepare for a potential commercial launch of our Gvoke HypoPen, including hiring our sales force;
- < 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.

We do not expect to generate significant product revenue unless or until we obtain marketing approval of, and begin to sell, our product candidates. 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

Revenue and Cost of Revenue

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, 2018, we are eligible to receive \$1.4 million in grants from the NIH and other philanthropic organizations that will help fund our ongoing clinical development for intermittent and chronic glucagon programs as well as our auto-injectable diazepam program for the treatment of epileptic seizures. These awards will be recognized as grant income when we have performed the services as outlined in the grant agreements.

Service revenue is derived 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.

Cost of revenue includes employees' time, materials and overhead applied to the feasibility studies.

Research and Development Expenses

Research and development expenses consist of expenses incurred in connection with the discovery and development of our product candidates. We expense 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:

- < 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;
- < manufacturing scale-up expenses, the cost of acquiring and manufacturing preclinical and clinical trial materials, including manufacturing validation batches, and the cost of manufacturing commercial supplies in advance of regulatory approval;
- < outsourced professional scientific development services;
- < employee-related expenses, which include salaries, benefits and stock-based compensation;
- < expenses relating to regulatory activities, including filing fees paid to regulatory agencies;
- < laboratory materials and supplies used to support our research activities; and
- < allocated expenses for facility-related costs.

Research and development activities are central to our business model. We expect our research and development expenses to increase as we conduct new clinical trials, prepare regulatory filings for our product candidates, and add headcount to support these efforts. In particular, we expect research and development expenses to increase in the near term as we (i) complete development and registration of our Gvoke HypoPen in the US and Europe; (ii) progress our intermittent and chronic glucagon programs for Post-Bariatric Hypoglycemia, Congenital Hyperinsulinism, Hypoglycemia-Associated Autonomic Failure, and Exercise-Induced Hypoglycemia; (iii) advance device development partnering efforts; (iv) continue preclinical and clinical development for our ready-to-use diazepam rescue pen; (v) conduct preclinical and clinical work for our Pramlintide-Insulin program; and (vi) continue to advance other pipeline candidates. Our research and development expenses may vary significantly over time due to uncertainties relating to the terms and timing of regulatory approvals and unexpected results of our clinical trials.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist principally of salaries, stock-based compensation and related costs for personnel in executive, marketing and administrative positions, facility costs not otherwise included in research and development, marketing expenses, professional fees for legal, audit and accounting services, fees paid for market research and trade shows, and travel costs for marketing and administrative employees.

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. We also expect selling and marketing costs to increase significantly as we prepare for the expected commercial launch of our Gvoke HypoPen in the United States, if approved, including the buildout of a sales force in 2019.

Other Income (Expense)

Other income (expense) consists primarily of interest expense related to our Loan and Security Agreement, interest income earned on short-term deposits and investments, and the change in the fair market value of our warrants.

Income Tax

We have incurred operating losses since inception and therefore do not have any taxable income. As of December 31, 2018, we had \$108.8 million in federal net operating loss carryforwards and \$35.6 million of various state net operating loss carryforwards, \$5.8 million in federal research and orphan drug credits that begin to expire in 2025, as well \$0.2 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, 2018 and 2017:

(in thousands)	Years Ended December 31,		\$ Change
	2018	2017	
Grant income	\$ 2,365	\$ 1,540	\$ 825
Service revenue	100	16	84
Cost of revenue	42	4	38
Gross profit	<u>2,423</u>	<u>1,552</u>	<u>871</u>
Operating expenses:			
Research and development	40,654	20,166	20,488
Selling, general and administrative	21,113	8,015	13,098
Expense from operations	<u>61,767</u>	<u>28,181</u>	<u>33,586</u>
Loss from operations	<u>(59,344)</u>	<u>(26,629)</u>	<u>(32,715)</u>
Other income (expense):			
Interest income	1,613	124	1,489
Interest expense	(2,545)	(2)	(2,543)
Change in fair value of warrants	196	(46)	242
Other expense	—	(1)	1
Total other income (expense)	<u>(736)</u>	<u>75</u>	<u>(811)</u>
Net loss	<u>\$ (60,080)</u>	<u>\$ (26,554)</u>	<u>\$ (33,526)</u>

Gross Profit

Gross profit increased by \$0.9 million for the year ended December 31, 2018 when compared to the year ended December 31, 2017, primarily driven by an increase in grant income of \$0.8 million. This increase was primarily driven by several clinical trials and preclinical studies for our CHI and PBH programs and our diazepam formulation for the treatment of epileptic seizures for which we received grants.

Research and Development Expenses

The following table summarizes our research and development expenses by functional area for the years ended December 31, 2018 and 2017:

(in thousands)	Years Ended December 31,		\$ Change
	2018	2017	
Clinical and preclinical	\$ 13,295	\$ 9,233	\$ 4,062
Product development	18,909	6,654	12,255
Compensation and related personnel costs	7,932	4,217	3,715
Stock-based compensation	518	62	456
Total research and development expenses	<u>\$ 40,654</u>	<u>\$ 20,166</u>	<u>\$ 20,488</u>

The following table summarizes our research and development expenses by program for the years ended December 31, 2018 and 2017:

(in thousands)	Years Ended December 31,		\$ Change
	2018	2017	
Gvoke HypoPen	\$ 20,865	\$ 10,339	\$ 10,526
Other ready-to-use glucagon programs	4,741	4,013	728
Pipeline product programs	2,434	60	2,374
Overhead (personnel, facilities and other expenses)	12,614	5,754	6,860
Total research and development expenses	\$ 40,654	\$ 20,166	\$ 20,488

Research and development expenses increased \$20.5 million for the year ended December 31, 2018 when compared to the year ended December 31, 2017. These increases were primarily driven by increased product development expenses of \$12.2 million in support of our Gvoke HypoPen NDA filing and additional pipeline programs as well as the manufacturing of commercial supplies of the Gvoke HypoPen prior to FDA approval, increased personnel expenses of \$4.2 million due to additional headcount and other employee-related costs, and increased expenses of \$4.1 million associated with our clinical and preclinical trials.

Selling, General and Administrative Expenses

Selling, general and administrative costs increased \$13.1 million for the year ended December 31, 2018 when compared to the year ended December 31, 2017. These increases were primarily driven by increases in personnel expenses due to additional headcount and other employee-related costs to support being a public company of \$7.0 million, marketing and market research expenses of \$3.3 million, costs of operating as a growing public company of \$1.7 million, and professional consulting fees of \$1.1 million.

Other Income (Expense)

For the year ended December 31, 2018, interest expense related to our current year debt issuances was \$2.5 million. Interest income earned on short-term investments and interest bearing accounts for the year ended December 31, 2018 was \$1.6 million. In addition, the fair market value of our warrants decreased for the year ended December 31, 2018 when compared to the year ended December 31, 2017 by \$0.2 million. The change in fair value of warrants decreased as the fair value of the stock into which the warrants convert decreased since their issuance and some of the warrants were exercised during the current year.

Liquidity and Capital Resources

Our primary uses of cash are to fund the development of our products, operating expenses and working capital requirements. Historically, we have funded our operations primarily through private placements of convertible preferred stock, issuance of debt, and grants awarded from the NIH and other philanthropic organizations. On June 25, 2018, we completed our IPO of 6,555,000 shares of our common stock at a price of \$15.00 per share for aggregate gross proceeds of approximately \$98.3 million, including 855,000 shares of our common stock pursuant to the exercise of the underwriters' option to purchase additional shares. We received aggregate net proceeds from the IPO of \$88.9 million after deducting underwriting discounts and commissions as well as other offering expenses. In addition, 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 the underwriters' partial exercise of their option to purchase additional shares of common stock. Net proceeds from the offering were approximately \$55.6 million after deducting underwriting discounts and commissions as well as other offering expenses. As of December 31, 2018, we had \$1.4 million in awarded unused grants that can be utilized to offset program costs for several of our intermittent and chronic glucagon programs as well as our diazepam program, in accordance with the grant agreements.

Capital Resources and Funding Requirements

We have incurred operating losses since inception, and we have an accumulated deficit of \$120.7 million at December 31, 2018. We believe that our cash and cash equivalents and short-term investments, net proceeds from our public offering in February 2019, expected revenue from sales of our Gvoke HypoPen, and available borrowing under our loan facility of \$10.0 million upon approval of our Gvoke HypoPen NDA by the FDA until the earlier of September 30, 2019 or the 30th day following NDA approval by the FDA will enable us to sustain operations and capital expenditure requirements through at least the first quarter of 2022. We expect to incur substantial additional expenditures in the near term to support our ongoing activities and the expected commercial launch of our Gvoke HypoPen. 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 the next several years. 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 our product candidates will depend on the amount and timing of cash received from planned financings. Our future capital requirements will depend on many factors, including:

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

Until we obtain regulatory approval to market our product candidates, if ever, we cannot generate revenues from sales of our products. Even if we are able to sell our products, we may not generate a sufficient amount of product revenues to finance our cash requirements. Accordingly, we may need to obtain additional financing in the future which may include public or private debt and 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 our product candidates. The issuance of equity securities may result in dilution to stockholders. If we raise additional funds through the issuance of debt securities, these securities may have rights, preferences and privileges senior to those of our common stock and the terms of the debt securities could impose significant restrictions on our operations. The failure to raise funds as and when needed could have a negative impact on our financial condition and ability to pursue our business strategies. If additional funding is not secured when required, we may need to delay or curtail our operations until such funding is received, which would have a material adverse impact on our business prospects and results of operations.

Cash Flows

(in thousands)	Years Ended December 31,	
	2018	2017
Net cash used in operating activities	\$ (56,279)	\$ (24,663)
Net cash used in investing activities	(68,261)	(700)
Net cash provided by financing activities	128,211	35,139
Increase in cash and cash equivalents	<u>\$ 3,671</u>	<u>\$ 9,776</u>

The increase in cash used in operating activities for the year ended December 31, 2018 when compared to the year ended December 31, 2017 was primarily due to an increase in net loss from operations resulting from increased spending on research and development and selling, general and administrative expenses.

The increase in cash used by investing activities for the year ended December 31, 2018 when compared to the year ended December 31, 2017 was primarily due to purchases of short-term investments with a portion of the net proceeds from the IPO.

The increase in cash provided by financing activities for the year period ended December 31, 2018 when compared to the year ended December 31, 2017 was primarily due to the net proceeds from the IPO of \$88.9 million after deducting payments for IPO costs, net proceeds from the Loan and Security Agreement of \$34.7 million and net proceeds from the sale of Series C Preferred Stock of \$4.4 million, partially offset by net proceeds from the sale of Series C Preferred Stock of \$35.0 million in the prior year.

Contractual Obligations and Commitments

During the year ended December 31, 2018 we entered into additional leases for office space in Chicago as well as executed the Loan and Security Agreement.

As of December 31, 2018, we were obligated to pay the following amounts:

(in thousands)	Total	2019	2020-2021	2022-2024	2025 and Beyond
Operating leases	\$ 18,566	\$ 891	\$ 3,798	\$ 5,318	\$ 8,559
Future principal payments under Loan and Security Agreement	35,000	—	21,000	14,000	—

In the first quarter of 2018, the Company signed a new lease for office space in Chicago, Illinois. In the fourth quarter of 2018, we signed an amendment to this lease to occupy additional space and expects to relocate from our existing premises to this additional space in March 2019. The lease term expires on June 30, 2031.

We enter into contracts in the normal course of business with clinical trial sites, manufacturing organizations and vendors for preclinical studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination after a notice period, and, therefore, are cancellable contracts and not included in the table above.

Off-Balance Sheet Arrangements

As of December 31, 2018, we had unused letters of credit of \$143,000 that are used to secure leases.

Internal Controls

Our internal policies and procedures relating to control over financial reporting are designed to provide reasonable assurance as to the reliability of our financial reporting. During 2017, we identified a material weakness in our internal control over financial reporting due to a lack of proper segregation of duties within our finance and accounting function, as one individual had control over two or more phases of a transaction or operation. This weakness was due to our inability to implement the appropriate segregation of duties within our historical enterprise resource planning system. Since August 2017, we have remediated this material weakness by implementing a new ERP system in December 2017 and adding additional personnel in order to develop an effective segregation of duties process.

CRITICAL ACCOUNTING POLICIES AND THE USE OF ESTIMATES

We have based our management's discussion and analysis of our financial condition and results of operations on our financial statements that have been prepared in accordance with generally accepted accounting principles, or 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 those related to 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.

While our significant accounting policies are more fully discussed in Note 2, "Summary of Significant Accounting Policies", of the notes to financial statements, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our financial statements. We have reviewed critical accounting policies and estimates with the audit committee of our board of directors.

Research and development expenses

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.

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 and restricted stock awards:

(in thousands)	Years Ended December 31,	
	2018	2017
Research and development	\$ 518	\$ 62
Selling, general and administrative	1,210	437
Total stock-based compensation expense	\$ 1,728	\$ 499

The Company accounts 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, net of estimated forfeitures, 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.

These 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 zero-coupon U.S. Treasury notes with remaining terms similar to the expected term of the options.
- *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.

Prior to our IPO in June 2018, our valuations were performed by a third-party valuation company using a discounted cash flow, or DCF, analysis. This method was chosen based on our sources of historical capital and potential future capital needs. For the December 31, 2017 valuation, we went from the DCF valuation technique to a hybrid method, which uses market approaches to estimate our enterprise value. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more of the scenarios is calculated using an option-pricing method, or OPM. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class

of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different. If there are any modifications or cancellations of the underlying unvested securities, we may be required to accelerate, increase or cancel any remaining unearned stock-based compensation expense.

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. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. We determine our 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.

We account for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, we recognize 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. As of December 31, 2018, we did not have any significant uncertain tax positions. Our 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. We did not accrue any interest or penalties on uncertain tax positions for the years ended December 31, 2018 and 2017.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its net operating losses, or NOLs, to offset future taxable income. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Section 382 of the Code. Our NOLs are also subject to international regulations, which could restrict our ability to utilize our NOLs. Furthermore, our ability to utilize NOLs of companies that we may acquire in the future may be subject to limitations. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to offset future income tax liabilities.

NEW ACCOUNTING STANDARDS

Refer to Note 2, "Summary of Significant Accounting Policies", of the notes to financial statements, 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 market risks related to changes in interest rates.

Interest Rate Risk

Cash and Cash Equivalents and Short-Term Investments—We are exposed to the risk of interest rate fluctuations on the interest income earned on our cash and cash equivalents and short-term investments. A hypothetical one-percentage point increase or decrease in interest rates applicable to our cash and cash equivalents and short-term investments outstanding at December 31, 2018 would increase or decrease interest income by approximately \$1.1 million on an annual basis. Any changes to interest income on short-term investments would only be realized if sold prior to maturity.

Loan and Security Agreement—Our interest rate risk relates primarily to U.S. dollar LIBOR-indexed borrowings. Based on our outstanding borrowings at December 31, 2018, a one-percentage point increase or decrease in interest rates would affect interest expense on the debt by \$0.4 million on an annualized basis.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Index to Financial Statements

	Page
Report of Independent Registered Public Accounting Firm	99
Financial Statements	
Balance Sheets as of December 31, 2018 and December 31, 2017	100
Statements of Operations and Comprehensive Loss for the years ended December 31, 2018 and 2017	101
Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit) for the years ended December 31, 2018 and 2017	102
Statements of Cash Flows for the years ended December 31, 2018 and 2017	103
Notes to Financial Statements	104

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Xeris Pharmaceuticals, Inc. (the Company) as of December 31, 2018 and 2017, the related 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, 2018, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these 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 financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

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

Chicago, Illinois
March 6, 2019

XERIS PHARMACEUTICALS, INC.

Balance Sheets

(in thousands, except share and par value)

	December 31, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	\$ 45,716	\$ 42,045
Short-term investments	66,917	—
Accounts receivable, net	2,869	1,199
Prepaid expenses and other current assets	2,397	809
Total current assets	117,899	44,053
Property and equipment, net	2,034	788
Other assets	95	157
Total assets	\$ 120,028	\$ 44,998
Liabilities, Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	\$ 866	\$ 1,976
Accrued expenses	8,214	2,557
Warrant liabilities	860	93
Deferred grant awards	232	234
Total current liabilities	10,172	4,860
Long-term debt, net of unamortized deferred costs	31,890	—
Other long-term liabilities	2,560	90
Total liabilities	44,622	4,950
Commitments and Contingencies (Note 9)		
Convertible Preferred Stock:		
Series A Convertible Preferred Stock—par value \$0.0001, 1,864,797 shares authorized and 1,843,965 shares issued and outstanding as of December 31, 2017	—	1,945
Series B Convertible Preferred Stock—par value \$0.0001, 5,732,338 shares authorized and 5,696,834 shares issued and outstanding as of December 31, 2017	—	18,536
Series C Convertible Preferred Stock—par value \$0.0001, 14,353,859 shares authorized and 12,834,912 shares issued and outstanding as of December 31, 2017	—	77,397
Total convertible preferred stock	—	97,878
Stockholders' Equity (Deficit):		
Preferred stock—par value \$0.0001, 10,000,000 shares authorized as of December 31, 2018 and no shares issued and outstanding as of December 31, 2017	—	—
Common stock—par value \$0.0001, 150,000,000 and 30,450,994 shares authorized as of December 31, 2018 and 2017, respectively; 20,808,366 and 2,159,068 shares issued and outstanding as of December 31, 2018 and 2017, respectively	2	1
Additional paid in capital	196,121	2,754
Accumulated deficit	(120,665)	(60,585)
Accumulated other comprehensive loss	(52)	—
Total stockholders' equity (deficit)	75,406	(57,830)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	\$ 120,028	\$ 44,998

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

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

	Years Ended December 31,	
	2018	2017
Grant income	\$ 2,365	\$ 1,540
Service revenue	100	16
Cost of revenue	42	4
Gross profit	2,423	1,552
Operating expenses:		
Research and development	40,654	20,166
Selling, general and administrative	21,113	8,015
Expense from operations	61,767	28,181
Loss from operations	(59,344)	(26,629)
Other income (expense):		
Interest income	1,613	124
Interest expense	(2,545)	(2)
Change in fair value of warrants	196	(46)
Other expense	—	(1)
Total other income (expense)	(736)	75
Net loss	\$ (60,080)	\$ (26,554)
Other comprehensive loss, net of tax:		
Unrealized losses on short-term investments	(52)	—
Comprehensive loss	\$ (60,132)	\$ (26,554)
Net loss per common share - basic and diluted	\$ (4.99)	\$ (13.09)
Weighted average common shares outstanding, basic and diluted	12,045,999	2,028,224

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

XERIS PHARMACEUTICALS, INC.

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

Years Ended December 31, 2018 and 2017

(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 LOSS	ACCUMULATED DEFICIT	TOTAL
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT				
Balance, December 31, 2016	1,843,965	\$ 1,945	5,696,834	\$ 18,536	7,177,398	\$ 42,417	1,927,237	\$ 1	\$ 2,096	\$ —	\$ (34,031)	\$ (31,934)
Net loss	—	—	—	—	—	—	—	—	—	—	(26,554)	(26,554)
Issuance of Series C Preferred Stock, net of cost of \$495	—	—	—	—	5,657,514	34,980	—	—	—	—	—	—
Exercise and vesting of stock-based awards	—	—	—	—	—	—	231,831	—	159	—	—	159
Stock-based compensation	—	—	—	—	—	—	—	—	499	—	—	499
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, net of cost of \$9,422	—	—	—	—	—	—	6,555,000	—	88,903	—	—	88,903
Issuance of Series C Preferred Stock, net of cost of \$24	—	—	—	—	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

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

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

	Years Ended December 31,	
	2018	2017
Cash flows from operating activities:		
Net loss	\$ (60,080)	\$ (26,554)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	320	225
Amortization of short-term investments	(218)	—
Amortization of debt issuance costs	560	—
Stock-based compensation	1,728	499
Change in fair value of warrants	(196)	46
Changes in operating assets and liabilities:		
Accounts receivable	(1,670)	(1,098)
Prepaid expenses and other current assets	(1,588)	(5)
Other assets	62	(111)
Accounts payable	(1,110)	661
Accrued expenses	5,630	1,703
Deferred grant awards	(2)	(29)
Deferred rent	285	—
Net cash used in operating activities	<u>(56,279)</u>	<u>(24,663)</u>
Cash flows from investing activities:		
Purchases of property and equipment	(1,510)	(700)
Purchases of short-term investments	(68,851)	—
Sales and maturities of short-term investments	2,100	—
Net cash used in investing activities	<u>(68,261)</u>	<u>(700)</u>
Cash flows from financing activities:		
Proceeds from Initial Public Offering	98,325	—
Payments for Initial Public Offering costs	(9,422)	—
Proceeds from sale of Series C Preferred Stock	4,438	35,475
Payments of Series C Preferred Stock offering costs	(24)	(495)
Proceeds from issuance of long-term debt	35,000	—
Payments of debt issuance costs	(333)	—
Proceeds from exercise of stock awards	227	159
Net cash provided by financing activities	<u>128,211</u>	<u>35,139</u>
Increase in cash and cash equivalents	3,671	9,776
Cash and cash equivalents, beginning of period	42,045	32,269
Cash and cash equivalents, end of period	<u>\$ 45,716</u>	<u>\$ 42,045</u>
Supplemental schedule of cash flow information:		
Cash paid for interest	<u>\$ 1,711</u>	<u>\$ 2</u>
Supplemental schedule of non-cash investing and financing activities:		
Allocation of debt costs to warrants	<u>\$ 1,012</u>	<u>\$ —</u>
Accrued debt issuance costs	<u>\$ 2,325</u>	<u>\$ —</u>
Vesting of early exercised awards	<u>\$ 169</u>	<u>\$ —</u>

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

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

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.

Basis of presentation

The financial statements are prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP").

Since its inception, the Company has devoted substantially all of its efforts to research and development, regulatory and technical activities. The Company has financed its operations through the issuance of common stock in its June 2018 initial public offering ("IPO"), issuance of convertible preferred stock and other equity instruments, issuance of debt, and grant funding from the National Institutes of Health ("NIH") and other philanthropic organizations.

The Company has not generated any revenue from product sales. The Company has incurred operating losses since inception and has an accumulated deficit of \$120.7 million as of December 31, 2018. The Company expects to continue to incur net losses for the next several years. Based on the Company's current operating plans and existing working capital at December 31, 2018, 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.

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 Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("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, contingent liabilities and expenses included in the financial statements and accompanying notes. Actual results could differ from those estimates.

Grant income

The Company has received several grants from the NIH and other philanthropic organizations for certain research and development projects the Company 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 also has grants where cash is received upfront. The Company defers the recognition of these awards until the research and development expenses are incurred.

Revenue

The Company recognizes revenue when persuasive evidence of an arrangement exists, the related services have been performed, the price is fixed and determinable and collectability is reasonably assured. The Company generates revenue through the performance of research and development activities on behalf of others.

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

Segment reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker in making decisions regarding resource allocation and assessing performance. The Company's chief executive officer uses summary financial information in determining how to allocate resources and assess performance. The Company has determined that it operates in one segment and all of the Company's assets are located 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.

Concentrations of risk

The Company has no off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements. Bank deposits are held by financial institutions, and these deposits may exceed insured limits. The Company is exposed to credit risk in the event of default by the financial institution holding our cash and cash equivalents and issuers of investments that are recorded on our balance sheets. The Company mitigates its risk by investing in high-grade instruments and limiting the concentration in any one issuer, which limits exposure.

The Company is dependent on several key suppliers and third-party manufacturers. A failure or disruption by one of the Company's key suppliers or third-party manufacturers may have a material impact to its planned operations.

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.

Short-term investments

The Company classifies its debt securities as short-term investments and available-for-sale securities. These short-term investments are classified as short-term on the balance sheets as they 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 us to record an impairment charge in the period any such determination is made. The Company considers factors such as the duration, severity and the 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 Loan and Security Agreement approximates fair value due to the variable interest rate on the debt. Items measured at fair value on a recurring basis include the Company's short-term investments and warrants.

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

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 impairment charges of \$0 and \$48,000 for the years ended December 31, 2018 and 2017, respectively. The impairment charge in 2017 was related to equipment that is no longer used in the Company's manufacturing of the Gvoke HypoPen due to process and formulation improvements.

Deferred rent

Certain of the Company's lease agreements provide for scheduled rent increases during the lease term and for rental payments commencing at a date after the initial occupancy date. Provisions are made for the excess of operating lease rentals, computed on a straight-line basis throughout the lease term, over cash rentals paid.

Debt issuance costs

Long-term debt is accounted for at amortized cost. 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.

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 or the services are performed.

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 to employees, including grants of employee stock options, to be recognized in

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

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, risk-free interest rates and expected dividend yields of the common stock. The Company recognizes stock-based compensation expense, net of estimated forfeitures, equal to the grant date fair value of stock options on a straight-line basis over the requisite service period. Restricted stock awards are valued based on the fair market value of the Company's common stock on the date they were granted. Restricted stock that vests and stock options that are authorized are issued out of authorized available shares.

The Company accounts for stock-based awards issued to non-employees based on the grant date fair value of such awards and recognizes compensation expense as the services are completed over the vesting period of the award.

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, 2018 and 2017, the Company did not accrue any interest or penalties on uncertain tax positions.

Impacts of the Tax Cuts and Jobs Act

On December 22, 2017, the Tax Cuts and Jobs Act (H.R. 1) (the "Tax Act") was signed into law. The Tax Act contains significant changes to corporate taxation, including (i) the reduction of the corporate income tax rate to 21%, (ii) the acceleration of expensing for certain business assets, (iii) the one-time transition tax related to the transition of U.S. international tax from a worldwide tax system to a territorial tax system, (iv) the repeal of the domestic production deduction, (v) additional limitations on the deductibility of interest expense, and (vi) expanded limitations on executive compensation. On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provides guidance on accounting for the tax effects of the Tax Act. SAB 118 provided a measurement period that should not extend beyond one year from the date of enactment for companies to complete the accounting under ASC 740, *Income Taxes*. The key impacts of the Tax Act on the Company's financial statements for the year ended December 31, 2017 were the remeasurement of deferred tax balances to the new corporate tax rate. The provisional amount determined, and recorded as of December 31, 2017, for the remeasurement of its deferred tax balances resulted in a net reduction in deferred tax assets of \$7.5 million and a corresponding reduction in the valuation allowance of \$7.5 million.

The SAB 118 measurement period ended as of December 22, 2018. The Company has obtained, prepared and analyzed the information needed to complete the accounting requirements under ASC 740. There were no material changes to the provisional amounts recorded as of December 31, 2018.

Equity financing costs

The Company capitalizes costs that are directly associated with in-process equity financings until such financings are consummated, at which time such costs are recorded in the additional paid in capital line on the balance sheet against the gross proceeds of the equity financings. The Company recognized \$9.4 million of direct costs associated with the IPO in additional paid in capital for the year ended December 31, 2018. As of December 31, 2018 and 2017, the Company did not have any deferred costs related to in-process equity financings.

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

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 the preferred stock, warrants, and stock awards 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 (shown below in common stock equivalent shares) were excluded from the computation of diluted weighted average common shares outstanding due to their anti-dilutive effect:

	December 31,	
	2018	2017
Convertible preferred stock	—	11,439,752
Vested and unvested stock options	3,130,700	1,979,306
Warrants	102,647	19,931
	3,233,347	13,438,989

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. Other comprehensive loss includes net loss and unrealized losses on debt securities classified as available-for-sale investments.

New accounting pronouncements

Recently adopted accounting pronouncements

In March 2016, the FASB issued ASU 2016-09, *Compensation—Stock Compensation (Topic 718): Improvements to Employee Share Based Payment Accounting* (“ASU 2016-09”), as part of the FASB simplification initiative. The new standard provides for changes to accounting for stock compensation including 1) excess tax benefits and tax deficiencies related to share-based payment awards being recognized as income tax expense in the reporting period in which they occur; 2) excess tax benefits being classified as an operating activity in the statement of cash flow; 3) the option to elect to estimate forfeitures or account for them when they occur; and 4) increased tax withholding requirements threshold to qualify for equity classification. As an emerging growth company, ASU 2016-09 was effective for the Company starting with the quarter ending March 31, 2018. Early adoption was permitted. The Company adopted this standard on January 1, 2018, and it did not have an impact on the financial statements.

Recently issued accounting pronouncements

In February 2016, the FASB issued ASU, No. 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 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. As an emerging growth company, ASU 2016-02 will be effective for the Company starting with the quarter ending March 31, 2020. Early adoption is permitted. 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 to report assets and liabilities related to these leases on the financial statements that have not been previously reported once adopted.

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

Note 3. Property and Equipment

Property and equipment consisted of the following:

(in thousands)	December 31, 2018	December 31, 2017
Lab equipment	\$ 1,658	\$ 860
Furniture and fixtures	541	128
Computer equipment	87	100
Office equipment	109	78
Software	110	52
Leasehold improvements	180	10
	<u>2,685</u>	<u>1,228</u>
Less: accumulated depreciation and amortization	(651)	(440)
Property and equipment, net	<u>\$ 2,034</u>	<u>\$ 788</u>

Depreciation and amortization expense relating to property and equipment was \$320,000 and \$177,000 for the years ended December 31, 2018 and 2017, respectively.

Note 4. Accrued Expenses

Accrued expenses consisted of the following:

(in thousands)	December 31, 2018	December 31, 2017
Accrued employee costs	\$ 4,326	\$ 1,581
Accrued research and development costs	2,221	566
Accrued other costs	1,667	410
Accrued expenses	<u>\$ 8,214</u>	<u>\$ 2,557</u>

Note 5. Long-term Debt

Senior Secured Loan Facility

In February 2018, the Company entered into the Loan and Security Agreement that provides 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 ("Term A Loan"). The second tranche was \$15.0 million and was drawn down in September 2018 ("Term B Loan"). The third tranche is \$10.0 million and is available beginning upon approval of the Company's Gvoke HypoPen New Drug Application ("NDA") by the U.S. Food & Drug Administration ("FDA") until the earlier of September 30, 2019 or the 30th day following NDA approval by the FDA.

The interest rate under the Loan and Security Agreement is the thirty-day U.S. LIBOR rate plus 6.75%, which was approximately 9.10% as of December 31, 2018. Payments on the Loan and Security Agreement are interest only for the first 24 months, which can be extended by an additional twelve months if the third tranche is drawn. The total term of the loan is fifty-nine months, and the principal payments will begin in 24 months from the beginning of the term or, should the third tranche be drawn, 36 months from the beginning of the term.

Pursuant to the Loan and Security Agreement, the Company provided a first priority security interest in all existing and future-acquired assets, excluding intellectual property and certain other assets, owned by the Company. The Loan and Security Agreement contains a negative pledge on intellectual property owned by the Company. The Company also issued warrants to the Lenders to purchase common stock, which is further discussed in Note 8, "Warrants", of the notes to financial statements.

The Loan and Security 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, 2020, the Company is subject to a prepayment penalty equal to 1.50% of the principal amount being prepaid. In the event the Company draws down the third tranche, the period subject to the 1.50% prepayment

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

penalty is extended to April 1, 2021. No prepayment fee exists for prepayments made after April 1, 2020, or April 1, 2021 in the event the third tranche is issued. A final payment fee of 6.5% multiplied by the original principal amount of each tranche drawn is due upon the earlier to occur of the maturity date of the Loan and Security Agreement, the acceleration of the Loan and Security Agreement or prepayment of such borrowings. The Loan and Security Agreement includes a non-utilization fee of 2.0% multiplied by the principal amount of tranche three payable to Lenders in October 2019, if the Company elects not to draw the third tranche.

The Loan and Security Agreement also contains customary indemnification obligations and customary events of default, including, among other things, failure to fulfill certain obligations under the Loan and Security Agreement and the occurrence of a material adverse change in the Company's business, operations or condition, a material impairment of the prospect of repayment of any portion of the loan, or a material impairment in the perfection or priority of the Lenders' lien in the collateral or in the value of such collateral. In the event of default under the Loan and Security Agreement, the Company would be required to pay interest on principal and all other due and unpaid obligations at the current rate in effect plus 5%. All such interest would be payable on demand and in cash. Further, the Lenders would be entitled to exercise their remedies thereunder, including the right to accelerate the debt, upon which the Company may be required to repay all amounts then outstanding under the Loan and Security Agreement.

The Loan and Security Agreement includes certain restrictions on, among other things, the Company's ability to incur additional indebtedness, change the name or location of the business, merge with or acquire other entities, pay dividends or make other distributions to holders of the Company's capital stock, make certain investments, engage in transactions with affiliates, create liens, open new deposit accounts, sell assets or pay subordinated debt.

The components of debt are as follows:

(in thousands)	December 31, 2018	December 31, 2017
Term A Loan	\$ 20,000	\$ —
Term B Loan	15,000	—
Less unamortized deferred costs	(3,110)	—
Long-term debt	<u>\$ 31,890</u>	<u>\$ —</u>

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

2018	\$ —
2019	—
2020	9,000
2021	12,000
2022	12,000
2023	2,000
	<u>\$ 35,000</u>

The Company incurred total debt issuance costs of \$3.7 million, 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. For the years 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 6. Reverse Stock Split and Initial Public Offering

On June 8, 2018, the Company effectuated a 1-for-1.78112 reverse stock split of its outstanding common stock, which was approved by the Company's board of directors on May 22, 2018 and by the Company's stockholders on June 8, 2018. The reverse stock split resulted in an adjustment to the preferred stock conversion prices to reflect a proportional decrease in the number of shares of common stock to be issued upon conversion. The accompanying financial statements and notes to financial statements give retroactive effect to the reverse stock split for all periods presented. The shares of common stock retained a par value of \$0.0001 per share. Accordingly, the stockholders' equity (deficit) reflects the reverse stock split by reclassifying from common stock to additional paid in capital an amount equal to the par value of the decreased shares resulting from the reverse stock split.

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

On June 25, 2018, the Company closed the 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 a public offering 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 offering were \$88.9 million after deducting underwriting discounts and commissions as well as other offering 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.

Note 7. 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. No such dividends were declared by the Company's 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 8. Warrants

In 2014 the Company issued 19,931 warrants ("2014 Warrants") to certain investors. The 2014 Warrants allow each holder to purchase one share of common stock for \$5.912. There have been 11,296 2014 Warrants exercised, and 8,635 warrants remain outstanding as of December 31, 2018.

As part of the Loan and Security Agreement discussed in Note 5, "Long-term Debt", in the notes to financial statements, the Lenders receive warrants equal to 3.0% of the principal borrowing amounts 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 ("Term A Warrants") upon the drawdown of the Term A Loan in February 2018, and the Company issued 40,292 warrants ("Term B Warrants") upon the drawdown of the 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, 2018, respectively.

Because the warrants are a freestanding instrument, indexed to the Company's stock, they do not meet the criteria for equity classification. Therefore, warrants are liability classified and subject to remeasurement at each reporting period until they are exercised, expired, or otherwise settled. The initial fair value of the warrant liability is recorded with a corresponding offset to deferred debt costs which is a reduction to the notional value of the debt.

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. The Company recognized a loss of \$(46,000) upon the change in fair value of the 2014 Warrants during the year ended December 31, 2017.

As of December 31, 2018, the following warrants were outstanding:

	<u>Outstanding Warrants</u>	<u>Exercise Price per Warrant</u>	<u>Expiration Date</u>
2014 Warrants	8,635	\$5.912	August 2020
Term A Warrants	53,720	\$11.169	February 2025
Term B Warrants	40,292	\$11.169	September 2025
	<u>102,647</u>		

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

Note 9. 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 new lease for office space in Chicago, Illinois. In the fourth quarter of 2018, the Company signed an amendment to this lease to occupy additional space and expects to relocate from its existing premises to this additional space in March 2019.

Future minimum lease payments under operating leases at December 31, 2018 are as follows:

(in thousands)

2019	\$	891
2020		1,580
2021		2,218
2022		2,273
2023		1,756
Thereafter		9,848
Total minimum lease payments	\$	<u>18,566</u>

Total rent expense under these operating leases was approximately \$1.3 million and \$0.5 million for the years ended December 31, 2018 and 2017, respectively.

As of December 31, 2018, we had unused letters of credit of \$143,000 that are used 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, 2018, management was not aware of any existing, pending or threatened legal actions that would have a material impact on the financial position or results of operations of the Company.

Note 10. Stock Compensation Plan

In 2011 the Company adopted the 2011 Stock Option Issuance Plan ("2011 Plan") and subsequently amended it to authorize the Board of Directors to issue up to 4,714,982 incentive grant and non-statutory awards.

The 2018 Stock Option and Incentive Plan ("2018 Plan") was adopted by our Board of Directors in April 2018 and approved by our stockholders in June 2018 to award up to 1,822,000 shares of our 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 our Board of Directors determined not to make additional awards under the 2011 Plan following the closing of our IPO, which occurred in June 2018. The 2018 Plan allows the compensation committee to make equity-based and cash-based incentive awards to our officers, employees, directors and other key persons (including consultants). As of December 31, 2018, there were 1,120,937 awards available for future issuance.

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 years 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 life 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

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

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 option exercises and 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,	
	2018	2017
Expected term (years)	6.0	6.1
Risk-free interest rate	2.48 %	2.06 %
Expected volatility	56.84 %	61.10 %
Expected dividends	—	—

Stock option activity for employee awards for the year ended December 31, 2018 was as follows:

	UNITS	WEIGHTED AVERAGE EXERCISE PRICE	WEIGHTED AVERAGE CONTRACTUAL LIFE (YEARS)
Outstanding - January 1, 2018	1,946,230	\$ 1.66	8.70
Issued	1,604,804	14.14	
Exercised	(225,986)	1.46	
Forfeited	(197,740)	1.89	
Outstanding - December 31, 2018	3,127,308	\$ 8.06	8.69
Exercisable - December 31, 2018	2,329,151	\$ 4.44	8.67
Vested and expected to vest at December 31, 2018	2,939,669	\$ 8.00	7.74

The weighted average fair value of awards granted during the year ended December 31, 2018 was \$8.17 per share. The total intrinsic value of options exercised during the year ended December 31, 2018 was \$2.4 million. The aggregate intrinsic value of awards vested and expected to vest as of December 31, 2018 was \$28.3 million.

The Company also granted stock options to non-employees. These awards are marked to fair value at the end of each reporting period until they vest. Stock option activity for these awards for the year ended December 31, 2018 was as follows:

	UNITS	WEIGHTED AVERAGE EXERCISE PRICE	WEIGHTED AVERAGE CONTRACTUAL LIFE (YEARS)
Outstanding - January 1, 2018	33,125	\$ 1.91	6.75
Issued	0	—	
Exercised	(22,996)	2.16	
Forfeited	(6,737)	0.82	
Outstanding - December 31, 2018	3,392	\$ 1.55	2.00
Exercisable - December 31, 2018	0	\$ 0.00	0.00
Vested and expected to vest at December 31, 2018	3,392	\$ 1.55	2.00

The aggregate intrinsic value of awards vested and expected to vest at December 31, 2018 was \$52,000. The aggregate intrinsic value of awards exercisable as of December 31, 2018 was \$0. The company recognized expense associated with these awards of \$114,000 and \$35,000 for the years ended December 31, 2018 and 2017, respectively.

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

The following table summarizes the reporting of total stock-based compensation expense resulting from employee and non-employee stock options:

(in thousands)	Years Ended December 31,	
	2018	2017
Research and development	\$ 518	\$ 62
Selling, general and administrative	1,210	437
Total stock-based compensation expense	<u>\$ 1,728</u>	<u>\$ 499</u>

At December 31, 2018, there was a total of \$7.3 million of unrecognized compensation expense that is expected to be recognized over a weighted average period of 1.83 years.

Note 11. 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 required 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, 2018 and 2017:

(in thousands)	Total as of December 31,			
	2018	Level 1	Level 2	Level 3
<i>Current Assets</i>				
Cash and cash equivalents:				
Money market funds	\$ 45,716	\$ 45,716	\$ —	\$ —
Short-term 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 short-term investments	<u>\$ 66,917</u>	<u>\$ 39,920</u>	<u>\$ 26,997</u>	<u>\$ —</u>
<i>Other Current Liabilities</i>				
Warrant liabilities	<u>\$ 860</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 860</u>

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

(in thousands)	Total as of December 31, 2017	Level 1	Level 2	Level 3
<i>Current Assets</i>				
Money market funds ^(a)	\$ 39,124	\$ 39,124	\$ —	\$ —
<i>Other current liabilities</i>				
Warrant liabilities	\$ 93	\$ —	\$ —	\$ 93

(a) The money market funds noted above are included in cash and cash equivalents.

There were no investments in commercial paper or short-term investments as of December 31, 2017.

The fair value of the Company's warrant liabilities at inception and for subsequent mark-to-market fair value measurements is based on management's valuation model and expected methods and timing of settlement. These estimates are prepared using models that consider various inputs including: (a) the Company's estimated future cash flows, (b) time value, (c) current market conditions, and (d) other relevant economic measures.

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)		\$	93
Balance at December 31, 2017		\$	93
Fair value of Term A Warrants issued under the Loan and Security Agreement			326
Fair value of Term B Warrants issued under the Loan and Security Agreement			686
Exercise of warrants			(49)
Change in fair value of warrants			(196)
Balance at December 31, 2018		\$	860

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

Note 12. Short-Term Investments

The Company classifies its debt securities as short-term investments and available-for-sale. Debt securities are comprised of highly liquid investments with minimum "A" rated securities and, as of December 31, 2018, consist of U.S. Treasury and agency bonds and corporate entity commercial paper and securities with maturities of more than three months but less than one year at the date of purchase. Debt securities as of December 31, 2018 have an average maturity of 0.40 years. The debt securities are reported at fair value with unrealized gains or losses recorded in accumulated other comprehensive loss in the balance sheets. Any differences between the cost and fair value of investments are represented by unrealized gains or losses. Refer to Note 11, "Fair Value Measurements", of the notes to financial statements for information related to the fair value measurements and valuation methods utilized.

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

The following table represents the Company's available for sale short-term investments by major security type as of December 31, 2018:

(in thousands)	Amortized Cost	Gross Unrealized Losses	Total Fair Value
Short-term 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 short-term investments	<u>\$ 66,969</u>	<u>\$ (52)</u>	<u>\$ 66,917</u>

There were no investments in short-term securities as of December 31, 2017.

The Company reviews available-for-sale investments for other-than-temporary impairment loss quarterly. The Company considers factors such as the duration, severity and the 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 quarter ended December 31, 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 13. 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. For the years ended December 31, 2018 and 2017, the Company has not made any matching contributions to the plan.

Note 14. Income Taxes

Due to reported losses, the Company recorded no income tax expense for the years ended December 31, 2018 and 2017. A reconciliation of the expected income tax benefit computed using the federal statutory income tax rate of 21% to the Company's effective income tax rate is as follows:

(in thousands)	December 31,	
	2018	2017
Federal tax benefit at statutory rate	\$ (12,617)	\$ (9,028)
State tax benefit, net of federal benefit	(1,842)	—
Impact of rate change	—	7,478
Research and development and orphan drug credits	(2,279)	(517)
Uncertain tax positions	603	—
Permanent adjustments to expenses	45	76
Stock compensation	76	42
Prior year adjustment	(2,470)	(100)
Rate impact of deferred tax balance	(63)	—
Other	9	—
Changes in valuation allowance	18,538	2,049
Total income taxes	<u>\$ —</u>	<u>\$ —</u>

During the years ended December 31, 2018 and 2017, the Company had no interest and penalties related to income taxes.

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

Deferred income taxes reflect the net tax effects of temporary difference 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, 2018, we have evaluated the need to maintain a valuation allowance for deferred tax assets based on our assessment of whether it is more likely than not that deferred tax benefits will be realized through the generation of future taxable income. Appropriate consideration is given to all available evidence, both positive and negative, in assessing the need for a valuation allowance.

Significant components of the Company's deferred tax assets and liabilities are as follows:

(in thousands)	December 31,	
	2018	2017
Deferred tax assets:		
Net operating losses	\$ 25,372	\$ 11,715
Federal research and orphan drug credits	5,426	2,045
Stock compensation	267	49
Other temporary differences	1,679	349
Valuation allowance	(32,662)	(14,124)
Total assets	82	34
Deferred tax liabilities:		
Fixed and intangible assets	(82)	(34)
Total liabilities	(82)	(34)
Net deferred tax assets	\$ —	\$ —

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. As of December 31, 2017, the Company had federal net operating loss carryforwards of \$55.8 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, 2018, the Company had \$5.8 million and \$0.2 million of federal and state income tax credits, respectively, to reduce future tax liabilities. As of December 31, 2017, the Company had \$2.0 million of federal income tax credits. 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 U.S. federal 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, 2018 and 2017 is as follows (in thousands):

Valuation allowance at December 31, 2016	\$ (12,075)
Increase for 2017 activity	(2,049)
Valuation allowance at December 31, 2017	(14,124)
Increase for 2018 activity	(18,538)
Valuation allowance at December 31, 2018	\$ (32,662)

XERIS PHARMACEUTICALS, INC.
Notes to Financial Statements
December 31, 2018

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, 2018 and 2017, excluding interest and penalties, consisted of the following:

(in thousands)	December 31,	
	2018	2017
Beginning balance - uncertain tax positions	\$ —	\$ —
Increases related to tax positions taken during the current year	228	—
Increases related to tax positions taken during the prior year	375	—
Ending balance - uncertain tax positions	\$ 603	\$ —

For the year ended December 31, 2018, 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 sheets, uncertain tax positions of \$0.6 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, 2018 and 2017.

Impacts of the Tax Cuts and Jobs Act

On December 22, 2017, the Tax Cuts and Jobs Act (H.R. 1) (the "Tax Act") was signed into law. The Tax Act contains significant changes to corporate taxation, including (i) the reduction of the corporate income tax rate to 21%, (ii) the acceleration of expensing for certain business assets, (iii) the one-time transition tax related to the transition of U.S. international tax from a worldwide tax system to a territorial tax system, (iv) the repeal of the domestic production deduction, (v) additional limitations on the deductibility of interest expense, and (vi) expanded limitations on executive compensation. On December 22, 2017, the SEC staff issued SAB 118, which provides guidance on accounting for the tax effects of the Tax Act. SAB 118 provided a measurement period that should not extend beyond one year from the date of enactment for companies to complete the accounting under ASC 740. The key impacts of the Tax Act on the Company's financial statements for the year ended December 31, 2017 were the remeasurement of deferred tax balances to the new corporate tax rate. The provisional amount determined, and recorded, for the remeasurement of its deferred tax balances resulted in a net reduction in deferred tax assets of \$7.5 million and a corresponding reduction in the valuation allowance of \$7.5 million.

The SAB 118 measurement period ended as of December 22, 2018. The Company has obtained, prepared and analyzed the information needed to complete the accounting requirements under ASC 740. There were no material changes to the provisional amounts recorded as of December 31, 2018.

Note 15. Related Party Transactions

There were no related party transactions for the year ended December 31, 2018. During the year ended December 31, 2017 the Company paid a spouse of an officer \$37,000 to help with the development of the Company's website.

Note 16. Subsequent Event

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 sold pursuant to a partial exercise of the underwriters' option to purchase up to an additional 882,000 shares of common stock. Net proceeds from the offering were approximately \$55.6 million after deducting underwriting discounts and commissions as well as other offering expenses.

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

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, the Company conducted an evaluation 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 their evaluation of these disclosure controls and procedures, the principal executive officer and principal financial officer concluded that the disclosure controls and procedures were effective as of December 31, 2018 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.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the three months ended December 31, 2018 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, 2018, or the Proxy Statement, 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 the Proxy Statement 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 the Proxy Statement 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 the Proxy Statement 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 the Proxy Statement 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

XERIS PHARMACEUTICALS, INC.
FORM 10-K

INDEX TO EXHIBITS

<u>Exhibit No.</u>	<u>Description</u>
3.1	<u>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)</u>
3.2	<u>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)</u>
4.1	<u>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)</u>
4.2	<u>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)</u>
10.1#	<u>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)</u>
10.2#	<u>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)</u>
10.3#	<u>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)</u>
10.4#	<u>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)</u>
10.5#	<u>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)</u>
10.6	<u>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)</u>
10.7#	<u>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)</u>
10.8#	<u>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)</u>
10.9#	<u>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)</u>
10.10#	<u>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)</u>
10.11#	<u>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)</u>
10.12#	<u>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)</u>
10.13#	<u>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)</u>

<u>Exhibit No.</u>	<u>Description</u>
10.14+	<u>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)</u>
10.15+	<u>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)</u>
10.16+	<u>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)</u>
10.17+	<u>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)</u>
10.18	<u>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)</u>
10.19+	<u>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)</u>
10.20#	<u>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)</u>
10.21+	<u>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)</u>
10.22#	<u>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)</u>
10.23	<u>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)</u>
23.1*	<u>Consent of Independent Registered Public Accounting Firm</u>
31.1*	<u>Certification of Principal Executive Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended</u>
31.2*	<u>Certification of Principal Financial Officer pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended</u>
32.1*	<u>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</u>
32.2*	<u>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</u>
101	The following materials from Xeris Pharmaceuticals, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2018, formatted in XBRL (Extensible Business Reporting Language): (i) the Balance Sheets, (ii) the Statements of Operations and Comprehensive Loss, (iii) the Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit), (iv) the Statements of Cash Flows and (v) Notes to Financial Statements

* 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 6, 2019

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 6th day of March, 2019.

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/ John Schmid

John Schmid

Director

/s/ BJ Bormann

BJ Bormann

Director

/s/ Jeffrey Sherman

Jeffrey Sherman

Director

/s/ Jonathan Rigby

Jonathan Rigby

Director

/s/ Marla Persky

Marla Persky

Director

/s/ Dawn Halkuff

Dawn Halkuff

Director

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors
Xeris Pharmaceuticals, Inc.:

We consent to the incorporation by reference in the Registration Statements on Form S-8 (File Nos. 333-229587 and 333-225802) of Xeris Pharmaceuticals, Inc. of our report dated March 6, 2019, with respect to the balance sheets of Xeris Pharmaceuticals, Inc. as of December 31, 2018 and 2017, the related 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, 2018, and the related notes, which report appears in the December 31, 2018 annual report on Form 10-K of Xeris Pharmaceuticals, Inc.

/s/ KPMG LLP

Chicago, Illinois
March 6, 2019

**CERTIFICATION PURSUANT TO RULE 13a-14(a) OR 15d-14(a) OF
THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, Paul R. Edick, certify that:

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

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

- a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- b) Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313;
- c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

- a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 6, 2019

By: /s/ Paul R. Edick

Paul R. Edick
President, Chief
Executive Officer and
Chairman
(Principal Executive
Officer)

**CERTIFICATION PURSUANT TO RULE 13a-14(a) OR 15d-14(a) OF
THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, Barry M. Deutsch, certify that:

1. I have reviewed this annual report on Form 10-K of Xeris Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b) Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313;
 - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 6, 2019

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

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Xeris Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ended December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Paul R. Edick, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material aspects, the financial condition and results of operations of the Company.

Date: March 6, 2019

By: /s/ Paul R. Edick
Paul R. Edick
President, Chief
Executive Officer and
Chairman
(Principal Executive
Officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Xeris Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ended December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Barry M. Deutsch, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material aspects, the financial condition and results of operations of the Company.

Date: March 6, 2019

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