LEXICON PHARMACEUTICALS, INC.
Form 10-K
March 15, 2019

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K
(Mark
One)

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

For the Fiscal Year 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: 000-30111
Lexicon Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware	76-0474169
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification Number)
8800 Technology Forest Place	(281) 863-3000
The Woodlands, Texas 77381	(Registrant's Telephone Number,
(Address of Principal Executive Offices and Zip Code)	Including Area Code)

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

Title of Each Class	Name of Each Exchange on which Registered
Common Stock, par value $0.001 per share	Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: None
Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act of 1933. Yes o No þ
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934. Yes o No þ
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 þ No o
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 þ No o
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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. þ
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Securities Exchange Act of

1934. (check one): Large accelerated filer o Accelerated filer þ Non-accelerated filer o Smaller reporting company o Emerging growth company o

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 Securities Exchange Act of 1934. o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes o No þ

The aggregate market value of voting stock held by non-affiliates of the registrant as of the last day of the registrant's most recently completed second quarter was approximately $491.5 million, based on the closing price of the common stock on the Nasdaq Global Select Market on June 30, 2018 of $12.00 per share. For purposes of the preceding sentence only, our directors, executive officers and controlling stockholders are assumed to be affiliates. As of March 8, 2019, 106,271,927 shares of common stock were outstanding.

Documents Incorporated by Reference

Certain sections of the registrant's definitive proxy statement relating to the registrant's 2019 annual meeting of stockholders, which proxy statement will be filed under the Securities Exchange Act of 1934 within 120 days of the end of the registrant's fiscal year ended December 31, 2018, are incorporated by reference into Part III of this annual report on Form 10-K.

Lexicon Pharmaceuticals, Inc.
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In this annual report on Form 10-K, "Lexicon Pharmaceuticals," "Lexicon," "we," "us" and "our" refer to Lexicon Pharmaceuticals, Inc. and its subsidiaries.

This annual report on Form 10-K contains forward-looking statements. These statements relate to future events or our future financial performance. We have attempted to identify forward-looking statements by terminology including "anticipate," "believe," "can," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "shou negative of these terms or other comparable terminology. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined under "Item 1A. Risk Factors," that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. We are not under any duty to update any of the forward-looking statements after the date of this annual report on Form 10-K to conform these statements to actual results, unless required by law.

PART I

Item 1. Business

Overview

Lexicon Pharmaceuticals is a biopharmaceutical company with a mission of pioneering medicines that transform patients' lives. We are devoting most of our resources to the commercialization or development of our four most advanced drug programs:

- We are commercializing XERMELO® (telotristat ethyl), an orally-delivered small molecule drug, in the United States for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog, or SSA, therapy in adults inadequately controlled by SSA therapy. We have granted Ipsen Pharma SAS, or Ipsen, an exclusive, royalty-bearing right to commercialize XERMELO outside of the United States and Japan. Ipsen is commercializing XERMELO in multiple countries, including the United Kingdom and Germany, and is preparing to commercialize XERMELO in certain additional countries. We are also developing telotristat ethyl as a treatment for biliary tract cancer and are conducting a Phase 2a clinical trial of telotristat ethyl in biliary tract cancer patients.
- We are developing sotagliflozin, an orally-delivered small molecule drug candidate, as a treatment for type 1 and type 2 diabetes. We have granted Sanofi-Aventis Deutschland GmbH, or Sanofi, an exclusive, worldwide (excluding Japan), royalty-bearing right to develop, manufacture and commercialize sotagliflozin. We have reported positive data from two pivotal Phase 3 clinical trials and a third Phase 3 clinical trial of sotagliflozin in type 1 diabetes patients. Sanofi has submitted applications for regulatory approval to market sotagliflozin for type 1 diabetes in the United States, the European Union and certain additional countries, and we and Sanofi are preparing for the commercial launch of sotagliflozin for the treatment of type 1 diabetes, if approved. Sanofi is also conducting a comprehensive Phase 3 development program for sotagliflozin in type 2 diabetes.
- We are developing LX9211, an orally-delivered small molecule drug candidate, as a treatment for neuropathic pain. We have reported positive top-line data from an initial Phase 1a clinical trial of LX9211 and are conducting a Phase 1b clinical trial of LX9211.
- We are developing LX2761, an orally-delivered small molecule drug candidate, as a treatment for diabetes. We have reported top-line data from two Phase 1 clinical trials of LX2761 and are presently evaluating the further clinical development of LX2761. We have granted Sanofi certain rights of first negotiation with respect to the future development and commercialization of LX2761.

Compounds from our most advanced drug programs, as well as compounds from a number of additional drug discovery and development programs that we have advanced into various stages of clinical and preclinical development, originated from our own internal drug discovery efforts. These efforts were driven by a systematic, target biology-driven approach in which we used gene knockout technologies and an integrated platform of advanced medical technologies to systematically study the physiological and behavioral functions of almost 5,000 genes in mice and assessed the utility of the proteins encoded by the corresponding human genes as potential drug targets. We have identified and validated in living animals, or in vivo, more than 100 targets with promising profiles for drug discovery.

We are working both independently and through strategic collaborations and alliances with third parties to capitalize on our drug target discoveries and drug discovery and development programs. We seek to retain exclusive or co-exclusive rights to the benefits of certain drug discovery and development programs by developing and commercializing drug candidates from those programs internally, particularly in the United States for indications treated by specialist physicians. We seek to collaborate with other pharmaceutical and biotechnology companies, such as Ipsen and Sanofi, with respect to drug discovery or the development and commercialization of certain of our drug candidates, particularly with respect to commercialization in territories outside the United States, commercialization in the United States for indications treated by primary care physicians, or when the collaboration may otherwise provide us with access to expertise and resources that we do not possess internally or are complementary to our own.

Lexicon Pharmaceuticals was incorporated in Delaware in July 1995, and commenced operations in September 1995. Our corporate headquarters are located at 8800 Technology Forest Place, The Woodlands, Texas 77381, and our telephone number is (281) 863-3000.

Our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 are made available

free of charge on our corporate website located at www.lexpharma.com as soon as reasonably practicable after the filing of those reports with the Securities and Exchange Commission. Information found on our website should not be considered part of this annual report on Form 10-K.

Drug Programs

We are devoting most of our resources to the commercialization or development of our four most advanced drug programs: XERMELO (telotristat ethyl), which we are commercializing for carcinoid syndrome diarrhea and developing for biliary tract cancer; sotagliflozin, which we are developing for type 1 and type 2 diabetes; LX9211, which we are developing for neuropathic pain; and LX2761, which we are developing for diabetes. We have also advanced a number of additional compounds into various stages of clinical and preclinical development.

XERMELO (telotristat ethyl)

We commercially launched XERMELO, an orally-delivered small molecule compound, following regulatory approval in the United States in February 2017 for the treatment of carcinoid syndrome diarrhea in combination with SSA therapy in adults inadequately controlled by SSA therapy. XERMELO was discovered by our scientists and inhibits tryptophan hydroxylase, or TPH, the rate-limiting enzyme for serotonin production found primarily in enterochromaffin cells of the gastrointestinal tract. Carcinoid syndrome is characterized by frequent and debilitating diarrhea and can result when these cells become cancerous and metastisize to the liver or other organs, where they overproduce serotonin. The recommended dose of XERMELO is 250mg three times daily, and the full prescribing information for XERMELO includes certain warnings and precautions relating to constipation.

We have entered into a license and collaboration agreement under which we granted Ipsen an exclusive, royalty-bearing right and license to commercialize XERMELO outside of the United States and Japan. Ipsen has received approval from the European Commission to market XERMELO for the treatment of carcinoid syndrome diarrhea in all member states of the European Union, Norway and Iceland and from certain other regulatory authorities to market XERMELO in additional countries. Ipsen has commercially launched XERMELO in multiple countries, including the United Kingdom and Germany, and is preparing to commercially launch XERMELO in certain additional countries.

As part of our life cycle management of the program, we are conducting a Phase 2a clinical trial evaluating the safety and tolerability of telotristat ethyl and its effects on biliary tract cancer. The trial is expected to enroll approximately 54 patients with unresectable, locally advanced, recurrent or metastatic biliary tract cancer in an open-label, two-stage study of a 250mg three times daily dose of telotristat ethyl over an initial 7-day treatment period, followed by a 500mg three times daily dose of telotristat ethyl over subsequent 21-day treatment cycles until cessation of treatment for disease progression, toxicity or patient withdrawal. Standard of care, first-line chemotherapy doses of cisplatin and gemcitabine will be administered on days one and eight of each 21-day treatment cycle. The trial is designed to be conducted in two stages, each of which is expected to enroll approximately 27 patients. The primary efficacy endpoint under evaluation is the progression-free survival rate at six months, with secondary endpoints including progression-free survival at 12 months, overall survival rates, disease control rates and weight change.

Sotagliflozin

Sotagliflozin is an orally-delivered small molecule compound that we and Sanofi are developing for the treatment of type 1 and type 2 diabetes mellitus. Sotagliflozin was discovered by our scientists and inhibits both sodium-glucose cotransporter type 2, or SGLT2, a transporter responsible for most of the glucose reabsorption performed by the kidney, and sodium-glucose cotransporter type 1, or SGLT1, a transporter responsible for glucose and galactose absorption in the gastrointestinal tract. Our scientists discovered that mice lacking SGLT1, SGLT2 or both exhibit potent anti-diabetic phenotypes across multiple measures of glucose control and metabolism, and found that

compounds inhibiting both targets had a favorable preclinical profile relative to compounds selective for SGLT2.

We have entered into a collaboration and license agreement with Sanofi under which we granted Sanofi an exclusive, worldwide (excluding Japan), royalty-bearing right and license to develop, manufacture and commercialize sotagliflozin.

Type 1 Diabetes.

We have completed three Phase 3 clinical trials evaluating the safety and tolerability of sotagliflozin and its effects on glycemic parameters associated with type 1 diabetes.

Our pivotal inTandem1 Phase 3 clinical trial enrolled 793 patients with type 1 diabetes in the United States and Canada in a randomized, double-blind, placebo-controlled study of 200mg and 400mg once daily doses of sotagliflozin over a 24-week treatment period, followed by a 28-week extension. Insulin therapy was optimized in patients over a 6-week period prior to dosing. The primary efficacy endpoint under evaluation in the trial was the reduction of hemoglobin A1c, or A1C, versus placebo on optimized insulin treatment at 24 weeks, with secondary endpoints including percentage of patients achieving A1C levels of less than 7% without experiencing an event of severe hypoglycemia or diabetic ketoacidosis, or DKA, change in meal-time, or bolus, insulin use, body weight, fasting plasma glucose and patient-reported assessments. Data from the study showed that patients treated with sotagliflozin experienced statistically significant reductions in A1C from baseline of 0.43% for the 200mg dose ($p<0.001$) and 0.48% for the 400mg dose ($p<0.001$), as compared to a reduction of 0.07% on placebo after 24 weeks of treatment, meeting the study's primary efficacy endpoint at both dose levels. The A1C benefit achieved with sotagliflozin was sustained with statistically significant results over the full 52-week duration of the study for both the 200mg and 400mg doses. Benefits in all secondary efficacy endpoints were observed in both the 200mg and 400mg dose arms compared to placebo, with statistically significant improvements in all secondary efficacy endpoints observed in the 400mg dose arm and in the percentage of patients achieving A1C levels of less than 7% without any severe hypoglycemia or DKA events and weight loss observed in the 200mg dose arm and statistically significant improvements in all secondary efficacy endpoints observed in the 400mg dose arm. Over the full 52-week treatment period, the incidences of treatment-emergent adverse events in the placebo, 200mg and 400mg dose arms were 80.6%, 81.7% and 79.8%, respectively; the incidences of serious adverse events were 7.5%, 10.3% and 11.1%, respectively; and the incidences of discontinuation due to adverse events were 4.1%, 4.9% and 6.5%, respectively. Potential cases of severe hypoglycemia and DKA were reviewed by a blinded adjudication panel, which determined whether such cases met pre-established diagnostic criteria. The number of patients with positively adjudicated severe hypoglycemic events during the full 52-week treatment period was 26 (9.7%), 17 (6.5%) and 17 (6.5%) in the placebo, 200mg and 400mg dose arms, respectively. The number of patients with positively adjudicated DKA events during the full 52-week treatment period was 1 (0.4%), 9 (3.4%) and 11 (4.2%) in the placebo, 200mg and 400mg dose arms, respectively.

Our pivotal inTandem2 Phase 3 clinical trial enrolled 782 patients with type 1 diabetes in Europe and Israel in a randomized, double-blind, placebo-controlled study of 200mg and 400mg once daily doses of sotagliflozin over a 24-week treatment period, followed by a 28-week extension. Insulin therapy was optimized in patients over a 6-week period prior to dosing. As with inTandem1, the primary efficacy endpoint under evaluation in the trial was the reduction of A1C versus placebo on optimized insulin treatment at 24 weeks, with secondary endpoints including percentage of patients achieving A1C levels of less than 7% without experiencing a severe hypoglycemia or DKA event, change in bolus insulin use, body weight, fasting plasma glucose and patient-reported assessments. Data from the study showed that patients treated with sotagliflozin experienced statistically significant reductions in A1C from baseline of 0.39% for the 200mg dose ($p<0.001$) and 0.37% for the 400mg dose ($p<0.001$), as compared to a reduction of 0.02% on placebo after 24 weeks of treatment, meeting the study's primary efficacy endpoint at both dose levels. The A1C benefit achieved with sotagliflozin was sustained with statistically significant results over the full 52-week duration of the study for both the 200mg and 400mg doses. Statistically significant improvements in all secondary efficacy endpoints were observed in both the 200mg and 400mg dose arms compared to placebo. Over the full 52-week treatment period, the incidences of treatment-emergent adverse events in the placebo, 200mg and 400mg dose arms were 61.2%, 68.2% and 68.8%, respectively; the incidences of serious adverse events were 6.6%, 10.0% and 8.0%, respectively; and the incidences of discontinuation due to adverse events were 3.5%, 3.8% and 6.8%, respectively. Potential cases of severe hypoglycemia and DKA were reviewed by a blinded adjudication panel, which determined whether such cases met pre-established diagnostic criteria. The number of patients with positively adjudicated severe hypoglycemic events during the full 52-week treatment period was 13 (5.0%), 13 (5.0%) and 6 (2.3%) in the placebo, 200mg and 400mg dose arms, respectively. The number of patients with positively adjudicated DKA events during the full 52-week treatment period was 0 (0.0%), 6 (2.3%) and 9 (3.4%) in the placebo, 200mg and 400mg dose arms, respectively.

We have additionally reported pooled continuous glucose monitoring, or CGM, data from the inTandem1 and inTandem2 clinical trials. The percentage of time during the initial 24-week treatment period spent inside the target range for CGM glucose (70-180 mg/dL) increased from 52.2% to 57.8% in patients treated with 200mg of sotagliflozin and from 50.7% to 64.1% in patients treated with 400mg of sotagliflozin, with no relevant change observed in patients receiving placebo. The differences from placebo were clinically significant for both the 200mg and 400mg dose groups ($p=0.026$ and $p<0.001$, respectively). The increase in time spent in range by both sotagliflozin dose groups was a result of significantly reduced time spent above 180 mg/dL, while the time spent below 70 mg/dL was not increased. These results translate into an additional 1.41 hours and 3.02 hours that a patient would spend within the 70-180 mg/dL target range in a 24-hour period, for the 200mg and 400mg dose groups respectively.

Our inTandem3 Phase 3 clinical trial enrolled 1,405 patients with type 1 diabetes in the United States and Europe in a randomized, double-blind, placebo-controlled study of a 400mg once daily dose of sotagliflozin over a 24-week treatment period. Insulin therapy was not optimized in patients and eligibility criteria included any background insulin therapy. The

primary efficacy endpoint under evaluation in the trial was the proportion of patients achieving A1C levels of less than 7% at 24 weeks without experiencing a severe hypoglycemic or DKA event, with secondary endpoints including the change from baseline in A1C, body weight, systolic blood pressure and bolus insulin use. Data from the study showed statistically significant superiority of sotagliflozin (28.6%) compared to placebo (15.2%) in the proportion of patients achieving A1C levels of less than 7% without experiencing a severe hypoglycemic or DKA event ($p<0.001$), meeting the study's primary endpoint. Patients treated with sotagliflozin also experienced statistically significant improvements in all secondary efficacy endpoints compared to placebo. The incidences of treatment-emergent adverse events in the placebo and 400mg dose arms were 52.5% and 55.1%, respectively; the incidences of serious adverse events were 3.3% and 6.9%, respectively; and the incidences of discontinuation due to adverse events were 2.3% and 6.3%, respectively. Potential cases of severe hypoglycemia and DKA were reviewed by a blinded adjudication panel, which determined whether such cases met pre-established diagnostic criteria. The number of patients with positively adjudicated severe hypoglycemic events during the 24-week treatment period was 17 (2.4%) and 21 (3.0%) in the placebo and 400mg dose arms, respectively. The number of patients with positively adjudicated DKA events during the 24-week treatment period was 4 (0.6%) and 21 (3.0%) in the placebo and 400mg dose arms, respectively. Results from the inTandem3 trial were published in the New England Journal of Medicine in September 2017.

Sanofi has submitted applications for regulatory approval to market sotagliflozin for type 1 diabetes in the United States, the European Union and certain additional countries. On January 17, 2019, the Endocrinologic and Metabolic Drugs Advisory Committee of the U.S. Food and Drug Administration, or FDA, voted eight to eight on the question of whether the overall benefits of sotagliflozin outweighed the risks to support approval. While the FDA is not required to follow the committee's vote, the FDA considers the committee's recommendations when making its decision on the United States application, which is anticipated by March 22, 2019 under the Prescription Drug User Fee Act.

On February 28, 2019, the European Medicines Agency, or EMA, Committee for Medicinal Products for Human Use adopted a positive opinion recommending regulatory approval of sotagliflozin for use as an adjunct to insulin therapy to improve glycemic control in adults with type 1 diabetes with a body mass index of 27 kg/m2 or greater, who have failed to achieve adequate glycemic control despite optimal insulin therapy. The European Commission is anticipated to make a final decision on the European Union application in the second quarter of 2019.

We and Sanofi are working with the FDA, EMA and other regulatory authorities in support of their review process and preparing for the commercial launch of sotagliflozin for the treatment of type 1 diabetes, if approved.

Type 2 Diabetes.

Sanofi is conducting a comprehensive Phase 3 development program for sotagliflozin in type 2 diabetes patients, including the following randomized, double-blind, placebo-controlled studies:

- 200mg and 400mg once daily doses of sotagliflozin as monotherapy in approximately 400 patients over a 26-week treatment period;
- 400mg once daily dose of sotagliflozin in approximately 500 patients on background metformin therapy over a 26-week treatment period, followed by a 53-week extension;
- 400mg once daily dose of sotagliflozin in approximately 500 patients added to sulfonylurea alone or in combination with metformin over a 26-week treatment period, followed by a 53-week extension;
- 200mg or 400mg once daily dose of sotagliflozin in approximately 10,500 patients with cardiovascular risk factors and moderately impaired renal function over a treatment period to be determined by cardiovascular outcome events, currently expected to be approximately four years;
- 200mg and 400mg once daily doses of sotagliflozin in approximately 780 patients with moderate renal impairment over a 52-week treatment period;
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200mg and 400mg once daily doses of sotagliflozin in approximately 276 patients with severe renal impairment over a 52-week treatment period;

- 200mg and 400mg once daily doses of sotagliflozin in approximately 560 patients on background basal insulin alone or in addition to other oral antidiabetic drug therapies over an 18-week treatment period, followed by a 34-week extension;

- 200mg and 400mg once daily doses of sotagliflozin in approximately 700 patients on dipeptidyl peptidase-4, or DPP-4, inhibitors, with or without metformin, compared to 25mg dose of empagliflozin over a 26-week treatment period;
- 200mg and 400mg once daily doses of sotagliflozin in approximately 930 patients on background metformin therapy compared to up to a 6mg dose of glimepiride over a 52-week treatment period;
- 200mg and 400mg once daily doses of sotagliflozin in approximately 360 patients aged 55 years or older, with or without any stable anti-diabetes therapy, evaluating efficacy and bone safety over a 26-week treatment period, followed by a 78-week extension; and
- 200mg or 400mg once daily doses of sotagliflozin in approximately 4,000 hemodynamically stable patients with type 2 diabetes post-worsening heart failure over a treatment period determined by cardiovascular outcome events, currently expected to be approximately three years.

We previously completed two Phase 2 clinical trials evaluating the safety and tolerability of sotagliflozin and its effects on glycemic parameters associated with type 2 diabetes.

The Phase 2b clinical trial enrolled 299 patients with type 2 diabetes who were not adequately controlled on metformin monotherapy in a double-blind, randomized, placebo-controlled study of 75mg once daily, 200mg once daily, 200mg twice daily and 400mg once daily doses of sotagliflozin, each administered in combination with standard metformin therapy over a 12 week treatment period. The primary efficacy endpoint under evaluation in the trial was the change in A1C from baseline to week 12. Secondary efficacy endpoints included percentage of patients achieving A1C levels of less than 7%, as well as changes in fasting plasma glucose levels, weight, blood pressure and triglyceride levels. Data from the study showed that treatment with sotagliflozin demonstrated statistically significant benefits in the primary and multiple secondary endpoints. Patients in each of the 75mg once daily, 200mg once daily, 200mg twice daily and 400mg once daily sotagliflozin treatment arms had mean A1C reductions from baseline of 0.43, 0.52, 0.79 and 0.92 percent, respectively ($p<0.001$ for all treatment arms), while in patients randomized to placebo, A1C decreased by 0.09 percent. We also observed that patients treated with sotagliflozin showed significant reductions in body weight and blood pressure. Sotagliflozin was well tolerated and adverse events were generally mild to moderate, with the overall incidence of adverse events with sotagliflozin being similar to placebo.

The Phase 2a clinical trial enrolled 36 patients with non-insulin dependent type 2 diabetes in a double-blind, randomized, placebo-controlled study of 150mg and 300mg doses of sotagliflozin, each administered once daily over a four-week treatment period. The efficacy endpoints under evaluation in the trial included urinary glucose excretion, fasting plasma glucose, response to oral glucose tolerance testing, and change in A1C. Data from the study showed that treatment with 150mg and 300mg of sotagliflozin provided improvements in glycemic control and demonstrated statistically significant benefits in the primary and multiple secondary efficacy endpoints. A marked and statistically significant decrease in fasting plasma glucose was observed at each measurement point throughout the treatment period in both treatment arms relative to placebo. After four weeks of dosing, patients in both dose groups exhibited statistically significant reductions in A1C as compared to patients receiving placebo ($p=0.001$ and $p<0.001$ for the 150mg and 300mg treatment arms, respectively). Patients in both treatment arms also exhibited statistically significant improvements in glucose tolerance in response to oral glucose tolerance testing ($p<0.001$ for both treatment arms). Consistent with the mechanism of action of sotagliflozin, there was also a significant, dose-dependent increase in 24-hour urinary glucose excretion in both treatment arms at each measurement point throughout the study period relative to placebo ($p<0.001$ at all time points measured). Patients in both treatment arms also showed positive trends in broader metabolic and cardiovascular parameters, including weight reduction, decreased blood pressure and lower triglyceride levels. Sotagliflozin was well tolerated in the trial, with no dose-limiting toxicities observed and adverse events being generally mild and equally distributed across all treatment groups, including the placebo group.

LX9211

LX9211 is an orally-delivered small molecule compound that we are developing for the treatment of neuropathic pain. LX9211 was discovered by scientists working within our drug discovery alliance with Bristol-Myers Squibb and

inhibits adaptor associated kinase 1, or AAK1. Our scientists discovered that mice lacking AAK1 exhibit increased resistance to induced neuropathic pain in preclinical models.

We reported top-line data in December 2018 from a Phase 1a clinical trial evaluating the safety, tolerability and pharmacokinetics of LX9211. The trial enrolled ten cohorts of healthy volunteers in a randomized, double-blind, placebo-controlled, ascending single dose study of daily doses of LX9211. LX9211 demonstrated a safety, tolerability and pharmacokinetics profile identifying the maximum tolerated dose and supportive of once daily, or less frequent, dosing.

Pharmacokinetics results were dose proportional over substantially all of the dose range. The most common adverse event was headache and there were no drug-related serious adverse events.

We are conducting a Phase 1b clinical trial further evaluating the safety, tolerability and pharmacokinetics of LX9211. The trial is expected to enroll up to 40 healthy volunteers in a randomized, double-blind, placebo-controlled, ascending multiple dose study of daily doses of LX9211 over a 14-day treatment period.

We have obtained exclusive research, development and commercialization rights to LX9211 and additional compounds acting through AAK1 from Bristol-Myers Squibb.

LX2761

LX2761 is an orally-delivered small molecule compound that we are developing for the treatment of diabetes. LX2761 was discovered by our scientists and is designed to inhibit SGLT1 locally in the gastrointestinal tract without any significant inhibition of SGLT2 in the kidney.

We reported top-line data in December 2018 from two Phase 1 clinical trials evaluating the safety, tolerability, pharmacodynamics and pharmacokinetics of LX2761. The Phase 1a trial enrolled five cohorts of healthy volunteers and two cohorts of type 2 diabetes patients in a randomized, double-blind, placebo-controlled, ascending single dose study of daily doses of LX2761. Patients with type 2 diabetes were washed off metformin for three days prior to dosing. LX2761 demonstrated minimal absorption and no systemic effect, with no increase in urine glucose excretion from baseline. LX2761 also reduced postprandial glucose in diabetic patients while increasing plasma levels of glucagon-like peptide-1, or GLP-1, a hormone produced in the small intestine that stimulates insulin secretion and inhibits glucagon secretion. The most common adverse and dose-limiting event was diarrhea.

The Phase 1b trial enrolled 51 patients with type 2 diabetes in a randomized, double-blind, placebo-controlled ascending multiple dose study of daily doses of LX2761, administered as a single dose or twice per day over an 8-day treatment period. Patients were treated with metformin at the time of screening and for the duration of the study. LX2761 showed reduced postprandial glucose, demonstrating delayed and reduced intestinal glucose absorption while increasing plasma levels of GLP-1 with minimal effect on urinary glucose excretion. The most common adverse event was diarrhea. We are presently evaluating the further clinical development of LX2761.

We have granted Sanofi certain rights of first negotiation with respect to the future development and commercialization of LX2761.

Drug Target Discoveries

Our internal drug discovery efforts were driven by a systematic, target biology-driven approach in which we used gene knockout technologies and an integrated platform of advanced medical technologies to systematically study the physiological and behavioral functions of almost 5,000 genes in mice and assessed the utility of the proteins encoded by the corresponding human genes as potential drug targets. We have identified and validated in living animals, or in vivo, more than 100 targets with promising profiles for drug discovery.

Collaborations

We are working both independently and through strategic collaborations and alliances with third parties to capitalize on our drug target discoveries and drug discovery and development programs. Consistent with this approach, we seek to retain exclusive rights to the benefits of certain drug discovery and development programs by developing and commercializing drug candidates from those programs internally, particularly in the United States for indications treated by specialist physicians, as we have with XERMELO in the United States. We seek to collaborate with other

pharmaceutical and biotechnology companies, such as Ipsen and Sanofi, with respect to drug discovery or the development and commercialization of certain of our drug candidates, particularly with respect to commercialization in territories outside the United States, commercialization in the United States for indications treated by primary care physicians, or when the collaboration may provide us with access to expertise and resources that we do not possess internally or are complementary to our own. We also seek to collaborate with other pharmaceutical and biotechnology companies, research institutes and academic institutions to capitalize on our drug target discoveries.

Strategic Collaborations

Sanofi. We entered into a collaboration and license agreement with Sanofi in November 2015 under which we granted Sanofi an exclusive, worldwide, royalty-bearing right and license to develop, manufacture and commercialize sotagliflozin. In December 2016, Sanofi terminated its rights under the agreement with respect to Japan. We received a $300 million upfront payment under the agreement and we are eligible to receive up to $210 million upon the achievement of specified clinical development milestones, up to $220 million upon the achievement of specified regulatory milestones and up to $990 million upon the achievement of specified commercial milestones. We are also entitled to tiered, escalating royalties ranging from low double digit percentages to 40 percent of net sales of sotagliflozin, based on indication and territory, with royalties for the higher band of such range attributable to net sales for type 1 diabetes in the United States, and subject in each case to customary royalty reduction provisions.

We are responsible for all clinical development activities relating to type 1 diabetes and have exercised an exclusive option to co-promote and have a significant role, in collaboration with Sanofi, in the commercialization of sotagliflozin for the treatment of type 1 diabetes in the United States. Under the terms of the exercised co-promotion option, we will fund 40 percent of the commercialization costs relating to such co-promotion activities. Sanofi is responsible for all clinical development and commercialization of sotagliflozin for the treatment of type 2 diabetes worldwide and is solely responsible for the commercialization of sotagliflozin for the treatment of type 1 diabetes outside the United States. We shared in the funding of a portion of the planned type 2 diabetes development costs over the first three years of the collaboration, up to an aggregate of $100 million, which was satisfied in 2018. Sanofi will book sales worldwide in all indications.

Ipsen. We entered into a license and collaboration agreement with Ipsen in October 2014 under which we granted Ipsen an exclusive, royalty-bearing right and license to commercialize XERMELO outside of the United States, Canada and Japan. The collaboration was expanded in March 2015 to include Canada. We have received $24.5 million in upfront payments and $20.5 million in regulatory and commercial launch milestones under the agreement. In addition, we are eligible to receive up to an additional $11.8 million upon the achievement of additional specified regulatory and commercial launch milestones and up to €72 million upon the achievement of specified sales milestones. We are also entitled to tiered, escalating royalties ranging from low twenties to mid-thirties percentages of net sales of XERMELO in the licensed territory, subject to a credit for Ipsen’s payments to us for the manufacture and supply of such units of XERMELO and customary royalty reduction provisions.

Bristol-Myers Squibb. We established a drug discovery alliance with Bristol-Myers Squibb Company in December 2003 to discover, develop and commercialize small molecule drugs in the neuroscience field. Bristol-Myers Squibb extended the target discovery term of the alliance in May 2006. We initiated the alliance with a number of neuroscience drug discovery programs at various stages of development and used our gene knockout technologies to identify additional drug targets with promise in the neuroscience field. For those targets that were selected for the alliance, we and Bristol-Myers Squibb worked together, on an exclusive basis, to identify, characterize and carry out the preclinical development of small molecule drugs. Bristol-Myers Squibb has the first option to assume full responsibility for clinical development and commercialization of any drugs resulting from the alliance which enter clinical trials, other than LX9211 and additional compounds acting through AAK1. We received $86 million in upfront payments and research funding under the agreement during the target discovery portion of the alliance, which expired in October 2009. In addition, we are entitled to receive clinical and regulatory milestone payments ranging, depending on the timing and extent of our efforts in the alliance, up to $76 million for each drug developed by Bristol-Myers Squibb under the alliance. We will also earn royalties on sales of drugs commercialized by Bristol-Myers Squibb under the alliance.

We jointly developed LX9211 with Bristol-Myers Squibb as part of the alliance, and separately obtained from Bristol-Myers Squibb exclusive research, development and commercialization rights to LX9211 and additional compounds acting through AAK1. We have agreed to pay Bristol-Myers Squibb up to $34.5 million in clinical and

regulatory milestones for the first indication and up to $16 million in clinical and regulatory milestones for each of the second and third indications, if applicable. We have also agreed to pay single digit royalties on worldwide net sales and up to $40 million in commercial milestones.

Genentech. We established a drug discovery alliance with Genentech, Inc. in December 2002 to discover novel therapeutic proteins and antibody targets. We and Genentech expanded the alliance in November 2005 for the advanced research, development and commercialization of new biotherapeutic drugs. Under the original alliance agreement, we used our target validation technologies to discover the functions of secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. In the expanded alliance, we conducted additional, advanced research on a broad subset of those proteins and targets. We have exclusive rights to develop and commercialize biotherapeutic drugs for two of these targets, while Genentech has exclusive rights to develop and commercialize biotherapeutic drugs for the other targets. We

retain certain other rights to discoveries made in the alliance, including non-exclusive rights, along with Genentech, for the development and commercialization of small molecule drugs addressing the targets included in the alliance. We received $58 million in upfront payments, research funding and research milestone payments under the agreement during the research collaboration term, which expired in November 2008. In addition, we are entitled to receive clinical and regulatory milestone payments ranging, depending on the extent of our efforts in the alliance, up to $25 million for each drug target for which Genentech develops a biotherapeutic drug under the alliance. We will also earn royalties on sales of biotherapeutic drugs commercialized by Genentech under the alliance. Genentech is entitled to receive milestone payments and royalties on sales of biotherapeutic drugs which we develop or commercialize under the alliance.

Other Collaborations

We have established collaborations with a number of pharmaceutical and biotechnology companies, research institutes and academic institutions under which we have received fees in exchange for generating knockout mice for genes requested by the collaborator, providing phenotypic data with respect to such knockout mice or otherwise granting access to some of our technologies and discoveries. In some cases, we remain eligible to receive milestone or royalty payments on the sale of mice and phenotypic data or on products that our collaborators discover or develop using our technology.

Manufacturing and Product Supply

We do not own or operate manufacturing or distribution facilities or resources for clinical or commercial production and distribution of XERMELO or any of our drug candidates. Instead, we have multiple contractual agreements in place with third-party contract manufacturing organizations, or CMOs, who, on our behalf, manufacture commercial supplies of XERMELO and clinical supplies of our drug candidates, and will continue to do so for the foreseeable future. Sanofi is responsible for the manufacture of all clinical and commercial supplies of sotagliflozin under the terms of our collaboration. We have selected well-established and reputable global CMOs for our active pharmaceutical ingredient, or API, and drug product manufacturing that have good regulatory standing, large manufacturing capacities, and multiple manufacturing sites within their business footprint. We employ highly skilled personnel with both technical and manufacturing experience to diligently manage the activities at our CMOs. Our quality department audits these suppliers on a periodic basis. Our commercial suppliers are subject to routine inspections by regulatory agencies. We work closely with our third-party manufacturers to ensure compliance with current good manufacturing practices, or cGMP, and other stringent regulatory requirements enforced by the FDA and foreign regulatory agencies in other territories, as applicable.

Raw materials that are used to manufacture our API are sourced from multiple third-party suppliers in Asia and Europe. Third-party API contract manufacturers in Asia and Europe stock sufficient quantities of these materials to ensure they can manufacture adequate API quantities per our requirements, for both clinical and commercial purposes. We store API at third-party facilities, and provide appropriate amounts to third-party drug product contract manufacturers in Asia and North America who then manufacture, package and label our specified quantities of finished goods for XERMELO and our drug candidates. We rely on sole source third-party drug product contract manufacturers in the United States to manufacture, package and label finished drug product for commercial distribution of XERMELO. We also rely on a single third-party logistics provider, with two distribution locations, to provide shipping and warehousing services for our commercial supply of XERMELO in the United States. Our third-party contract manufacturers also need to obtain materials such as excipients, components and reagents to manufacture our API and finished drug products.

Within our supply chain, we have established safety stock amounts for both our API and drug products, and store those quantities for XERMELO in multiple locations. The quantities that we store are based on our business needs and take into account scenarios for demand, production lead times, potential supply interruptions and shelf life for our API

and drug products. In parallel, for business continuity reasons, we have established a backup supplier for our API and are in the process of evaluating and expect to establish an additional or backup supplier for our drug product in the near future. We believe that our current manufacturing network has the appropriate capacity to produce sufficient commercial quantities of XERMELO for both our and Ipsen's commercialization efforts in support of the current approved indication of carcinoid syndrome diarrhea, as well as the potential indication of biliary tract cancer, if clinical development in that indication proves to be successful and gains regulatory approval in the future.

Marketing, Sales and Distribution

We have a fully integrated commercial team consisting of sales, marketing, market access, and commercial operations functions. Our specialized sales team promotes XERMELO in the United States, concentrating their efforts on oncologists, oncology nurses and pharmacists. We have also built an internal medical affairs function with responsibility for responding to external inquiries regarding the appropriate use of XERMELO with regularly updated and well-substantiated scientific and

medical information. We have contracted with two independent specialty pharmacies to dispense XERMELO and provide specialty pharmacy services in fulfillment of prescriptions in the United States, allowing for efficient delivery of XERMELO by mail directly to patients. We rely on Ipsen for the commercialization and distribution of XERMELO in territories outside of the United States.

To help ensure that all eligible patients in the United States have appropriate access to XERMELO, we have established a comprehensive reimbursement and support program called LexCares. Through LexCares, we provide co-pay assistance to qualified, commercially insured patients to help minimize out-of-pocket costs and provide free drug to uninsured or under-insured patients who meet certain clinical and financial criteria. In addition, LexCares is designed to provide comprehensive reimbursement support services, such as benefits investigation and, if needed, appeals support.

Competition

The biotechnology and pharmaceutical industries are highly competitive and characterized by rapid technological change. We face significant competition in each of the aspects of our business from other pharmaceutical and biotechnology companies, as well as academic research institutions, clinical reference laboratories and governmental agencies that are pursuing research or development activities similar to ours. Many of our competitors have substantially greater research, development and commercialization capabilities and financial, scientific, marketing and human resources than we do. As a result, our competitors may succeed in developing products earlier than we do, obtaining approvals from the FDA or other regulatory agencies for those products more rapidly than we do, developing products that are more effective than those we develop or commercializing products more effectively and profitably than we do. Similarly, our collaborators face similar competition from other competitors who may succeed in developing products more quickly, developing products that are more effective than those developed by our collaborators or commercialize products more effectively and profitably than our collaborators.

The competition for our products and drug candidates includes both marketed products and drug candidates that are being developed by others, including pharmaceutical products that are currently in a more advanced stage of clinical development or commercialization than are our own drug candidates. These competitive marketed products and drug candidates include compounds that employ different mechanisms of action in addressing diseases and conditions for which we are developing our own drug candidates and, in some cases such as sotagliflozin, that employ the same or similar mechanisms of action.

We believe that our ability to successfully compete with these potentially competitive drug candidates and other competitive products currently on the market will depend on, among other things:

- the efficacy, safety and reliability of our products;
- our ability, and the ability of our collaborators, to complete preclinical and clinical development and obtain regulatory approvals for our drug candidates;
- the timing and scope of regulatory approvals of our products;
- our ability, and the ability of our collaborators, to obtain product acceptance by physicians and other health care providers and secure coverage and adequate reimbursement for product use in approved indications;
- our ability, and the ability of our collaborators, to manufacture and sell commercial quantities of our products;
- the skills of our employees and our ability to recruit and retain skilled employees;

- protection of our intellectual property; and

- the availability of substantial capital resources to fund development and commercialization activities.

Our principal competition for XERMELO includes the use, above their maximum labeled dose, of the established SSA therapies octreotide and lanreotide, injectable products currently marketed by Novartis and Ipsen, respectively, as well as lutetium Lu 177 dotatate, a radiopharmaceutical product currently marketed for the treatment of gastroenteropancreatic neuroendocrine tumors by Advanced Accelerator Applications (a subsidiary of Novartis).

If approved for the treatment of type 1 diabetes, we expect that our principal competition for sotagliflozin will include established insulin therapies, as well as selective SGLT2 inhibitors currently being prescribed off-label, but which may gain regulatory approval, for the treatment of type 1 diabetes. Such selective SGLT2 inhibitors include dapagliflozin, empagliflozin and canagliflozin, currently marketed for the treatment of type 2 diabetes by AstraZeneca, Boehringer Ingelheim and Eli Lilly, and Janssen (a subsidiary of Johnson & Johnson), respectively. The EMA Committee for Medicinal Products for Human Use has adopted a positive opinion recommending regulatory approval for AstraZeneca to market dapagliflozin for the treatment of insufficiently controlled type 1 diabetes as an adjunct to insulin in adult patients with a body mass index of 27 kg/m2 or greater, when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy. If approved for the treatment of type 2 diabetes, we expect that our principal competition for sotagliflozin will include such selective SGLT2 inhibitors, as well as DPP-4 inhibitors such as sitagliptin, currently marketed for the treatment of type 2 diabetes by Merck.

Government Regulation

The development, manufacture and sale of pharmaceutical products are subject to extensive regulation by United States and foreign governmental authorities, including federal, state and local authorities. In the United States, new drugs are subject to regulation under the Federal Food, Drug and Cosmetic Act and the regulations promulgated thereunder, or the FDC Act. The FDA and comparable governmental authorities regulate, among other things, research and development activities and the testing, manufacture, quality control, safety, efficacy, record keeping, reporting, labeling, storage, approval, advertising, promotion, sale, distribution, export and import of pharmaceutical products.

The standard process required by the FDA before a drug candidate may be marketed in the United States generally includes the following:

- preclinical laboratory and animal tests performed under current good laboratory practices, or cGLP;
- submission of an IND, which must become effective before human clinical trials may commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for its intended use;
- submission of a New Drug Application, or NDA, for approval of commercial marketing and sale, or of an NDA supplement, or sNDA, for approval of a new indication if the product is already approved for another indication;
- pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with cGMP and current good clinical practices, or cGCP;
- if FDA convenes an advisory committee, satisfactory completion of the advisory committee review; and
- FDA approval of the NDA or sNDA.

This process for the testing and approval of drug candidates requires substantial time, effort and financial resources. Preclinical development of a drug candidate can take from one to several years to complete, with no guarantee that an IND based on those studies will become effective to even permit clinical testing to begin. Before commencing the first clinical trial of a drug candidate in the United States, we must submit an IND to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial. In such a case, we and the FDA must resolve any outstanding concerns before the clinical trial may begin. Submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, and the FDA must grant permission for each clinical trial to start and continue. Further, an independent institutional review board for each medical center proposing to participate in the clinical trial must review and approve the plan for any clinical trial before it commences at that center. Regulatory authorities or an institutional review board or we may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

For purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1 clinical trials are conducted in a limited number of healthy human volunteers or, in some cases, patients, to evaluate the safety, dosage tolerance, absorption, metabolism, distribution and excretion of the drug candidate;
- Phase 2 clinical trials are conducted in groups of patients afflicted with a specified disease or condition to obtain preliminary data regarding efficacy as well as to further evaluate safety and optimize dosing of the drug candidate.

Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials; and

- Phase 3 clinical trials are conducted in larger patient populations at multiple clinical trial sites to obtain statistically significant evidence of the efficacy of the drug candidate for its intended use and to further test for safety in an expanded patient population.

In addition, the FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied after a drug receives approval. Failure to satisfy such post-marketing commitments can result in FDA enforcement action, up and to including withdrawal of NDA approval. The results of phase 4 studies can confirm the effectiveness of a drug candidate and can provide important safety information to augment the FDA's adverse drug reaction reporting system.

After completion of clinical trials, FDA approval of an NDA must be obtained before a new drug may be marketed in the United States. The submission of an NDA requires payment of a substantial user fee to the FDA. An NDA must contain, among other things, information on chemistry, manufacturing controls and potency and purity, non-clinical pharmacology and toxicology, human pharmacokinetics and bioavailability and clinical data. There can be no assurance that the FDA will accept an NDA for filing and, even if accepted for filing, that approval will be granted. The FDA may convene an advisory committee to provide clinical insight on NDA review questions. Although the FDA is not required to follow the recommendations of an advisory committee, the agency typically does so. Among other things, the FDA reviews an NDA to determine whether a product is safe and effective for its intended use and whether the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may deny approval of an NDA by way of a Complete Response letter if the applicable regulatory criteria are not satisfied, or it may require additional clinical data or an additional pivotal Phase 3 clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. An NDA may be approved with significant restrictions on its labeling, marketing and distribution under a Risk Evaluation and Mitigation Strategy or otherwise that could restrict the commercial applications of a product or impose costly procedures in connection with the commercialization or use of the product. Once issued, the FDA may withdraw product approval if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

In addition to obtaining FDA approval for each product, each drug manufacturing establishment must be inspected and approved by the FDA. All manufacturing establishments are subject to inspections by the FDA and by other federal, state and local agencies and must comply with current Good Manufacturing Practices requirements. Non-compliance with these requirements can result in, among other things, total or partial suspension of production, failure of the government to grant approval for marketing and withdrawal, suspension or revocation of marketing approvals.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes many years, with the actual time required varying substantially based on, among other things, the nature, novelty and complexity of the drug candidate and of the disease or condition. Government regulation may delay or prevent marketing of drug candidates or new diseases for a considerable period of time and impose costly procedures upon our activities. The FDA or any other regulatory agency may not grant approvals for new indications for our product candidates on a timely basis, if at all. Success in earlier-stage clinical trials does not ensure success in later-stage clinical trials. Targets and pathways identified in vitro may be determined to be less relevant in clinical studies and results in animal model studies may not be predictive of human clinical results. Furthermore, data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Even if a drug candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product

or even complete withdrawal of the product from the market.

Once the FDA approves a product, a manufacturer must provide certain updated safety and efficacy information. Product changes as well as certain changes in a manufacturing process or facility would necessitate additional FDA review and approval. Other post-approval changes may also necessitate further FDA review and approval. Additionally, a manufacturer must meet other requirements including those related to adverse event reporting and record keeping.

Products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their subcontractors 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 cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers.

The FDA closely regulates the marketing and promotion of drugs, including restricting the promotion of uses for which a drug is not approved by the agency. Not only must a company have appropriate substantiation to support claims made about a drug, under the FDA's current interpretation of relevant laws, a company can make only those claims relating to safety and efficacy that are for indications for which FDA has approved the drug and are otherwise consistent with the FDA-approved label for the drug. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may, in their independent medical judgment, prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturers' communications on the subject of off-label use. Additionally, a significant number of pharmaceutical companies have been the target of inquiries and investigations by various United States federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for off-label uses and other sales practices. These investigations have alleged violations of various United States federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDC Act, false claims laws, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement.

The United States Orphan Drug Act is intended to incentivize the development of products for rare diseases or conditions that affect fewer than 200,000 people in the United States. If a drug is being developed for a rare disease or condition, to be eligible for designation as an orphan drug, the FDA must not have previously approved a drug considered the "same drug" for the same orphan indication. If the FDA has previously approved another same drug for the same indication, the sponsor of the subsequent drug would be required to provide a plausible hypotheses of clinical superiority over the previously approved drug to obtain an orphan designation. Upon FDA receipt of orphan drug designation, the sponsor is eligible for tax credits of up to 25% for qualified clinical trial expenses, the ability to apply for annual grant funding and waiver of PDUFA application fee. In addition, upon marketing approval, an orphan-designated drug could be eligible for seven years of market exclusivity for the approved orphan-designated indication. Such orphan drug exclusivity, if awarded, would only block the approval of any drug considered the same drug for the same orphan indication. Moreover, a subsequent same drug could break a previously approved drug's orphan exclusivity through a demonstration of clinical superiority over the previously approved drug.

The FDA has various programs, including Fast Track, priority review and accelerated approval, which are intended to expedite or simplify the process for developing and reviewing promising drugs, or to provide for the approval of a drug on the basis of a surrogate endpoint. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious or life-threatening diseases or conditions and fill unmet medical needs. Priority review is designed to give drugs that treat serious conditions and offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months of NDA filing as compared to a standard review time of 10 months from NDA filing. Certain other types of drug applications are also eligible for priority review. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track-designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval provides for an earlier approval for a new drug that is intended to treat a serious or life-threatening disease or condition and that fills an unmet medical need based on a surrogate endpoint. As a condition of approval, the FDA may require that a sponsor of a product candidate receiving accelerated approval perform post-marketing clinical trials to confirm the clinically meaningful outcome as predicted by the surrogate marker trial. In addition to the Fast Track, accelerated approval and priority review

programs, the FDA also designates Breakthrough Therapy status to drugs that are intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient drug development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.

Additional programs intended to expedite the development of drug products were included in the 21st Century Cures Act, or the Cures Act. The Cures Act includes various provisions to accelerate the development and delivery of new treatments, such as those intended to expand the types of evidence manufacturers may bring to the FDA to support drug

approval, to encourage patient-centered drug development, to liberalize the communication of healthcare economic information to payers, and to create greater transparency with regard to manufacturer expanded access programs. Central to the Cures Act are provisions that enhance and accelerate the FDA's processes for reviewing and approving new drugs and supplements to approved NDAs, including provisions that:

- require the FDA to establish a program to evaluate the potential use of real world evidence to help support the approval of a new indication for an approved drug and to help support or satisfy post-approval study requirements;
- provide that the FDA may rely upon qualified data summaries to support the approval of a supplemental application with respect to a qualified indication for an already approved drug;
- require the FDA to issue guidance for purposes of assisting sponsors in incorporating complex adaptive and other novel trial designs into proposed clinical protocols and applications for new drugs; and
- require the FDA to establish a process for the qualification of drug development tools for use in supporting or obtaining FDA approval for or investigational use of a drug.

The Cures Act amends Section 114 of the Food and Drug Administration Modernization Act of 1997 to help clarify and facilitate the dissemination of healthcare economic information, including by broadening the definition of healthcare economic information, expressly extending the dissemination of healthcare economic information to payors, and clarifying that healthcare economic information must only relate to an FDA-approved indication rather than directly relate to the indication.

Regulation Outside of the United States

In addition to regulations in the United States, we are subject to the regulations of other countries governing clinical trials and the manufacturing, commercial sales and distribution of our products outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the United States before we can commence clinical trials in such countries and approval of the regulators of such countries or economic areas, such as the European Union, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company may submit marketing authorization applications, or MAAs, either under a centralized or decentralized procedure. Under the centralized procedure, MAAs are submitted to the European Medicines Agency, or EMA, whose Committee for Medicinal Products for Human Use reviews the application and issues an opinion on it. The opinion is considered by the European Commission which is responsible for deciding applications. If the application is approved, the European Commission grants a single marketing authorization that is valid for all European Union member states as well as Iceland, Liechtenstein and Norway, or the EEA. The national authorization procedures, the decentralized and mutual recognition procedures, as well as national applications, are available for products for which the centralized procedure is not compulsory. The mutual recognition procedure provides for the European Union member states selected by the applicant to mutually recognize a national marketing authorization that has already been granted by the competent authority of another member state, referred to as the Reference Member State, or RMS. The decentralized procedure is used when the product in question has yet to be granted a marketing authorization in any member state. Under this procedure the applicant can select the member state that will act as the RMS. In both the mutual recognition and decentralized procedures, the RMS reviews the application and submits its assessment of the application to the member states where marketing authorizations are being sought, referred to as Concerned Member States or CMS. Within 90 days of receiving the application and assessment report, each CMS must decide whether to recognize the RMS assessment. If a member state does not agree with the assessment, and the disputed points cannot be resolved the matter is eventually referred to the European Commission, whose decision is binding on all member states. If the application is successful national marketing authorizations will be granted by the competent authorities in each of the member states chosen by the applicant.

Conditional marketing authorizations may be granted for a limited number of medicinal products for human use referenced in European Union law applicable to conditional marketing authorizations where the clinical dataset is not comprehensive, if the risk-benefit balance of the product is positive, it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, unmet medical needs will be fulfilled and the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, such as the completion of ongoing or new studies and obligations relating to the collection of pharmacovigilance data, may be amongst the conditions stipulated in the marketing authorization.

As in the United States, we may apply for designation of a product as an Orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. In the European Union, orphan designation is available for products in development which are either intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union, or intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the community and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the medicinal product. Additionally, the sponsor of an application for orphan drug designation must establish that there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition or even if such treatment exists, the product will be of significant benefit to those affected by that condition.

Orphan drugs in the European Union enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product. The period of market exclusivity may be reduced to six years if at the end of the fifth year it is established that the criteria for orphan designation are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Healthcare Regulation

Federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, also apply to our business. If we fail to comply with those laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected. The laws that may affect our ability to operate include, but are not limited to: the federal Anti-Kickback Statute, which prohibits. among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs; and federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent. Additionally, we are subject to state law equivalents of each of the above federal laws, which may be broader in scope and apply regardless of whether the payer is a federal healthcare program, and many of which differ from each other in significant ways and may not have the same effect, further complicate compliance efforts.

Numerous federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use and disclosure of personal information. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. In addition, most healthcare providers who are expected to prescribe our products and from whom we obtain patient health information, are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology and Clinical Health Act, or HIPAA. Although we are not directly subject to HIPAA, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity, including healthcare providers, in a manner that is not authorized or permitted by HIPAA. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost of doing business. International laws, such as the EU Data Privacy Directive and Swiss Federal Act on Data Protection, regulate the processing of personal data within the European Union and between countries in the European Union and countries outside of the European Union, including the United States. Failure to provide adequate privacy protections and maintain compliance with safe harbor mechanisms could jeopardize business transactions across borders and result in significant penalties.

In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the PPACA, created a federal requirement under the federal Open Payments program, that requires certain manufacturers to track and report to the Centers for Medicare and Medicaid Services, or CMS, annually certain payments and other transfers of value provided to physicians and teaching hospitals made in the previous calendar year. In addition, there are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. These laws may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state and federal authorities.

For those marketed products which are covered in the United States by the Medicaid program, we have various obligations, including government price reporting and rebate requirements, which generally require products be offered at substantial rebates/discounts to Medicaid and certain purchasers. We are also required to discount such products to authorized users of the Federal Supply Schedule of the General Services Administration, under which additional laws and requirements

apply. These programs require submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations, and the guidance governing such calculations is not always clear. Compliance with such requirements can require significant investment in personnel, systems and resources, but failure to properly calculate our prices, or offer required discounts or rebates could subject us to substantial penalties.

Other Regulations

In addition to the foregoing, our business is subject to regulation under various state and federal environmental laws, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act and the Toxic Substances Control Act. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in and wastes generated by our operations. We believe that we are in material compliance with applicable environmental laws and that our continued compliance with these laws will not have a material adverse effect on our business. We cannot predict, however, whether new regulatory restrictions will be imposed by state or federal regulators and agencies or whether existing laws and regulations will adversely affect us in the future.

Patents and Proprietary Rights

We are able to protect our proprietary rights from unauthorized use by third parties only to the extent that those rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. Accordingly, patents and other proprietary rights are an essential element of our business. We own or exclusively license patents and/or patent applications throughout the world that claim our products and drug candidates, including:

- issued patents and pending patent applications in Europe, the United States, and other countries throughout the world, including Australia, Argentina, Brazil, Canada, China, Europe, India, Israel, Japan, Mexico, New Zealand, South Africa, and South Korea, that claim telotristat ethyl and associated crystalline forms, pharmaceutical compositions comprising telotristat ethyl, and methods of its manufacture and use;
- issued patents and pending patent applications in Europe, the United States, and other countries throughout the world, including Australia, Argentina, Brazil, Canada, China, Europe, India, Israel, Japan, Mexico, New Zealand, South Africa, and South Korea, that claim sotagliflozin and associated crystalline forms, pharmaceutical compositions comprising sotagliflozin, and methods of its manufacture and use;
- pending patent applications in Europe, the United States, and other countries throughout the world, including Australia, Argentina, Brazil, Canada, China, Europe, India, Israel, Japan, Mexico, New Zealand, South Africa, and South Korea, that disclose and/or claim LX9211, pharmaceutical compositions comprising LX9211, and methods of its use; and
- pending patent applications in Europe, the United States, and other countries throughout the world, including Australia, Argentina, Brazil, Canada, China, Europe, India, Israel, Japan, Mexico, New Zealand, South Africa, and South Korea, that disclose and/or claim LX2761, pharmaceutical compositions comprising LX2761, and methods of its use.

Additionally, we hold rights to a number of patents and patent applications under license agreements with third parties. Many of these licenses are nonexclusive, although some are exclusive in specified fields. Most of the licenses have terms that extend for the life of the licensed patents.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country. We have filed patent applications and hold issued patents covering our approved drug, XERMELO, and each of our drug candidates. None of our United States patents that claim XERMELO or one of our drug candidates has a normal expiration date earlier than 2026.

All of our employees, consultants and advisors are required to execute a proprietary information agreement upon the commencement of employment or consultation. In general, the agreement provides that all inventions conceived by the employee or consultant, and all confidential information developed or made known to the individual during the term of the agreement, shall be our exclusive property and shall be kept confidential, with disclosure to third parties allowed only in

specified circumstances. We cannot assure you, however, that these agreements will provide useful protection of our proprietary information in the event of unauthorized use or disclosure of such information.

Our patent and intellectual property rights are subject to certain rights and uncertainties. See “Risks Related to Our Intellectual Property” under “Item 1A. Risk Factors.”

Executive Officers

Our executive officers and their ages and positions are listed below.

Name	Age	Position with the Company
Lonnel Coats	54	President and Chief Executive Officer and Director
Pablo Lapuerta, M.D.	55	Executive Vice President and Chief Medical Officer
Alan J. Main, Ph.D.	65	Executive Vice President, Commercial Supply Operations
Alexander A. Santini	60	Executive Vice President and Chief Commercial Officer
Praveen Tyle, Ph.D.	58	Executive Vice President, Research and Development
Jeffrey L. Wade	54	Executive Vice President, Corporate and Administrative Affairs and Chief Financial Officer
James F. Tessmer	59	Vice President, Finance and Accounting

Lonnel Coats has been our president and chief executive officer and a director since July 2014. Mr. Coats previously served in a series of executive leadership positions at Eisai Inc. and Eisai Corporation of North America, where he worked for 18 years before joining our company, most recently as chief executive officer from 2010 to 2014. Prior to joining Eisai, Mr. Coats spent eight years with Janssen Pharmaceuticals, Inc., a division of Johnson & Johnson, where he held a variety of management and sales positions. Mr. Coats serves as a director of Blueprint Medicines Corporation and holds a B.S. from Oakland University.

Pablo Lapuerta, M.D. has been our executive vice president and chief medical officer since February 2015 and previously served in a series of medical and clinical leadership positions since joining our company in 2011. Dr. Lapuerta was formerly vice president at Bristol-Myers Squibb Company with responsibility for global development of an Alzheimer’s disease drug candidate, and prior to that served as senior vice president, clinical strategy and chief medical officer of Cogentus Pharmaceuticals, Inc. and in a variety of clinical development leadership roles at Bristol-Myers Squibb, where he worked for 11 years before joining Cogentus. He holds a B.A. in biology from Harvard College and an M.D. from Harvard Medical School.

Alan J. Main, Ph.D. has been our executive vice president, commercial supply operations since May 2017 and previously served in a series of manufacturing and scientific leadership positions since joining our company in 2001. Dr. Main was president and chief executive officer of Coelacanth Corporation, a leader in using proprietary chemistry technologies to rapidly discover new chemical entities for drug development, until our acquisition of Coelacanth in 2001. Dr. Main was formerly senior vice president, U.S. Research at Novartis Pharmaceuticals Corporation, where he worked for 20 years before joining Coelacanth. Dr. Main holds a B.S. from the University of Aberdeen, Scotland and a Ph.D. in organic chemistry from the University of Liverpool, England and completed postdoctoral studies at the Woodward Research Institute.

Alexander A. Santini has been our executive vice president and chief commercial officer since November 2016 and previously served in a series of commercial leadership positions since joining our company in April 2015. Mr. Santini was formerly vice president of market access and an executive member at Bayer Healthcare Pharmaceuticals, where he had executive responsibility for market access, pricing, trade and channel management and payer account management, and prior to that served in a variety of commercial leadership roles of increasing responsibility during eight years of service at Bayer and 22 years of service at Berlex Laboratories. Mr. Santini served as a non-commissioned officer in the United States Air Force, where he completed the Radiologic Technology Program at the United States Air Force School of Health Care Science and an AAS in business marketing from Westchester

Community College.

Praveen Tyle, Ph.D. has been our executive vice president of research and development since May 2016. Dr. Tyle was previously a member of the executive management team at Osmotica Pharmaceutical Corp., serving as president and chief executive officer from January 2013 through April 2016 and prior to that as executive vice president and chief scientific officer. Prior to his service at Osmotica, Dr. Tyle held a series of scientific leadership positions within the pharmaceutical industry, including executive vice president and chief science officer for the United States Pharmacopeia, senior vice president and global head of research and development and business development and licensing at Novartis OTC, corporate senior vice president of global research and development and chief scientific officer at Bausch & Lomb Incorporated and vice president and global head of pharmaceutical sciences at Pharmacia Corporation. Dr. Tyle serves as director of Eyegate Pharmaceuticals,

Inc. and Orient Europharma Ltd. Dr. Tyle received his B.Pharm. from the Indian Institute of Technology, Banaras Hindu University and his Ph.D. in pharmaceutics and pharmaceutical chemistry from the Ohio State University.

Jeffrey L. Wade has been our executive vice president, corporate and administrative affairs and chief financial officer since February 2015 and previously served in a series of finance and legal leadership positions since joining our company in 1999. Mr. Wade was previously a corporate securities and finance attorney for ten years with the law firm of Andrews & Kurth L.L.P., where he represented companies in the biotechnology, information technology and energy industries. Mr. Wade is a member of the board of directors of the Texas Healthcare and Bioscience Institute. He received his B.A. and J.D. from the University of Texas.

James F. Tessmer has been our vice president, finance and accounting since November 2007 and previously served in a series of finance and accounting leadership positions since joining our company in 2001. Mr. Tessmer was previously assistant controller for Mariner Health Network, Inc. and prior to that served in a variety of financial and accounting management positions for HWC Distribution Corp. and American General Corporation. Mr. Tessmer is a certified public accountant and received his B.B.A. from the University of Wisconsin – Milwaukee and his M.B.A. from the University of Houston.

Employees

As of February 28, 2019, we employed 202 persons, of whom 34 hold M.D. or Ph.D. degrees and another 63 hold other advanced degrees. All of our employees are located in the United States. None of our employees are represented by a labor union and we believe that our relationship with our employees is good.

Research and Development Expenses

In 2018, 2017 and 2016, respectively, we incurred expenses of $100.2 million, $152.2 million and $164.0 million in company-sponsored as well as collaborative research and development activities, including $6.0 million, $4.9 million and $3.9 million of stock-based compensation expense in 2018, 2017 and 2016, respectively.

Item 1A. Risk Factors

The following risks and uncertainties are important factors that could cause actual results or events to differ materially from those indicated by forward-looking statements. The factors described below are not the only ones we face and additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Business and Industry

We depend heavily on the commercial success of XERMELO. If we do not achieve commercial success with XERMELO, our business will suffer and our stock price will likely decline.

We expect that a significant portion of our total revenues for the next several years will be attributable to sales of XERMELO in the United States, but we cannot be certain that XERMELO will be commercially successful. Our future sales of XERMELO will depend on numerous factors, including:

- the number of patients with carcinoid syndrome diarrhea who are inadequately controlled by SSA therapy, as well as the number of newly diagnosed carcinoid syndrome diarrhea patients;
- competition from SSA therapies, radiopharmaceutical products and any additional products for the treatment of carcinoid syndrome diarrhea that may be approved by the FDA in the future;
- the safety profile of XERMELO, including whether previously unknown side effects or increased incidence or severity of known side effects as compared to those seen during development are identified with the increased use of XERMELO after approval;
- the effectiveness of our commercial strategy for marketing XERMELO and our execution of that strategy, including our pricing strategy and the effectiveness of our efforts to obtain adequate third-party reimbursement;
- the acceptance of XERMELO by patients, the medical community and third-party payers; and
- our ability to meet the demand for commercial supplies of XERMELO and to maintain and successfully monitor commercial manufacturing arrangements for XERMELO with third-party manufacturers to ensure they meet our standards and those of the FDA, which extensively regulates and monitors pharmaceutical manufacturing facilities.

While we believe that XERMELO has a competitive commercial profile, our current estimates of the revenues that XERMELO could generate in future periods may change based upon the above factors, and could prove to be incorrect. If our revenues, market share or other indicators of market acceptance of XERMELO fail to meet the expectations of investors or public market analysts, the market price of our common stock could decline. In addition, if one or more of the factors above negatively affects XERMELO sales, our business and financial condition could be materially harmed and we may be more heavily dependent on the success of our other drug programs.

We depend heavily on our and Sanofi's ability to obtain regulatory approval in the United States and the European Union for sotagliflozin in type 1 diabetes. If we and Sanofi fail to obtain such regulatory approvals or fail to successfully commercialize sotagliflozin for type 1 diabetes upon such regulatory approvals, our business will suffer and our stock price will likely decline.

Sanofi has submitted applications for regulatory approval to market sotagliflozin for type 1 diabetes in the United States and the European Union, as well as additional countries. On January 17, 2019, the Endocrinologic and Metabolic Drugs Advisory Committee of the FDA voted eight to eight on the question of whether the overall benefits of sotagliflozin outweighed the risks to support approval. While the FDA is not required to follow the committee's vote, the FDA considers the committee's recommendations when making its decision on the United States application, which is anticipated by March 22, 2019 under the Prescription Drug User Fee Act.

On February 28, 2019, the EMA Committee for Medicinal Products for Human Use adopted a positive opinion recommending regulatory approval of sotagliflozin for use as an adjunct to insulin therapy to improve glycemic control in adults with type 1 diabetes with a body mass index of 27 kg/m2 or greater, who have failed to achieve adequate glycemic control despite optimal insulin therapy. The European Commission is anticipated to make a final decision on the European Union application in the second quarter of 2019.

We cannot offer any assurances or predict with any certainty that the FDA and/or EMA will grant marketing approval for sotagliflozin in type 1 diabetes, in either case on the expected timelines. Furthermore, regulatory approvals for sotagliflozin in type 1 diabetes, even if obtained, may limit the type of patients in which sotagliflozin may be used, such as on the basis of body mass index as recommended by the EMA Committee for Medicinal Products for Human Use, or otherwise require specific warning or labeling language, each of which may reduce the commercial potential of sotagliflozin in type 1 diabetes. Even if approved, we and Sanofi might not be successful in commercializing sotagliflozin for type 1 diabetes. Should we and Sanofi fail to obtain regulatory approval in the United States and/or the European Union for sotagliflozin in type 1 diabetes or fail to successfully commercialize sotagliflozin upon such regulatory approvals, our business and financial condition could be materially harmed and we may be more heavily dependent on the success of our other drug programs.

We depend heavily on Sanofi's ability to successfully complete Phase 3 clinical development and obtain regulatory approvals for sotagliflozin in type 2 diabetes. If Sanofi fails to successfully complete such Phase 3 clinical development and obtain such regulatory approvals, or fails to successfully commercialize sotagliflozin for type 2 diabetes upon such regulatory approvals, our business will suffer and our stock price will likely decline.

Sanofi is presently conducting a comprehensive Phase 3 development program for sotagliflozin in type 2 diabetes patients. We cannot offer any assurances or predict with any certainty that such Phase 3 clinical development will be successfully completed, that positive clinical data will be obtained from such Phase 3 clinical development efforts or that regulatory authorities will grant marketing approval for sotagliflozin in type 2 diabetes, in any such case on the expected timelines. Furthermore, regulatory approvals for sotagliflozin, even if obtained, may limit the type of patients in which sotagliflozin may be used for type 2 diabetes or otherwise require specific warning or labeling language, each of which may reduce the commercial potential of sotagliflozin in type 2 diabetes. Even if approved, Sanofi might not be successful in commercializing sotagliflozin for type 2 diabetes. Should Sanofi fail to obtain regulatory approvals for sotagliflozin in type 2 diabetes or fail to successfully commercialize sotagliflozin upon such regulatory approvals, our business and financial condition could be materially harmed and we may be more heavily dependent on the success of our other drug programs.

Clinical testing of our drug candidates in humans is an inherently risky and time-consuming process that may fail to demonstrate safety and efficacy, which could result in the delay, limitation or prevention of regulatory approval.

In order to obtain regulatory approvals for the commercial sale of any products that we or our collaborators may develop in addition to XERMELO, we or our collaborators are required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our drug candidates. We or our collaborators may not be able to obtain authority from the FDA, or other equivalent foreign regulatory agencies to initiate or complete any clinical trials. In addition, we have limited internal resources for making regulatory filings and interacting with regulatory authorities. Clinical trials are inherently risky and the results from nonclinical testing of a drug candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger-scale, advanced stage clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after achieving positive results in earlier trials. Although Phase 2 proof-of-concept clinical trials of sotagliflozin in type 2 diabetes patients were positive, we cannot assure you that the Phase 3 clinical development program for sotagliflozin being conducted by Sanofi in type 2 diabetes patients will yield positive results. Negative or inconclusive results from a nonclinical study or a clinical trial could cause us, our collaborators or the FDA or other equivalent foreign regulatory agencies to terminate a nonclinical study or clinical trial or require that we or our collaborators repeat or modify it. Furthermore, we, one of our collaborators or a regulatory agency with jurisdiction over the trials may suspend clinical trials at any time if the subjects or patients participating in such trials are being exposed to unacceptable health risks or for other reasons.

Any nonclinical or clinical test may fail to produce results satisfactory to the FDA or foreign regulatory authorities. Nonclinical and clinical data can be interpreted in different ways, which could delay, limit or prevent regulatory approval. The FDA or institutional review boards at the medical institutions and healthcare facilities where we or our collaborators sponsor clinical trials may suspend any trial indefinitely if they find deficiencies in the conduct of these trials. Clinical trials must be conducted in accordance with the FDA's current Good Clinical

Practices. The FDA and these institutional review boards have authority to oversee our and our collaborators' clinical trials, and the FDA may require large numbers of subjects or patients. In addition, we or our collaborators must manufacture, or contract for the manufacture of, the drug candidates that we use in our clinical trials under the FDA's current Good Manufacturing Practices.

The rate of completion of clinical trials is dependent, in part, upon the rate of enrollment of patients. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study, the nature of the study, the existence of competitive clinical trials and the availability of alternative

treatments. Delays in planned patient enrollment may result in increased costs and prolonged clinical development, which in turn could allow our competitors to bring products to market before we do and impair our ability to commercialize our products or potential products.

We or our collaborators may not be able to successfully complete any clinical trial of a drug candidate within any specified time period. In some cases, we or our collaborators may not be able to complete the trial at all. Moreover, clinical trials may not show our drug candidates to be both safe and effective. Thus, the FDA and other regulatory authorities may not approve any additional drug candidates that we develop for any indication or may limit the approved indications or impose other conditions.

Our drug candidates are subject to a lengthy and uncertain regulatory process that may not result in the necessary regulatory approvals, which could adversely affect our and our collaborators' ability to commercialize products.

Our drug candidates, as well as the activities associated with their research, development and commercialization, are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for any drug candidate would prevent us from commercializing that drug candidate. Other than XERMELO, we and our collaborators have not received regulatory approval to market any of our drug candidates in any jurisdiction. The process of obtaining regulatory approvals is expensive, and often takes many years, if approval is obtained at all, and can vary substantially based upon the type, complexity and novelty of the drug candidates involved. Before a new drug application can be filed with the FDA, the drug candidate must undergo extensive clinical trials, which can take many years and may require substantial expenditures. Any clinical trial may fail to produce results satisfactory to the FDA. For example, the FDA could determine that the design of a clinical trial is inadequate to produce reliable results. Furthermore, prior to approving a new drug, the FDA typically requires that the efficacy of the drug be demonstrated in two double-blind, controlled studies. The regulatory process also requires nonclinical testing, and data obtained from nonclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval periods of our drug candidates may cause delays in the approval or rejection of an application. Even if the FDA or a comparable authority in another country approves a drug candidate, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, marketing and/or production of such product and may impose ongoing requirements for post-approval studies, including additional research and development and clinical trials. These agencies also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

The commercial success of XERMELO and any other products that we or our collaborators may develop will depend upon the degree of market acceptance among physicians, patients, health care payers and the medical community.

Our ability to commercialize XERMELO and our or our collaborators' ability to commercialize any other products that we or they may develop will be highly dependent upon the extent to which XERMELO and such other products gain market acceptance among physicians, patients, health care payers, such as commercial health insurers, Medicare and Medicaid, and the medical community. If XERMELO and such other products do not achieve an adequate level of acceptance, we may not generate adequate product revenues and we may not become profitable. The degree of market acceptance of XERMELO and such other products will depend upon a number of factors, including:

- the effectiveness, or perceived effectiveness, of our products in comparison to competing products;

- the existence of any significant side effects, as well as their severity in comparison to any competing products;

- potential advantages or disadvantages in relation to alternative treatments;
- current and future indications for which our products may be approved;
- the ability to offer our products for sale at competitive prices;
- relative convenience and ease of administration;
- the strength of marketing and distribution support; and
- sufficient third-party coverage or reimbursement.

If we are unable to maintain an effective sales force, marketing infrastructure and distribution capabilities, we will not be able to successfully commercialize XERMELO or any other products that we or our collaborators may develop.
In order to successfully commercialize XERMELO, we have built a marketing organization and a specialized sales force for XERMELO and established distribution capabilities in the United States. However, we had no prior experience in building and maintaining such a commercialization infrastructure. Factors that may hinder our efforts to effectively manage and maintain such infrastructure for XERMELO or establish, manage and maintain such infrastructure for other products that we or our collaborators may develop include:

- inability to recruit, retain and effectively manage adequate numbers of effective sales and marketing personnel;
- inability to maintain relationships with third-party logistics providers, specialty pharmacies, third-party manufacturers and other third parties instrumental in the commercial manufacture and distribution of XERMELO and any other products;
- inability to establish or implement internal controls and procedures required in connection with sales of pharmaceutical products;
- inability of sales personnel to obtain access to or convince adequate numbers of physicians to prescribe XERMELO or any other products; and
- lack of complementary products to be offered by our sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines.

If we are unable to sustain our sales force, marketing infrastructure and distribution capability for XERMELO or any other products, we may not be able to generate any product revenue, may generate increased expenses and may never become profitable.
We will need to continue to expend significant time and resources to train our sales force to be credible, persuasive and compliant in discussing XERMELO and any other products with the specialists treating the patients indicated under the label. We will also need to continue to train our sales force to ensure that a consistent and appropriate message about XERMELO and any other products is being delivered to our potential customers. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits and risks of XERMELO and any other products and their proper administration, our ability to successfully commercialize XERMELO and any other products could be diminished, which could have a material adverse effect on our financial condition, stock price and operations.
If we are unable to maintain adequate coverage and reimbursement from third-party payers for XERMELO and any other products that we or our collaborators may develop, our revenues and prospects for profitability will suffer.

Our ability to successfully commercialize XERMELO and any other products that we or our collaborators may develop is highly dependent on the extent to which coverage and reimbursement for such products are available from third-party payers, including governmental payers, such as Medicare and Medicaid, and private health insurers, including managed care organizations and group purchasing organizations. Many patients are not capable of paying themselves for XERMELO and some or all of the other products that we or our collaborators may develop, and rely on third-party payers to pay for, or subsidize, their medical needs. If third-party payers do not provide coverage or reimbursement for XERMELO or any other products, our revenues and prospects for profitability will suffer. In addition, even if third-party payers provide some coverage or reimbursement for such products, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans often varies based on the type of contract or plan purchased.

In addition, in some foreign countries, particularly the countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, price negotiations with governmental

authorities can take six to 12 months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement and/or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost effectiveness of our drug candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in the commercialization of our drug candidates. Third-party payers are challenging the prices charged for medical products and services, and many third-party payers limit reimbursement for newly approved health care products. In particular, third-party payers may limit the indications for which they will reimburse patients who use any

products that we or our collaborators may develop. Cost-control initiatives could decrease prices we or our collaborators might establish for products that may be developed, which would result in lower product revenues to us.

We may not be able to manufacture XERMELO and any other products that we or our collaborators may develop in commercial quantities, which would impair our ability to commercialize such products.

Other than XERMELO, our drug candidates have been manufactured in relatively small quantities for nonclinical and clinical trials. If any of these drug candidates are approved by the FDA or other regulatory agencies for commercial sale, we or our collaborators will need to manufacture them in larger quantities. We may not be able to successfully increase the manufacturing capacity, whether in collaboration with third-party manufacturers or on our own, for any of such drug candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. If we or our collaborators are unable to successfully increase the manufacturing capacity for a drug candidate, the regulatory approval or commercial launch of that drug candidate may be delayed or there may be a shortage in supply. Our drug candidates require precise, high-quality manufacturing. The failure to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously hurt our business.

We and our collaborators are subject to extensive and rigorous ongoing regulation relating to XERMELO and any other products that we or our collaborators may develop.

We are subject to extensive and rigorous ongoing domestic and foreign government regulation of, among other things, the research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing of XERMELO and any other products which receive regulatory approvals from the FDA or foreign regulatory authorities. The failure to comply with these requirements or the identification of safety problems during commercial marketing could lead to the need for product marketing restrictions, product withdrawal or recall or other voluntary or regulatory action, which could delay further marketing until the product is brought into compliance. The failure to comply with these requirements may also subject us or our collaborators to stringent penalties.

We are subject to certain healthcare laws, regulation and enforcement; our failure to comply with those laws could have a material adverse effect on our results of operations and financial condition.

We are subject to certain healthcare laws and regulations and enforcement by the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include, without limitation:

- the federal Anti-Kickback Law, which constrains our business activities, which includes our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent;

- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

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state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

- the Foreign Corrupt Practices Act, a United States law which regulates certain financial relationships with foreign government officials (which could include, for example, certain medical professionals);

- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- state and federal government price reporting laws that require us to calculate and report complex pricing metrics to government programs, where such reported price may be used in the calculation of reimbursement and/or discounts on our marketed drugs (participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on our products, increased infrastructure costs, and potentially limit our ability to offer certain marketplace discounts); and

- state and federal marketing expenditure tracking and reporting laws, which generally require certain types of expenditures in the United States to be tracked and reported. Compliance with such requirements may require investment in infrastructure to ensure that tracking is performed properly, and some of these laws result in the public disclosure of various types of payments and relationships, which could potentially have a negative effect on our business and/or increase enforcement scrutiny of our activities.

In addition, certain marketing practices, including off-label promotion, may also violate certain federal and state health regulatory fraud and abuse laws as well as false claims laws, including the civil False Claims Act. Suits filed under the civil False Claims Act, known as “qui tam” actions, can be brought by any individual on behalf of the government and such individuals, commonly known as “whistleblowers,” may share in any amounts paid by the entity to the government in fines or settlement. The filing of qui tam actions has caused a number of pharmaceutical, medical device and other healthcare companies to defend a civil False Claims Act action. When an entity is determined to have violated the civil False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties for each separate false claim.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we, or our officers or employees, may be subject to penalties, including administrative civil and criminal penalties, damages, fines, withdrawal of regulatory approval, the curtailment or restructuring of our operations, the exclusion from participation in Medicare, Medicaid and other federal and state healthcare programs, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to sell our products or operate our business and also adversely affect our financial results. Defending against any such actions can be costly, 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.

Numerous federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use and disclosure of personal information. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. In addition, most healthcare providers who may be expected to prescribe our products and from whom we may obtain patient health information are subject to privacy and security requirements under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA. Although we are not directly subject to HIPAA, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost of doing business. International laws, such as the EU Data Privacy Directive and Swiss Federal Act on Data Protection, regulate the processing of personal data within Europe and between European countries and the United States. Failure to provide adequate privacy protections and maintain compliance with safe harbor mechanisms could jeopardize business transactions across borders and result in significant penalties.

Current healthcare laws and regulations and future legislative or regulatory reforms to the healthcare system may negatively affect our revenues and prospects for profitability.

A primary trend in the United States and some foreign countries is toward reform and cost containment in the health care industry. The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals that may have the effect of reducing the prices that we are able to charge for XERMELO and other products we or our collaborators may develop. Healthcare reform measures which may be adopted in the future in the United States and foreign jurisdictions may result in more rigorous coverage criteria and significant downward pressure on the prices drug manufacturers may charge. As a result, our revenues and prospects for profitability could be significantly harmed.

As a result of the overall trend towards cost-effectiveness criteria and managed healthcare in the United States, third-party payers are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. They may use tiered reimbursement and may adversely affect demand for XERMELO and other products we or our collaborators may develop by placing them in an expensive tier. They may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payers will reimburse for newly approved drugs, which in turn will put pressure on the pricing of drugs. Further, we do not have experience in ensuring approval by applicable third-party payers outside of the United States for coverage and reimbursement of pharmaceutical products. We also anticipate pricing pressures in connection with the sale of XERMELO and other products we or our collaborators may develop due to the increasing influence of health maintenance organizations and additional legislative proposals.

Pricing for pharmaceutical products has come under increasing scrutiny by governments, legislative bodies and enforcement agencies. These activities may result in actions that have the effect of reducing our revenue or harming our business or reputation.

Many companies in our industry have received a governmental request for documents and information relating to drug pricing and patient support programs. We may become subject to similar requests, which would require us to incur significant expense and result in distraction for our management team. Additionally, to the extent there are findings, or even allegations, of improper conduct on the part of our company, such findings could further harm our business, reputation and/or prospects. It is possible that such inquiries could result in negative publicity or other negative actions that could harm our reputation, changes in our product pricing and distribution strategies, reduced demand for our approved products and/or reduced reimbursement of approved products, including by federal health care programs such as Medicare and Medicaid and state health care programs.

Our competitors may develop products that impair the value of XERMELO or any other products that we or our collaborators may develop.

The pharmaceutical and biotechnology industries are highly diversified and are characterized by rapid technological change. We and our collaborators face, and will continue to face, intense competition from biotechnology and pharmaceutical companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research and development activities similar to ours. In addition, significant delays in the development of our drug candidates could allow our competitors to bring products to market before us, which would impair our or our collaborators' ability to commercialize our drug candidates. XERMELO and any other products that we or our collaborators develop will compete in highly competitive markets. Further, our competitors may be more effective at using their technologies to develop commercial products. Many of the organizations competing with us have greater capital resources, larger research and development staff and facilities, more experience in obtaining regulatory approvals and more extensive product manufacturing and marketing capabilities. As a result, our competitors may be able to more easily develop products that would render XERMELO and any other products that we or our collaborators develop obsolete and noncompetitive. For example, dapagliflozin, empagliflozin and canagliflozin are currently being marketed by AstraZeneca, Boehringer Ingelheim and Eli Lilly, and Janssen (a subsidiary of Johnson & Johnson), respectively, for the treatment of type 2 diabetes. In addition, the EMA Committee for Medicinal Products for Human Use has adopted a positive opinion recommending regulatory approval for AstraZeneca to market dapagliflozin for the treatment of insufficiently controlled type 1 diabetes as an adjunct to insulin in adult patients with a body mass index of 27 kg/m2 or greater, when insulin alone does not provide adequate glycemic control despite optimal insulin therapy. Each of those products act through SGLT2, one of the targets of sotagliflozin. In addition, there may be drug candidates of which we are not aware at an earlier stage of development that may compete with our drug candidates.

Risks Related to Our Capital Requirements and Financial Results

We will need additional capital in the future and, if it is unavailable, we will be forced to delay, reduce or eliminate our commercialization efforts or product development programs. If additional capital is not available on reasonable terms, we will be forced to obtain funds, if at all, by entering into financing agreements on unattractive terms.

As of December 31, 2018, we had $160.1 million in cash, cash equivalents and investments. We anticipate that our existing capital resources and the cash and revenues we expect to derive from product revenues, collaborations and other sources will enable us to fund our currently planned operations for at least the next 12 months. However, we caution you that we may generate less cash and revenues or incur expenses more rapidly than we currently anticipate. Our currently planned operations for the next twelve months include the continued commercialization of XERMELO in the United States; the continued support of the regulatory review process for sotagliflozin in type 1 diabetes; preparations for the commercial launch of sotagliflozin for type 1 diabetes in the United States, if approved; and the continued nonclinical and clinical development of telotristat ethyl, sotagliflozin, LX9211, LX2761 and our other drug candidates.

Although difficult to accurately predict, the amount of our future capital requirements will be substantial and will depend on many factors, including:

- the success of our sales, marketing, distribution and other commercialization activities for XERMELO in the United States and the revenues we generate from that approved product;
- the success of Ipsen's sales, marketing, distribution and other commercialization activities for XERMELO outside of the United States and Japan;
- our and Sanofi's ability to obtain regulatory approvals for the marketing and sale of sotagliflozin for type 1 diabetes;
- if approved, our and Sanofi's ability to successfully commercialize sotagliflozin for type 1 diabetes;
- the progress and scope of Sanofi's development activities with respect to sotagliflozin in type 2 diabetes patients;
- if approved, Sanofi's ability to successfully commercialize sotagliflozin for type 2 diabetes;
- the timing, progress and results of our clinical trials of telotristat ethyl, sotagliflozin, LX9211, LX2761 and our other drug candidates;
- the amount and timing of payments, if any, under our existing collaboration agreements with Sanofi, Ipsen and other entities and any future collaboration agreements;
- the amount and timing of our research, development and commercialization expenditures;
- future results from clinical trials of our other drug candidates;
- the cost and timing of regulatory approvals and commercialization of additional drug candidates that we successfully develop;
- the market acceptance and commercial success of additional products that we successfully develop and commercially launch;
- the effect of competing programs and products, and of technological and market developments;
- the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights; and
- the cost and timing of establishing or contracting for commercialization capabilities of any other approved drug candidate.

Our capital requirements have and will continue to be substantial as we market XERMELO in the United States, support the regulatory review process for sotagliflozin in type 1 diabetes, prepare for the commercial launch of sotagliflozin for type 1 diabetes in the United States, conduct nonclinical and clinical development of telotristat ethyl, sotagliflozin, LX9211 and LX2761 and advance new drug candidates into clinical development. Our capital requirements will also be affected by any expenditures we make in connection with license agreements and acquisitions of and investments in complementary products and technologies. For all of these reasons, our future capital requirements cannot easily be quantified.

If our capital resources are insufficient to meet future capital requirements, we will need to raise additional funds to continue our currently planned operations. Our ability to raise additional capital is dependent on a number of factors, including the market demand for our securities, which itself is subject to a number of pharmaceutical development and business risks and uncertainties, as well as uncertainty that we would be able to raise such additional capital at a price or on terms that are favorable to us. If we raise additional capital by issuing equity securities, our then-existing stockholders will experience dilution and the terms of any new equity securities may have preferences over our common stock. The affirmative and restrictive covenants and the pledge of substantially all of our assets as collateral under our existing term loan with BioPharma Credit PLC and BioPharma Credit Investments IV Sub LP, or the BioPharma Term Loan, restrict our ability to raise additional capital by issuing debt securities. We cannot be certain that additional financing, whether debt or equity, will be available in amounts or on terms acceptable to us, if at all. We may be unable to raise sufficient additional capital on reasonable terms, and if so, we will be forced to delay, reduce or eliminate our clinical development programs or commercialization efforts or obtain funds, if at all, by entering into financing agreements on unattractive terms.

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We have a history of net losses, and we expect to continue to incur net losses and may not achieve or maintain profitability.

We have incurred net losses since our inception, including net losses of $120.5 million for the year ended December 31, 2018, $123.0 million for the year ended December 31, 2017 and $131.4 million for the year ended December 31, 2016. As of December 31, 2018, we had an accumulated deficit of $1.5 billion. Because of the numerous risks and uncertainties associated with successfully developing and commercializing drugs, we are unable to predict the extent of any future losses or whether or when we will become profitable, if at all. The size of our net losses will depend, in part, on the rate of decline or growth in our revenues and on the amount of our expenses. We expect to continue to incur significant expenses over the next several years as we expect to make significant investments in the commercialization of XERMELO in the United States, the commercialization of sotagliflozin for type 1 diabetes in the United States, if approved, and the continued nonclinical and clinical development of telotristat ethyl, sotagliflozin, LX9211, LX2761 and our other drug candidates.

Prior to the commercial launch of XERMELO, we derived substantially all of our revenues from strategic collaborations and other research and development collaborations and technology licenses. Future revenues from our commercialization of XERMELO are uncertain because they depend on a number of factors, including market acceptance of XERMELO, the success of our sales, marketing, distribution and other commercialization activities and the cost and availability of reimbursement for XERMELO. Future revenues from our existing collaborations are uncertain because they depend, to a large degree, on the achievement of milestones and payment of royalties we earn from any future products developed under the collaborations. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future collaborators and licensees, and to negotiate agreements that we believe are in our long-term best interests. We may determine, as we have with certain of our drug candidates, including XERMELO in the United States and Japan, that our interests are better served by retaining rights to our discoveries and advancing our therapeutic programs to a later stage, which could limit our near-term revenues and increase expenses. Because of these and other factors, our operating results have fluctuated in the past and are likely to do so in the future, and we do not believe that period-to-period comparisons of our operating results are a good indication of our future performance.

We expect to spend significant amounts to fund our commercialization activities with respect to XERMELO in the United States, our preparations for the commercial launch of sotagliflozin for type 1 diabetes in the United States and our planned nonclinical and clinical development of telotristat ethyl, sotagliflozin, LX9211, LX2761 and our other drug candidates. As a result, we will need to generate substantial additional revenues 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 operating results have been and likely will continue to fluctuate, and we believe that period-to-period comparisons of our operating results are not a good indication of our future performance.

Our operating results have fluctuated in the past and are likely to fluctuate in the future. A number of factors, many of which we cannot control, could subject our operating results to volatility, including:

- our ability to successfully commercialize XERMELO in the United States and the amount of revenues generated from such commercialization efforts;
- our and Sanofi's ability to obtain regulatory approval for the marketing and sale of sotagliflozin for type 1 diabetes;
- the amount and timing of payments, if any, under our existing collaboration agreements with Sanofi, Ipsen and other entities;
- the success of our ongoing nonclinical and clinical development efforts;

- the timing and amount of expenses incurred with respect to our nonclinical and clinical development and commercialization efforts;

- our success in establishing new collaborations and technology licenses, and the timing of such arrangements;

- the success rate of our development efforts leading to opportunities for new collaborations and licenses, as well as milestone payments and royalties;

- the timing and willingness of our collaborators to commercialize pharmaceutical products that would result in milestone payments and royalties;

- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our products and technologies;

- general and industry-specific economic conditions, which may affect our and our collaborators' research and development expenditures.

Because of these and other factors, including the risks and uncertainties described in this section, our operating results have fluctuated in the past and are likely to do so in the future. Due to the likelihood of fluctuations in our revenues and expenses, we believe that period-to-period comparisons of our operating results are not a good indication of our future performance.

We have substantial indebtedness that may limit cash flow available to invest in the ongoing needs of our business.

We have incurred $245.0 million of indebtedness. Although the affirmative and restrictive covenants and the pledge of substantially all of our assets as collateral under the BioPharma Term Loan restrict our ability to obtain additional debt financing, we could in the future incur additional indebtedness beyond such amount. Our substantial debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate a substantial portion of cash flow from operations to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product commercialization and development efforts and other general corporate purposes;

- increasing our vulnerability to adverse changes in general economic, industry and market conditions;

- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and

- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents and marketable securities and funds from external sources. However, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our existing debt. Funds from external sources may not be available on acceptable terms, if at all. In addition, a failure to comply with the covenants under our existing debt instruments could result in an event of default under those instruments. In the event of an acceleration of amounts due under our debt instruments as a result of an event of default, including upon the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, properties, assets or condition or a failure to pay any amount due, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness or to make any accelerated payments, and the lenders could seek to enforce their security interests in the collateral securing such indebtedness.

If we do not effectively manage our affirmative and restrictive covenants under the BioPharma Term Loan, our financial condition and results of operations could be adversely affected.
Our obligations under the BioPharma Term Loan are secured by a first lien security interest in substantially all of our assets. In addition, the BioPharma Term Loan requires that we comply with certain affirmative and restrictive covenants, including among other things, covenants restricting dispositions, fundamental changes in our business, mergers or acquisitions, indebtedness, encumbrances, distributions, investments, transactions with affiliates and subordinated debt, any of which could restrict our business and operations, particularly our ability to respond to changes in our business or to take specified actions to take advantage of certain business opportunities that may be

presented to us. Our failure to comply with any of these covenants could result in a default under the BioPharma Term Loan, which could permit the lenders to declare all or part of any outstanding borrowings to be immediately due and payable. If we are unable to repay those amounts, the lenders could enforce the security interest granted to them to secure that debt, which would seriously harm our business.

Risks Related to Our Relationships with Third Parties

We are significantly dependent upon our collaborations with Ipsen, Sanofi and other pharmaceutical and biotechnology companies. If pharmaceutical products are not successfully and timely developed and commercialized under our collaborations, our opportunities to generate revenues from milestones and royalties will be greatly reduced.

We have entered into collaboration agreements with Ipsen for the commercialization of XERMELO outside of the United States and Japan and with Sanofi for the worldwide (excluding Japan) development and commercialization of sotagliflozin. We have also established collaborative arrangements with other pharmaceutical and biotechnology companies with respect to the research, development and commercialization of drug candidates from other programs. We have derived a substantial majority of our revenues to date from these strategic collaborations and other research and development collaborations and technology licenses. Future revenues from our existing collaborations depend upon the achievement of milestones and payment of royalties we earn from any future products developed under the collaborations. If our relationship terminates with any of our collaborators, particularly Ipsen and Sanofi, our reputation in the business and scientific community may suffer and revenues will be negatively impacted to the extent such losses are not offset by additional collaboration agreements. If milestones are not achieved under our collaborations or our collaborators are unable to successfully develop and commercialize products from which milestones and royalties are payable, we will not earn the revenues contemplated by those collaborations.

We have limited or no control over the resources that any collaborator may devote to the development and commercialization of products under our alliances. For example, Sanofi is responsible for all clinical development activities relating to sotagliflozin for the treatment of type 2 diabetes and we have limited influence on the manner in which Sanofi may conduct such clinical development. Any of our present or future collaborators may not perform their obligations as expected. These collaborators may breach or terminate their agreements with us or otherwise fail to conduct research, development or commercialization activities successfully or in a timely manner. Further, our collaborators may elect not to develop pharmaceutical products arising out of our collaborative arrangements or may not devote sufficient resources to the development, regulatory approval, manufacture, marketing or sale of these products. If any of these events occurs, we may not receive collaboration revenue or otherwise realize anticipated benefits from such collaborations, our product development efforts may be delayed and our business, operating results and financial condition could be adversely affected.

Conflicts with our collaborators could jeopardize the success of our collaborative agreements and harm our product development efforts.

We may pursue opportunities in specific disease and therapeutic modality fields that could result in conflicts with our collaborators, if any of our collaborators takes the position that our internal activities overlap with those activities that are exclusive to our collaboration. Moreover, disagreements could arise with our collaborators over rights to our intellectual property or our rights to share in any of the future revenues of compounds or therapeutic approaches developed by our collaborators. Any conflict with or among our collaborators could result in the termination of our collaborative agreements, delay collaborative research or development activities, impair our ability to renew or obtain future collaborative agreements or lead to costly and time consuming litigation. Conflicts with our collaborators could also have a negative impact on our relationship with existing collaborators, materially impairing our business and revenues. Some of our collaborators are also potential competitors or may become competitors in the future. Our collaborators could develop competing products, preclude us from entering into collaborations with their competitors or terminate their agreements with us prematurely. Any of these events could harm our product development efforts.

We depend on third-party manufacturers, including sole source suppliers, to manufacture commercial quantities of XERMELO. We may not be able to maintain these relationships and could experience supply disruptions outside of our control.

We rely on a network of third-party manufacturers to manufacture and supply XERMELO for commercial sale. As a result of our reliance on these third-party manufacturers and suppliers, including sole source suppliers for certain steps in the manufacture of XERMELO, we could be subject to significant supply disruptions. Our supply chain for sourcing raw materials and manufacturing drug product ready for distribution is a multi-step endeavor. Third-party contract manufacturers procure raw materials, convert these raw materials into API, and then convert the API into final dosage form. Establishing and managing this supply chain requires a significant financial commitment and the creation and maintenance of numerous third party contractual relationships. Although we attempt to effectively manage the business relationships with companies in our supply chain, we do not have control over their operations.

We require our own commercial supply of XERMELO for sale in the United States, and are required under our collaboration agreement to supply Ipsen's commercial requirements of XERMELO in the European Union and other territories outside of the United States and Japan. We currently rely, and expect to continue to rely, on sole source third-party manufacturers to produce final drug product and package and label XERMELO. While we have identified and expect to qualify and engage back-up third-party manufacturers as additional or alternative suppliers for the production of final drug product and packaging and labeling of XERMELO, we currently do not have such arrangements in place. Moreover, some of these alternative manufacturers will need to be approved by the FDA before we can use them for manufacturing XERMELO. It is also possible that supplies of materials that cannot be second-sourced can be managed with inventory planning. There can be

no assurance, however, that failure of any of our sole source third-party manufacturers to meet our and Ipsen's commercial demands for XERMELO in a timely manner, or our failure to engage qualified additional or back-up suppliers for the production of final drug product and packaging and labeling of XERMELO, would not have a material adverse effect on commercialization of XERMELO and our business.

Supply disruptions may result from a number of factors, including shortages in product raw materials, labor or technical difficulties, regulatory inspections or restrictions, shipping or customs delays or any other performance failure by any third-party manufacturer on which we rely. Any supply disruptions could disrupt sales of XERMELO, which could have a material adverse impact on our business.

We rely on a single third-party logistics provider and two independent specialty pharmacies for distribution of XERMELO in the United States, and their failure to distribute XERMELO effectively would adversely affect sales of XERMELO.

We rely on a single third-party logistics provider for shipping and warehousing of our commercial supply of XERMELO and two independent specialty pharmacies for dispensation of XERMELO to patients in fulfillment of prescriptions in the United States. Although our third-party logistics provider stores our commercial supply of XERMELO at two separate warehouses, the use of a single third-party logistics provider increases the risk that a fire or damage from another type of disaster at either of the warehouses may result in a disruption of our commercialization efforts. A specialty pharmacy is a pharmacy that specializes in the dispensing of medications for complex or chronic conditions, which often require a high level of patient education and ongoing management. The use of specialty pharmacies involves certain additional risks, including, but not limited to, risks that these specialty pharmacies will:

- not provide us accurate or timely information regarding their inventories, the number of patients who are using XERMELO or complaints about XERMELO;
- reduce or discontinue their efforts to sell or support or otherwise not effectively sell or support XERMELO;
- not devote the resources necessary to sell XERMELO in the volumes and within the time frames that we expect;
- be unable to satisfy their financial obligations to us; or
- cease operations.

If our third-party logistics provider or either or both of our specialty pharmacies do not fulfill their contractual obligations to us, or refuse or fail to adequately distribute XERMELO and serve patients, or the agreements are terminated without adequate notice, shipments of XERMELO, and associated revenues, would be adversely affected. In addition, we expect that it may take a significant amount of time if we were required to change our third-party logistics provider or either of our specialty pharmacies.

We rely on third parties to carry out drug development activities.
We rely on clinical research organizations and other third-party contractors to carry out many of our drug development activities, including the performance of nonclinical laboratory and animal tests under the FDA's current Good Laboratory Practices regulations and the conduct of clinical trials of our drug candidates in accordance with protocols we establish. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, our drug development activities may be delayed, suspended or terminated. Such a failure by these third parties could significantly impair our ability to develop and commercialize the affected drug candidates.

We lack the capability to manufacture materials for nonclinical studies, clinical trials or commercial sales and rely on third parties to manufacture our drug candidates, which may harm or delay our product development and commercialization efforts.

We currently do not have the manufacturing capabilities or experience necessary to produce materials for nonclinical studies, clinical trials or commercial sales and intend in the future to continue to rely on collaborators and third-party contractors to produce such materials. We will rely on selected manufacturers to deliver materials on a timely basis and to comply with applicable regulatory requirements, including the current Good Manufacturing Practices of the FDA, which relate to manufacturing and quality control activities. These manufacturers may not be able to produce material on a timely basis or manufacture material at the quality level or in the quantity required to meet our development timelines and applicable regulatory requirements. In addition, there are a limited number of manufacturers that operate under the FDA's current Good Manufacturing Practices and that are capable of producing such materials, and we may experience difficulty finding

manufacturers with adequate capacity for our needs. If we are unable to contract for the production of sufficient quantity and quality of materials on acceptable terms, our product development and commercialization efforts may be delayed. Moreover, noncompliance with the FDA's current Good Manufacturing Practices can result in, among other things, fines, injunctions, civil and criminal penalties, product recalls or seizures, suspension of production, failure to obtain marketing approval and withdrawal, suspension or revocation of marketing approvals.

Risks Related to Our Intellectual Property

If we are unable to adequately protect our intellectual property, third parties may be able to use our products and technologies, which could adversely affect our ability to compete in the market.

Our success will depend in part upon our ability to obtain patents and maintain adequate protection of the intellectual property related to our products and technologies. The patent positions of biotechnology and pharmaceutical companies, including our patent position, are generally uncertain and involve complex legal and factual questions. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our products and technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We will continue to apply for patents covering our products and technologies as, where and when we deem appropriate. However, pending patent applications do not provide protection against competitors because they are not enforceable until they issue as patents. Further, the disclosures contained in our current and future patent applications may not be sufficient to meet statutory requirements for patentability and our applications may fail to result in issued patents. Once issued, patents still may not provide commercially meaningful protection. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from developing competing products and technologies. Furthermore, others may independently develop similar or alternative products or technologies or design around our patents. If anyone infringes upon our or our collaborators' patent rights, enforcing these rights may be difficult, costly and time-consuming and, as a result, it may not be cost-effective or otherwise expedient to pursue litigation to enforce those patent rights.

Our patents may be challenged by third parties as invalid or unenforceable under U.S. or foreign laws, or they may be infringed by third parties. As a result, we may be involved in the defense and enforcement of our patent or other intellectual property rights in a court of law, U.S. Patent and Trademark Office inter partes review or reexamination proceeding, foreign opposition proceeding or related legal and administrative proceeding in the United States and elsewhere. The costs of defending our patents or enforcing our proprietary rights in post-issuance administrative proceedings and litigation may be substantial and the outcome can be uncertain. An adverse outcome may allow third parties to use our intellectual property without a license and negatively impact our business.

In addition, because patent applications can take many years to issue, third parties may have pending applications, unknown to us, which may later result in issued patents that cover the production, manufacture, commercialization or use of our products and drug candidates. If any such patents are issued to other entities, we will be unable to obtain patent protection for the same or similar discoveries that we make relating to our products and drug candidates. Moreover, we may be blocked from using our drug targets or drug candidates or developing or commercializing our products and other drug candidates, or may be required to obtain a license that may not be available on reasonable terms, if at all. Further, others may discover uses for our drug targets and drug candidates other than those covered in our issued or pending patents, and these other uses may be separately patentable. Even if we have a patent claim on a particular technology or product, the holder of a patent covering the use of that technology or product could exclude us from selling a product that is based on the same use of that product.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, if the patent owner has failed to "work" the invention in that country or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Compulsory licensing of life-saving drugs is also becoming increasingly popular in developing countries either through direct legislation or international initiatives. Such compulsory licenses could be extended to include some of our products and drug candidates, which could limit our potential revenue opportunities. Moreover, the legal systems of certain countries,

particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement.

We rely on trade secret protection for some of our confidential and proprietary information. We have taken security measures to protect our proprietary information and trade secrets, but these measures may not provide adequate protection. While we seek to protect our proprietary information by entering into confidentiality agreements with employees,

collaborators and consultants, we cannot assure you that our proprietary information will not be disclosed, or that we can meaningfully protect our trade secrets. In addition, our competitors may independently develop substantially equivalent proprietary information or may otherwise gain access to our trade secrets.

We may be involved in patent litigation and other disputes regarding intellectual property rights and may require licenses from third parties for our planned nonclinical and clinical development and commercialization activities. We may not prevail in any such litigation or other dispute or be able to obtain required licenses.

Our products and those of our collaborators, as well as our nonclinical and clinical development efforts, may give rise to claims that they infringe the patents of others. We are aware that other companies and institutions are developing products acting through the same drug targets through which some of our drug candidates currently in clinical development act, have conducted research on many of the same targets that we have identified and have filed patent applications potentially covering drug targets that we have identified and certain therapeutic products addressing such targets. In some cases, patents have issued from these applications. In addition, many companies and institutions have well-established patent portfolios directed to common techniques, methods and means of developing, producing and manufacturing pharmaceutical products. These or other companies or institutions could bring legal actions against us or our collaborators for damages or to stop us or our collaborators from engaging in certain nonclinical or clinical development activities or from manufacturing and marketing therapeutic products that allegedly infringe their patent rights. If any of these actions are successful, in addition to our potential liability for damages, these entities would likely require us or our collaborators to obtain a license in order to continue engaging in the infringing activities or to manufacture or market the infringing therapeutic products or may force us to terminate such activities or manufacturing and marketing efforts.

We may deem it advisable to pursue litigation against others to enforce our patents and intellectual property rights and may be the subject of litigation brought by third parties to enforce their patent and intellectual property rights. In addition, we may become involved in litigation based on intellectual property indemnification undertakings that we have given to certain of our collaborators. Patent litigation is expensive and requires substantial amounts of management attention. The eventual outcome of any such litigation is uncertain and involves substantial risks.

We believe that there will continue to be significant litigation in our industry regarding patent and other intellectual property rights. We have expended and many of our competitors have expended and are continuing to expend significant amounts of time, money and management resources on intellectual property litigation. If we become involved in future intellectual property litigation, it could consume a substantial portion of our resources and could negatively affect our results of operations.

Data breaches and cyber-attacks could compromise our intellectual property or other sensitive information and cause significant damage to our business and reputation.

In the ordinary course of our business, we collect, maintain and transmit sensitive data on our networks and systems, including our intellectual property and proprietary or confidential business information (such as research data and personal information) and confidential information with respect to our customers, clinical trial patients and our business partners. We have also outsourced significant elements of our information technology infrastructure and, as a result, third parties may or could have access to our confidential information. The secure maintenance of this information is critical to our business and reputation. We believe that companies have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access. These threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state-sponsored attack and motive (including corporate espionage). Cyber threats may be generic, or they may be custom-crafted against our information systems. Our network and storage applications and those of our vendors may be subject to unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. It is often difficult to anticipate or immediately detect such incidents and the damage caused by such incidents. These data breaches and any unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose sensitive business information. A data security breach could also lead to public exposure of personal information of our clinical trial patients, customers and others. Cyber-attacks could cause us to incur significant remediation costs, result in product development delays, disrupt key business operations and divert attention of management and key information technology resources. Our network security and data recovery measures

and those of our vendors may not be adequate to protect against such security breaches and disruptions. These incidents could also subject us to liability, expose us to significant expense and cause significant harm to our reputation and business.

We may be subject to damages resulting from claims that we, our employees or independent contractors have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees and independent contractors were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, independent contractors or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. 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 divert management's attention. If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key research personnel and/or their work product could hamper or prevent our ability to commercialize certain drug candidates, which could severely harm our business.

Risks Related to Employees and Facilities Operations

If we are unable to manage our growth, our business, financial condition, results of operations and prospects may be adversely affected.

We have experienced and expect to continue to experience growth in the number of our employees and in the scope of our operations. This growth places significant demands on our management, operational and financial resources, and our current and planned personnel, systems, procedures and controls may not be adequate to support our growth. To effectively manage our growth, we must continue to improve existing, and implement new, operational and financial systems, procedures and controls and must expand, train and manage our growing employee base, and there can be no assurance that we will effectively manage our growth without experiencing operating inefficiencies or control deficiencies. We expect that we may need to increase our medical, clinical, commercial and other personnel, and recruiting and retaining qualified individuals is difficult. If we are unable to manage our growth effectively, or are unsuccessful in recruiting qualified personnel when advisable, our business, financial condition, results of operations and prospects may be adversely affected.

The loss of key personnel or the inability to attract and retain additional personnel could impair our ability to operate and expand our operations.

We are highly dependent upon the principal members of our management, as well as medical, clinical and commercial staff, the loss of whose services might adversely impact the achievement of our objectives. Retaining and, where advisable, recruiting qualified medical, clinical and commercial personnel will be critical to support activities related to successfully executing on our commercial plan for XERMELO and advancing our nonclinical and clinical development programs for telotristat ethyl, sotagliflozin, LX9211, LX2761 and our other drug candidates. Competition is intense for experienced medical, clinical and commercial personnel, and we may be unable to retain or recruit such personnel with the expertise or experience necessary to allow us to successfully develop and commercialize our products. Further, all of our employees are employed "at will" and, therefore, may leave our employment at any time.

Facility security breaches may disrupt our operations, subject us to liability and harm our operating results.

Any break-in or trespass of our facilities that results in the misappropriation, theft, sabotage or any other type of security breach with respect to our proprietary and confidential information, including research or clinical data, or that results in damage to our equipment and assets could subject us to liability and have a material adverse impact on our business, operating results and financial condition.

Our facilities are located near coastal zones, and the occurrence of a hurricane or other disaster could damage our facilities and equipment, which could harm our operations.

Our facilities are located in The Woodlands, Texas and Basking Ridge, New Jersey, and therefore our facilities are vulnerable to damage from hurricanes. We are also vulnerable to damage from other types of disasters, including fire, floods, power loss, communications failures, terrorism and similar events and any insurance we may maintain may not be adequate to cover our losses. If any disaster were to occur, our ability to operate our business at our facilities could be seriously, or potentially completely, impaired.

Risks Related to Environmental and Product Liability

We have used hazardous chemicals and radioactive and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes have historically involved the controlled use of hazardous materials, including chemicals and radioactive and biological materials. Our operations have produced hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may face liability for any injury or contamination that results from our use or the use by third parties of these materials, and such liability may exceed our insurance coverage and our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

In addition, our collaborators may use hazardous materials in connection with our collaborative efforts. In the event of a lawsuit or investigation, we could be held responsible for any injury caused to persons or property by exposure to, or release of, these hazardous materials used by these parties. Further, we may be required to indemnify our collaborators against all damages and other liabilities arising out of our development activities or products produced in connection with these collaborations.

Our business has a substantial risk of product liability and we face potential product liability exposure far in excess of our limited insurance coverage.

We may be held liable if XERMELO or any other product that we or our collaborators develop or commercialize, or any product that is made with the use or incorporation of any of our technologies, causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Regardless of merit or eventual outcome, product liability claims could result in decreased demand for our products and product candidates, injury to our reputation, withdrawal of patients from our clinical trials, product recall, substantial monetary awards to third parties and the inability to commercialize any products that we may develop. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling or testing our products. We have obtained limited product liability insurance coverage for our clinical trials and commercial activities. However, our insurance may not reimburse us or may not be sufficient to reimburse us for expenses or losses we may suffer. Moreover, if insurance coverage becomes more expensive, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. On occasion, juries have awarded large judgments in class action lawsuits for claims based on drugs that had unanticipated side effects. In addition, the pharmaceutical and biotechnology industries, in general, have been subject to significant medical malpractice litigation. A successful product liability claim or series of claims brought against us could harm our reputation and business.

Risks Related to Our Common Stock

Invus, L.P., Invus C.V. and their affiliates own a controlling interest in our outstanding common stock and may have interests which conflict with those of our other stockholders.

Invus, L.P. and Invus C.V., which we collectively refer to as Invus, and their affiliates currently own approximately 61.0% of the outstanding shares of our common stock and are thereby able to control the election and removal of our directors and determine our corporate and management policies, including potential mergers or acquisitions, asset sales, the amendment of our articles of incorporation or bylaws and other significant corporate transactions. This concentration of ownership may delay or deter possible changes in control of our company, which may reduce the value of an investment in our common stock. The interests of Invus and its affiliates may not be aligned with the interests of other holders of our common stock.

Invus has additional rights under our stockholders' agreement with Invus, L.P. relating to the membership of our board of directors, which provides Invus with substantial influence over significant corporate matters.

Under our stockholders' agreement with Invus, L.P., Invus has the right to designate a number of directors equal to the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates, rounded up to the nearest whole number of directors. Invus has designated three of the nine current members of our board of directors. While Invus has not presently exercised its director designation rights in full, it may exercise them at any time in the future in its sole discretion. To facilitate the exercise of such rights, we have agreed, upon written request from Invus, to take all necessary steps in accordance with our obligations under the stockholders' agreement to (1) increase the number of directors to the number specified by Invus (which number shall be no greater than reasonably necessary for the exercise of Invus' director designation rights under the

stockholders' agreement) and (2) cause the appointment to the newly created directorships of directors so designated by Invus pursuant to its rights under the stockholders' agreement.

Invus also has the right to require proportionate representation of Invus-appointed directors on the audit, compensation and corporate governance committees of our board of directors, subject to certain restrictions. Invus-designated directors currently serve as one of the three members of each of the compensation committee and the corporate governance committee of our board of directors. No Invus-designated directors currently serve on the audit committee of our board of directors.

The provisions of the stockholders' agreement relating to Invus' rights to designate members of our board of directors and its audit, compensation and corporate governance committees will terminate if the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%. Invus also has the right to terminate these provisions at any time in its discretion.

Our stock price may be extremely volatile.

The trading price of our common stock has been highly volatile, and we believe the trading price of our common stock will remain highly volatile and may fluctuate substantially due to factors such as the following, many of which we cannot control:

- the commercial success of XERMELO and the revenues we generate from sales of XERMELO;
- adverse results or delays in our or our collaborators' clinical trials;
- the timing and achievement of milestones under our collaboration agreements;
- the announcement of FDA approval or non-approval, or delays in the FDA review process, of our or our collaborators' drug candidates or those of our competitors or actions taken by regulatory agencies with respect to our, our collaborators' or our competitors' clinical trials;
- actions taken by regulatory agencies with respect to XERMELO, sotagliflozin, LX9211, LX2761 and our other drug candidates;
- the announcement of new products by our competitors;
- quarterly variations in our or our competitors' results of operations;
- developments in our relationships with our collaborators, including conflicts, litigation or the termination or modification of our agreements;
- the announcement of an in-licensed drug candidate or strategic acquisition;
- litigation, including intellectual property infringement and product liability lawsuits, involving us;
- failure to achieve operating results projected by securities analysts;
- changes in earnings estimates or recommendations by securities analysts;
- the satisfaction of outstanding debt obligations or entry into new financing arrangements;
- developments in the biotechnology or pharmaceutical industry;
- sales of large blocks of our common stock or sales of our common stock by our executive officers, directors and significant stockholders;
- departures of key personnel or board members;
- FDA or international regulatory actions;
- third-party coverage and reimbursement policies;

- disposition of any of our drug programs or other technologies; and
- other factors, including general market, economic and political conditions and other factors unrelated to our operating performance or the operating performance of our competitors.

These factors may materially adversely affect the market price of our common stock. In addition, the stock markets in general, and the markets for biotechnology and pharmaceutical stocks in particular, have historically experienced significant volatility that has often been unrelated or disproportionate to the operating performance of particular companies. For example, negative publicity regarding drug pricing and price increases by pharmaceutical companies has negatively impacted, and may continue to negatively impact, the markets for biotechnology and pharmaceutical stocks. Likewise, the broader financial markets could experience significant volatility that could also negatively impact the markets for biotechnology and pharmaceutical stocks. These broad market fluctuations have adversely affected and may in the future adversely affect the trading price of our common stock. Excessive volatility may continue for an extended period of time.

In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs and divert management's attention and resources, which could have a material and adverse effect on our business.

We are subject to securities litigation, which is expensive and could divert management attention.

Companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation and we are currently a target of this type of litigation. On January 28, 2019, a purported securities class action complaint captioned Daniel Manopla v. Lexicon Pharmaceuticals, Inc., Lonnel Coats and Jeffrey L. Wade was filed against us, and certain of our officers in the U.S. District Court for the Southern District of Texas, Houston Division. The lawsuit purports to be a class action brought on behalf of purchasers of our securities during the period from March 11, 2016 through January 17, 2019. The complaint alleges that the defendants violated federal securities laws by making materially false and misleading statements and/or omissions concerning data from our Phase 3 clinical trials of sotagliflozin in type 1 diabetes patients and the prospects of FDA approval of sotagliflozin for the treatment of type 1 diabetes. The complaint purports to assert claims for violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder. The complaint seeks, on behalf of the purported class, an unspecified amount of monetary damages, interest, fees and expenses of attorneys and experts, and other relief. This case, and other litigation of this type, could result in substantial costs and diversion of management's attention and resources, which could adversely impact our business. Any adverse determination in litigation could also subject us to significant liabilities.

Future sales of our common stock, or the perception that such sales may occur, may depress our stock price.

A substantial number of shares of our common stock is reserved for issuance upon conversion of notes evidencing our current indebtedness, upon the exercise of stock options and upon vesting of restricted stock units. If our stockholders sell substantial amounts of our common stock (including shares issued upon the conversion of notes, exercise of stock options or vesting of restricted stock units) in the public market, or if the market perceives that such sales may occur, the market price of our common stock could fall and it may become more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem appropriate. For example, following an acquisition, a significant number of shares of our common stock held by new stockholders may become freely tradable or holders of registration rights could cause us to register their shares for resale. Sales of these shares of common stock held by existing stockholders could cause the market price of our common stock to decline.

Conversion of our 5.25% Convertible Senior Notes due 2021 may dilute the ownership interest of our existing stockholders, including holders who had previously converted their notes, or may otherwise depress the price of our common stock.

The conversion of some or all of our 5.25% Convertible Senior Notes due 2021 will dilute the ownership interests of existing stockholders to the extent we deliver shares upon conversion of any of the notes. Any sales in the public market of the common stock issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of the notes may encourage short selling by market participants because the conversion of the notes could be used to satisfy short positions, or anticipated conversion of the notes into shares of our common stock could depress the price of our common stock.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our stock or publish inaccurate or u