

HERE. NOW. NEXT...

ANNUAL  
REPORT  
2023



TO OUR SHAREHOLDERS

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2023 was a transformative year for Lexicon as we commercially launched INPEFA<sup>®</sup> (sotagliflozin) within weeks of its approval by the U.S. Food and Drug Administration (FDA) while simultaneously continuing the advancement of our innovative research and development pipeline.

This journey began with our Genome5000 program, a 10-year project in which our scientists gained foundational insights into the human genome by discovering the functions of approximately 5,000 genes in mammalian physiology and behavior.

Through this program, we identified more than 100 targets with significant therapeutic potential across a wide range of diseases and focused our drug discovery and development efforts on those targets with the most promising profiles. We have always followed the science, which has led us **here to this moment**.

We have thus far advanced two compounds from our own discovery efforts, through preclinical and clinical development and into market – most recently INPEFA, an inhibitor of SGLT1 and SGLT2 which was approved by the FDA in May 2023 with a broad label for heart failure. We have built a fully-integrated commercial team consisting of sales, marketing, market access and commercial operations who are now promoting INPEFA to prescribers across the United States.

**Now is also the time** to elevate additional treatment options for patients in areas of high unmet medical need, so our talented team has remained focused on advancing the other important drug programs in our pipeline.

We are enrolling patients in a Phase 2b clinical trial of LX9211 in diabetic peripheral neuropathic pain (DPNP), with top-line results expected in the second quarter of 2025. LX9211 is an inhibitor of AAK1, which represents a novel, non-opioid approach to treating DPNP and presents an opportunity to become the first drug with a new mechanism of action approved for the treatment of neuropathic pain in more than two decades.

Our ongoing commitment to following the science also keeps us **looking ahead to what's next**.

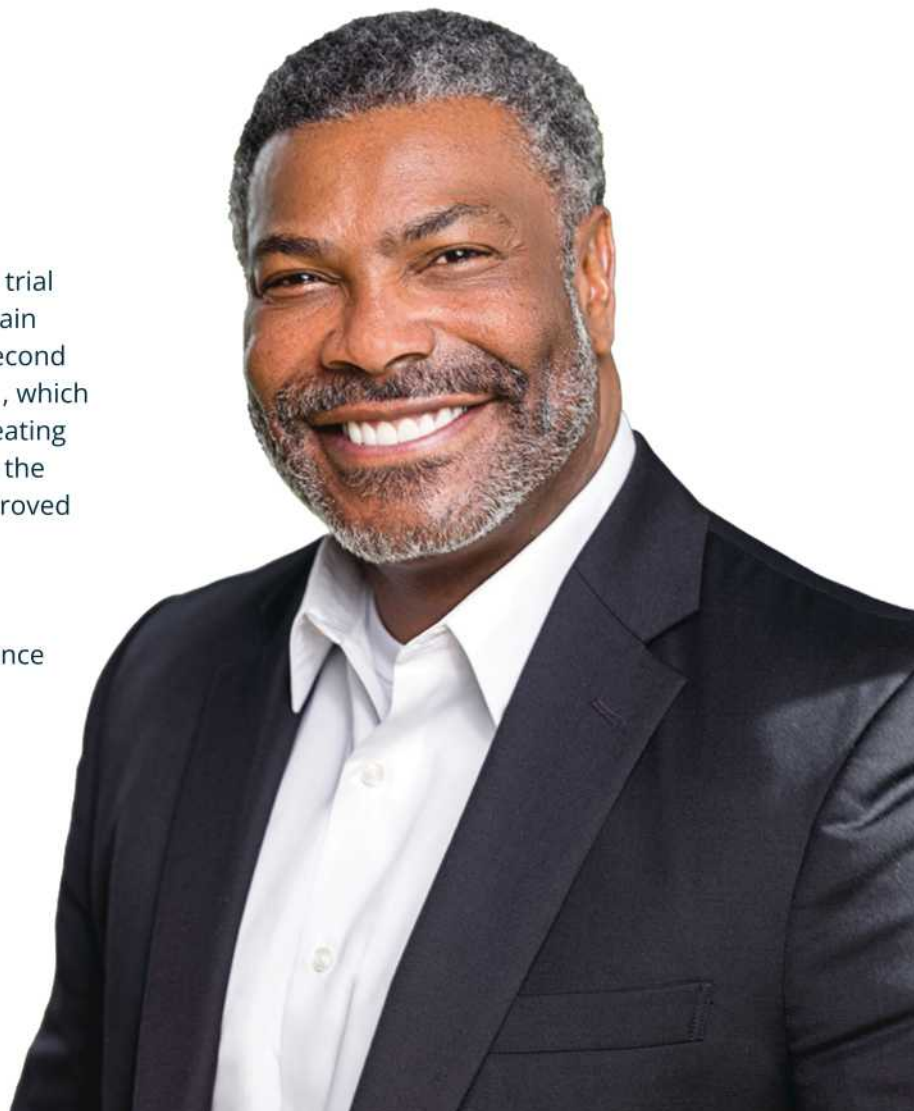
We are preparing for Phase 3 development of sotagliflozin in hypertrophic cardiomyopathy (HCM), an area of high unmet need with very few treatments in development. Following feedback from the FDA, we are preparing to resubmit our New Drug Application (NDA) for sotagliflozin as an adjunct to insulin therapy in patients with type 1 diabetes and chronic kidney disease. We are conducting preclinical development of the lead compound in our LG985 program for obesity and weight management and continuing to evaluate other new and innovative opportunities to address high unmet medical needs.

2023 was a pivotal year for our company and 2024 presents even greater opportunity. Thank you for your continued support,



**Lonnel Coats**

Chief Executive Officer and Director





FORM 10K...



**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549  
FORM 10-K**

(Mark One)

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

For the Fiscal Year Ended **December 31, 2023**

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**

(State or Other Jurisdiction of Incorporation or Organization)

**76-0474169**

(I.R.S. Employer Identification Number)

**2445 Technology Forest Blvd., 11th Floor**

**The Woodlands, TX 77381**

(Address of Principal Executive Offices and Zip Code)

**(281) 863-3000**

(Registrant's Telephone Number, Including Area Code)

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

<u>Title of Each Class</u>	<u>Trading Symbol(s)</u>	<u>Name of Each Exchange on which Registered</u>
Common Stock, par value \$0.001 per share	LXX	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  No

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  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes  No

Indicate by check mark 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  Accelerated filer  Non-accelerated filer  Smaller reporting company  Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Securities Exchange Act of 1934.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

If securities are registered pursuant to Section 12(b) of the Securities Exchange Act of 1934, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

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   
No

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 \$273.7 million, based on the closing price of the common stock on the Nasdaq Global Select Market on June 30, 2023 of \$2.29 per share. For purposes of the preceding sentence only, our directors, executive officers and controlling stockholders are assumed to be affiliates. As of March 21, 2024, 246,236,753 shares of common stock were outstanding.

#### **Documents Incorporated by Reference**

Certain sections of the registrant's definitive proxy statement relating to the registrant's 2024 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, 2023, are incorporated by reference into Part III of this annual report on Form 10-K.

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# Lexicon Pharmaceuticals, Inc.

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The Lexicon name and logo and INPEFA<sup>®</sup> are registered trademarks of Lexicon Pharmaceuticals, Inc. INPEFA Together<sup>™</sup> is a trademark of Lexicon Pharmaceuticals, Inc.

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

### **Factors Affecting Forward-Looking Statements**

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,” “should” or “will” or the 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

We are a biopharmaceutical company with a mission of pioneering medicines that transform patients' lives. We are devoting most of our resources to the commercialization of our approved drug, INPEFA<sup>®</sup> (sotagliflozin), for heart failure and the research and development of our most advanced drug candidates:

- We are commercializing INPEFA, an orally-delivered small molecule drug, in the United States to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visits in adults with heart failure or type 2 diabetes mellitus, chronic kidney disease, or CKD, and other cardiovascular risk factors.

We are separately pursuing regulatory approval of sotagliflozin as a treatment for type 1 diabetes. The U.S. Food and Drug Administration, or FDA, issued a complete response letter regarding our New Drug Application, or NDA, for sotagliflozin in type 1 diabetes in March 2019, which we appealed. Following FDA feedback from recent discussions, we are now preparing to resubmit our NDA for patients with type 1 diabetes and CKD. We have reported positive results from three Phase 3 clinical trials of sotagliflozin in type 1 diabetes.

We are also developing sotagliflozin as a treatment for hypertrophic cardiomyopathy, or HCM, and are preparing to initiate a Phase 3 clinical trial of sotagliflozin in HCM.

- We are developing LX9211, an orally-delivered small molecule drug candidate, as a treatment for neuropathic pain. We are conducting a Phase 2b clinical trial of LX9211 in diabetic peripheral neuropathic pain, or DPNP, and have received Fast Track designation from the FDA for development of LX9211 in that indication. We have reported positive results from a Phase 2 clinical trial of LX9211 in DPNP and top-line results from a separate Phase 2 clinical trial of LX9211 in post-herpetic neuralgia which also demonstrated evidence of effect.
- We are conducting preclinical development of LX9851, an orally-delivered small molecule drug candidate, as a treatment for obesity and tool for weight management.
- We are conducting preclinical research and development and preparing to conduct clinical development of compounds from a number of additional drug programs originating from our internal drug discovery efforts.

INPEFA, LX9851 and compounds from a number of additional drug programs originated from our own internal drug discovery efforts, and LX9211 originated from our collaborative neuroscience drug discovery efforts with Bristol-Myers Squibb. Our 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 have worked both independently and through collaborations and strategic alliances with third parties to capitalize on our drug target discoveries and research and development programs. We seek to retain exclusive or co-exclusive rights to the benefits of certain research 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 with respect to the research, development and commercialization of certain of our drug candidates, particularly with respect to commercialization in territories outside the United States or 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.

We were incorporated in Delaware in July 1995, commenced operations in September 1995 and were listed on The Nasdaq Global Select Market in April 2000. Our corporate headquarters are located at 2445 Technology Forest Blvd., 11th Floor, 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](http://www.lexpharma.com) as soon as reasonably practicable after the filing of

those reports with the Securities and Exchange Commission, or the SEC. Information found on our website should not be considered part of this annual report on Form 10-K. Alternatively, you may access these reports on the SEC's website at [www.sec.gov](http://www.sec.gov).

## **Drugs and Drug Candidates**

We are devoting most of our resources to the commercialization of INPEFA and the research and development of sotagliflozin, LX9211 and LX9851. We have also advanced a number of additional compounds into various stages of preclinical research and development.

### ***INPEFA (sotagliflozin)***

INPEFA (sotagliflozin) is an orally-delivered small molecule compound that we are commercializing for heart failure and developing for type 1 diabetes and HCM. Our scientists identified the targets of sotagliflozin, sodium-glucose cotransporter type 1, or SGLT1, and sodium-glucose cotransporter type 2, or SGLT2, in our target discovery efforts based on their discovery that mice lacking SGLT1, SGLT2 or both exhibited favorable phenotypes across multiple measures of metabolism and glucose control in preclinical models. Preclinical studies of sotagliflozin demonstrated that compounds inhibiting both targets had a favorable preclinical profile relative to compounds selective for SGLT2.

We use "INPEFA" when referring to our FDA-approved drug and "sotagliflozin" when referring to our development of INPEFA for type 1 diabetes, HCM and any additional indications.

#### *Heart Failure*

We commercially launched INPEFA, a once-daily oral tablet, following regulatory approval in the United States in May 2023 to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure or type 2 diabetes, CKD, and other cardiovascular risk factors.

We have a fully integrated commercial team consisting of sales, marketing, market access and commercial operations functions. Our sales force of approximately 150 cardiovascular specialty representatives is focused on promoting INPEFA to high-volume prescribers and institutions in the United States, concentrating their efforts on cardiologists specializing in heart failure. We have also built an internal medical affairs function with responsibility for responding to external inquiries regarding the appropriate use of INPEFA with regularly updated and well-substantiated scientific and medical information. We principally sell INPEFA to a limited number of major wholesalers, as well as selected regional wholesalers, most of whom in turn resell INPEFA to retail pharmacies, hospitals, government agencies and other institutions for subsequent resale to patients and healthcare providers.

Major cardiology societies in the United States and elsewhere have issued treatment guidelines recommending the use of SGLT inhibitors, such as INPEFA, as an important element in the standard of care for treating heart failure. SGLT inhibitors are the only class of therapy recommended by such treatment guidelines as a foundational treatment for heart failure regardless of left ventricular ejection fraction, with our Phase 3 SOLOIST-WHF study of INPEFA specifically cited as part of the basis for such recommendation.

To ensure that all eligible patients in the United States have appropriate access to INPEFA, we have established a comprehensive reimbursement and support program called INPEFA Together™. Through INPEFA Together, 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, INPEFA Together is designed to provide comprehensive reimbursement support services, such as benefits investigation and, if needed, appeals support.

#### *Type 1 Diabetes*

The FDA issued a complete response letter in March 2019 regarding our NDA for sotagliflozin in type 1 diabetes and confirmed that position in denying two appeals of the complete response letter in November 2019 and March 2020. At our request, the FDA issued a public Notice of Opportunity for Hearing, or NOOH, in March 2021 on whether there are grounds for denying approval of our NDA. We and the FDA agreed to pause the NOOH proceedings in September 2023 in order to engage in discussions regarding a potential path forward for the approval of sotagliflozin in type 1 diabetes. Following FDA feedback from such discussions, we are now preparing to resubmit our NDA for sotagliflozin as an adjunct to insulin therapy for patients with type 1 diabetes and CKD.

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 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.

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.

### *Hypertrophic Cardiomyopathy*

We are preparing to initiate a Phase 3 clinical trial evaluating the safety and tolerability of sotagliflozin and its effects on HCM. The trial is expected to enroll approximately 500 patients experiencing obstructive or non-obstructive HCM in a randomized, double-blind, placebo-controlled study of a 400mg once daily dose of sotagliflozin over a 26-week treatment period. Doses for patients not tolerating treatment may be reduced to 200mg beginning at week 4. The primary efficacy endpoint under evaluation will be change from baseline in the patient-reported Kansas City Cardiomyopathy Questionnaire, or KCCQ, clinical summary score at 26 weeks, with secondary endpoints including change in KCCQ total symptom score and New York Heart Association class improvement at 26 weeks.

### **LX9211**

LX9211 is an orally-delivered small molecule compound that we are developing as a treatment for neuropathic pain. We have received Fast Track designation from the FDA for development of LX9211 in DPNP. Our scientists identified the target of LX9211, adapter-associated kinase 1, or AAK1, in our target discovery efforts based on their discovery that mice lacking AAK1 exhibited increased resistance to induced neuropathic pain in preclinical models. LX9211 and another development candidate were discovered by scientists working within our drug discovery alliance with Bristol-Myers Squibb from which we hold exclusive development and commercialization rights. Preclinical studies of LX9211 demonstrated central nervous system penetration and reduction in pain behavior in models of neuropathic pain without affecting opiate pathways.

We are conducting a Phase 2b clinical trial, PROGRESS, evaluating the safety and tolerability of LX9211 and its effects on DPNP. The trial is expected to enroll approximately 416 patients with type 1 or type 2 diabetes and experiencing moderate to severe DPNP in a randomized, double-blind, placebo-controlled study evaluating three treatment groups receiving once daily LX9211 doses of 10mg, 20mg or 20mg for seven days followed by 10mg thereafter. The effects of LX9211 will be assessed over a 16-week evaluation period, which includes a screening period of up to two weeks and a blinded evaluation period of 14 weeks. The primary efficacy endpoint under evaluation is the reduction in an average daily pain score at 8 weeks, with secondary endpoints including reduction in burning pain and reduction in pain interference on sleep at 8 weeks. Certain patient-reported outcome measures will also be assessed.

We have completed two Phase 2 clinical trials evaluating the safety and tolerability of LX9211 and its effects on neuropathic pain.

Our RELIEF-DPN-1 Phase 2 clinical trial enrolled 319 patients experiencing DPNP in a randomized, double-blind, placebo-controlled study of LX9211 evaluating three treatment groups receiving an initial loading dose of 100mg or 200mg of LX9211 or placebo, followed by once daily doses of 10mg or 20mg of LX9211 or placebo, respectively. The effects of LX9211 were assessed over an 11-week evaluation period, which included a 5-week placebo run-off period following the initial 6-week treatment period. The primary efficacy endpoint under evaluation in the study was the change from baseline to week 6 in average daily pain score, or ADPS, based on the 11-point numerical rating scale in patients treated with LX9211 compared with placebo. Data from the study showed a statistically significant reduction from baseline to week 6 in ADPS of 1.39 points in the low dose arm, compared to 0.72 in the placebo arm ( $p=0.007$  versus placebo), meeting the study's primary endpoint. The high dose arm demonstrated a reduction from baseline to week 6 in ADPS of 1.27 points ( $p=0.030$  versus placebo), narrowly missing statistical significance. Consistent and statistically significant benefits in burning pain, pain interference with sleep and other measures of particular importance in DPNP were also observed in both LX9211 treatment arms as compared to placebo during the initial 6-week treatment period. During the blinded 5-week placebo run-off period, there was a gradual tapering of efficacy in both treatment arms with no evidence of rebound pain or withdrawal symptoms. Adverse events were more frequent in the LX9211 treatment arms and at the higher dose during the initial 6-week treatment period, with the most common being dizziness, headache and nausea and nearly all being reported as mild or moderate. There were no observed differences in drug-related treatment-emergent adverse events between the treatment and placebo arms during the run-off period, and no drug-related serious adverse events or deaths were reported in the study.

Our RELIEF-PHN-1 Phase 2 clinical trial enrolled 79 patients experiencing post-herpetic neuralgia, or PHN, in a randomized, double-blind, placebo-controlled study of LX9211 evaluating two treatment groups receiving an initial loading

dose of 200mg of LX9211 or placebo, followed by once daily doses of 20mg of LX9211 or placebo, respectively. The effects of LX9211 were assessed over an 11-week evaluation period, which included a 5-week placebo run-off period following the initial 6-week treatment period. The primary efficacy endpoint under evaluation in the study was the change from baseline to week 6 in ADPS based on the 11-point numerical rating scale in patients treated with LX9211 compared with placebo. Topline data from the study showed a reduction from baseline to week 6 in ADPS of 2.42 points in the LX9211 arm, compared to a reduction of 1.62 points in the placebo arm ( $p=0.120$  versus placebo), missing statistical significance in the study's primary endpoint but demonstrating evidence of effect. Separation of LX9211 from placebo on ADPS was observed at week 1 and maintained consistently thereafter, with an average placebo-adjusted reduction over the 6-week treatment period of 0.80 points ( $p=0.031$  versus placebo). Adverse events were consistent with those observed in our RELIEF-DPN-1 clinical trial, with dizziness as the most commonly reported and the most frequently associated with patient dropouts from the study. No drug-related serious adverse events or deaths were reported in the study.

### ***LX9851***

We are developing LX9851, an orally-delivered small molecule drug candidate, for the treatment of obesity and as a tool for weight management. We have commenced preclinical studies of the compound and its associated back-up molecules and are preparing to initiate clinical development. Our scientists identified the target of LX9851 in our target discovery efforts based on their discovery that mice lacking such target exhibited favorable phenotypes across multiple measures of metabolic syndrome in preclinical models, including resistance to diet-induced obesity and improved body composition.

### ***Additional Research and Development Programs***

We are conducting preclinical research and development of compounds from a number of additional drug programs originating from our internal drug discovery efforts. Those 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 and Strategic Alliances**

We have worked both independently and through collaborations and strategic alliances with third parties to capitalize on our drug target discoveries and research and development programs. Consistent with this approach, we seek to retain exclusive rights to the benefits of certain research 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 INPEFA in the United States. We seek to collaborate with other pharmaceutical and biotechnology companies with respect to the research, development and commercialization of certain of our drug candidates, particularly with respect to commercialization in territories outside the United States or 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.

### ***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, for which we hold exclusive development and commercialization rights under the alliance. 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.

LX9211 and another development compound acting through AAK1 were discovered by scientists working within our alliance with Bristol-Myers Squibb. 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.

### ***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 commercial production and distribution of INPEFA or clinical production and distribution of sotagliflozin, LX9211, LX9851 or our other 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 INPEFA and clinical supplies of our drug candidates, and will continue to do so for the foreseeable future. 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 inspection 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 quantities of API sufficient to meet our commercial and clinical requirements. We store API at third-party facilities in North America, and provide appropriate amounts to third-party drug product contract manufacturers in North America who then manufacture, package and label our specified quantities of finished commercial goods for INPEFA and clinical goods for our drug candidates. 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 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. We believe that our current manufacturing network has the appropriate capacity to produce sufficient commercial quantities of INPEFA and clinical quantities of sotagliflozin, LX9211, LX9851 and our other drug candidates.

For business continuity reasons, we are establishing a backup supplier for the API necessary to manufacture commercial supplies of INPEFA. We rely on a sole source third party drug product contract manufacturer in the United States to manufacture, package and label finished drug product for commercial distribution of INPEFA, and are in the process of evaluating a backup supplier for our commercial INPEFA drug product. 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 INPEFA.

### **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 have and may in the future succeed in developing products earlier than we do and obtaining approvals from the FDA or other regulatory agencies for those products more rapidly than we do. In addition, our competitors may develop products that are more effective than those we develop or commercialize 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 drugs 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 commercialization or clinical development than are our own drugs and 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 INPEFA, that employ the same or similar mechanisms of action.

We believe that our ability to successfully compete with these competitive products currently on the market and potentially competitive drug candidates 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 commercialization and development activities.

Our principal competition for INPEFA for the treatment of heart failure includes drugs which selectively inhibit SGLT2, or selective SGLT2 inhibitors, which have gained or may gain regulatory approval for the treatment of heart failure. Such selective SGLT2 inhibitors include dapagliflozin and empagliflozin, currently marketed for the treatment of heart failure by AstraZeneca and through an alliance between Boehringer Ingelheim and Eli Lilly, respectively. Such competition also includes, to some extent, other classes of drugs used in the treatment of heart failure, such as the combination drug sacubitril/valsartan, currently marketed for the treatment of heart failure by Novartis, and vericiguat, currently marketed for the treatment of heart failure by Merck.

We expect that our principal competition for sotagliflozin in the treatment of type 1 diabetes would include established insulin therapies, and potentially, to some extent, selective SGLT2 inhibitors currently being prescribed off-label. Such selective SGLT2 inhibitors include dapagliflozin, empagliflozin and canagliflozin, currently marketed for the treatment of type 2 diabetes by AstraZeneca, through an alliance between Boehringer Ingelheim and Eli Lilly, and by Janssen (a subsidiary of Johnson & Johnson), respectively.

We expect that our principal competition for sotagliflozin in the treatment of hypertrophic cardiomyopathy would include generic beta blockers and calcium channel blockers and cardiac myosin inhibitors, such as mavacamten marketed by Bristol Myers Squibb and aficamten in development by Cytokinetics.

We expect that our principal competition for LX9211 for the treatment of DPNP would include duloxetine and pregabalin, which are currently marketed for the treatment of DPNP by Eli Lilly and Pfizer, respectively, and are also available as generics. We also expect that we would experience competition from gabapentin, which is available as a generic and is frequently prescribed off-label for the treatment of DPNP.

We expect that our principal competition for LX9851 would include drugs approved for weight loss, including GLP-1 analogs and similar drugs.

## Government Regulation

### *Regulation in the United States*

The development, manufacture and sale of pharmaceutical products are subject to extensive regulation by United States 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 Investigational New Drug application, or 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 an 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 the 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 cGMP 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 the 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 Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act of 2010, or the ACA, 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 certain advanced non-physician health care practitioners and teaching hospitals made in the previous calendar year, as well as ownership and investment interests held by physicians and their immediate family members. 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.

### ***Healthcare Reform***

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of pharmaceutical products, restrict or regulate post-approval activities, and affect the ability to profitably sell pharmaceutical products that obtain marketing approval. The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of drug candidates. Moreover, among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access.

For example, the ACA has had a significant impact on the health care industry in the United States. The ACA was designed to expand coverage for the uninsured while at the same time contain overall healthcare costs. With regard to biopharmaceutical products, the ACA, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program. Additionally, the Creating and Restoring Equal Access to Equivalent Samples Act of 2019, or the CREATES Act, aimed to address the concern articulated by both the FDA and others in the industry that some brand manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a risk evaluation and mitigation strategies, or REMS, program for certain products, to deny generic product developers access to samples of brand products. Because generic product developers need samples to conduct certain comparative testing required by the FDA, some have attributed the inability to timely obtain samples as a cause of delay in the entry of generic products. To remedy this concern, the CREATES Act established a private cause of action that permits a generic product developer to sue the brand manufacturer to compel it to furnish the necessary samples on "commercially reasonable, market-based terms." Whether and how generic product developments will use this new pathway, as well as the likely outcome of any legal challenges to provisions of the CREATES Act, remain highly uncertain and its potential effects on future competition are unknown.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA and we expect there will be additional challenges and amendments to the ACA in the future. Members of the United States Congress have indicated that they may continue to seek to modify, repeal or otherwise invalidate all, or certain provisions of, the ACA. For example, the Tax Cuts and Jobs Act, among other things, removed penalties for not complying with the ACA's individual mandate to carry health insurance, commonly referred to as the "individual mandate." It is unclear how this and other efforts to repeal and replace the ACA will impact the implementation of the ACA, the pharmaceutical industry more generally, and our business.

In addition, the Inflation Reduction Act of 2022, or the Inflation Reduction Act, imposed significant changes to how drugs are covered and paid for under the Medicare program, including the creation of financial penalties for drugs whose prices rise faster than the rate of inflation, redesign of the Medicare Part D program to require manufacturers to bear more of the liability for certain drug benefits, and government price-setting for certain Medicare Part D drugs, starting in 2026, and Medicare Part B drugs starting in 2028. The long-term implications of the Inflation Reduction Act remain uncertain and subject to various factors, including the manner in which the Department of Health and Human Services, or DHHS, decides to implement the statute. Many experts and analysts, both within the industry and outside, have predicted that the law will harm innovation in the pharmaceutical industry and result in fewer new treatments being developed and approved over time.

As another example, the 2021 Consolidated Appropriations Act incorporated extensive healthcare provisions and amendments to existing laws, including a requirement that all manufacturers of drugs and biological products covered under Medicare Part B report the product's average sales price to the DHHS, subject to enforcement via civil money penalties.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. DHHS has solicited feedback on some of various measures intended to lower drug prices and reduce the out of pocket costs of drugs and implemented others under its existing authority. Congress and the executive branch have each indicated that it will

continue to seek new legislative and/or administrative measures to control drug costs, making this area subject to ongoing uncertainty.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the United States Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers and other members of the health care and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services.

### ***Environmental and Worker Safety Matters***

In addition to the foregoing, our business is subject to regulation under various state and federal environmental and worker safety laws, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act, the Comprehensive Environmental Response, Compensation and Liability Act and the Toxic Substances Control Act, each as amended from time to time. These and other laws and their implementing regulations govern our manufacture, use, storage, handling, transport and disposal of various biological, chemical, radioactive and other hazardous substances used in our operations and the wastes generated by those activities. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these substances. We may face liability for any injury or contamination that results from our use or the use by third parties of those substances, and such liability may exceed our insurance coverage and our total assets. Historically, our environmental and worker safety compliance costs have not had a material adverse effect on our results of operations, but there can be no assurance that such costs will not be material in the future or that such future compliance will not have a material adverse effect on our business and operational results. The trend in environmental and occupational health and safety laws and regulations is to typically place more restrictions and limitations on activities that may adversely affect the environment or expose workers to injury. If existing regulatory requirements or enforcement policies change or new regulatory or enforcement initiatives are developed and implemented in the future, we may be required to make significant, unanticipated capital and operating expenditures.

### **Patents and Proprietary Rights**

We can 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 patent applications throughout the world that claim our drugs 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 INPEFA, crystalline forms of INPEFA, pharmaceutical compositions comprising INPEFA, 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, Brazil, Canada, China, Europe, India, Israel, Japan, Mexico, New Zealand, South Africa, and South Korea, that claim LX9211, pharmaceutical compositions comprising LX9211, and methods of its use; and
- a pending United States patent application that claims LX9851, pharmaceutical compositions comprising it, and methods of its manufacture and use.

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 each of our drugs and drug candidates. The earliest normal expiration date of our United States patents that claim INPEFA is 2028, but we have applied for an extension of patent term based on the FDA's approval of the drug. We expect that upon acceptance of that application, an additional five years will be added to the term of a patent that claims INPEFA itself, pushing its expiration date out to 2033. None of our United States patents that claim LX9211 has a normal expiration date earlier than 2035.



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.

<b><u>Name</u></b>	<b><u>Age</u></b>	<b><u>Position with the Company</u></b>
Lonnel Coats	59	Chief Executive Officer and Director
Jeffrey L. Wade	59	President and Chief Financial Officer
Brian T. Crum	51	Senior Vice President and General Counsel
Thomas A. Garner	48	Senior Vice President and Chief Commercial Officer
Craig B. Granowitz, M.D., Ph.D.	59	Senior Vice President and Chief Medical Officer
Kenneth B. Kassler-Taub, M.D.	67	Senior Vice President, Regulatory and Quality Assurance
Alan J. Main, Ph.D.	70	Executive Vice President, Innovation and Chemical Sciences
Wendy E. McDermott	53	Vice President, Human Resources
Kristen L. Alexander	56	Vice President, Finance and Accounting

*Lonnel Coats* has been our 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 Verve Therapeutics, Inc., and holds a B.S. from Oakland University.

*Jeffrey L. Wade* has been our president and chief financial officer since October 2021, having previously served in a series of finance, corporate development, administrative and legal leadership positions since joining our company in 1999. Before joining Lexicon, Mr. Wade was a partner with the law firm of Andrews & Kurth L.L.P., where he represented companies in the biotechnology, information technology and energy industries in venture capital financings, public offerings and private placements, mergers and acquisitions, collaborations and licensing, and other corporate matters. Mr. Wade is a member of the boards of directors of the Texas Healthcare and Bioscience Institute and BioHouston. He received his B.A. and J.D. from the University of Texas.

*Brian T. Crum* has been our senior vice president and general counsel since October 2021 and previously served in a series of legal leadership positions since joining our company in 2001. Mr. Crum was previously a corporate securities attorney with the law firms of Brobeck, Phleger & Harrison LLP and Andrews & Kurth L.L.P., where he represented companies in the energy and information technology industries. Mr. Crum received his B.B.A. and J.D. from the University of Texas.

*Thomas A. Garner* has been our senior vice president and chief commercial officer since October 2023. Mr. Garner previously served in a series of commercial leadership positions at Bristol-Myers Squibb Company, where he worked for more than 20 years at local, country and global levels across multiple brands and therapeutic areas before joining our company. At Bristol-Myers Squibb, he most recently served as senior vice president and head of the U.S. cardiovascular and established brand business unit from August 2022 to October 2023 and as vice president and U.S. brand lead for mavacamten from January 2019 to August 2022. Prior to joining Bristol-Myers Squibb, Mr. Garner served in various commercial roles with Eli Lilly and Company and Boehringer Ingelheim. Mr. Garner holds a BSc (Honors) degree from the Royal Agricultural University in the United Kingdom and a certification in General Management from INSEAD in France.

*Craig B. Granowitz, M.D., Ph.D.* has been our senior vice president and chief medical officer since August 2021. Dr. Granowitz previously served as chief medical officer of Amarin Corporation plc since 2016. Prior to joining Amarin, Dr. Granowitz served as senior vice president and head of global medical affairs, global human health of Merck & Co., Inc. and in a

variety of medical and commercial management positions for Schering-Plough Corporation. Dr. Granowitz received his B.A. from Dartmouth College and his M.D. and Ph.D. from Columbia University.

*Kenneth B. Kassler-Taub, M.D.* has been our senior vice president, regulatory affairs and quality assurance since October 2021 and previously served as vice president, clinical operations and in other senior capacities since joining our company in 2014. Dr. Kassler-Taub previously served in various senior clinical and medical leadership positions at Becton Dickinson and Company, where he worked for 12 years, most recently as vice president, corporate clinical development. Prior to joining Becton Dickinson, Dr. Kassler-Taub spent 14 years with Bristol-Myers Squibb Company Pharmaceutical Research Institute, where he held a variety of clinical and drug safety positions. Dr. Kassler-Taub received his B.A. from Amherst College and M.D. from the Boston University School of Medicine.

*Alan J. Main, Ph.D.* has been our executive vice president of innovation and chemical sciences since September 2020 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.

*Wendy E. McDermott* has been our vice president, human resources since January 2022. Ms. McDermott previously served as chief people officer of Rafael Pharmaceuticals, Inc. since 2019, vice president, human resources of Sanofi from 2017 to 2019 and in a variety of human resources positions with Sanofi, Schering-Plough Corporation and other companies in the tobacco, media and talent and event management industries. Ms. McDermott received her B.A. from State University of New York at Plattsburgh.

*Kristen L. Alexander* has been our vice president of finance and accounting and principal accounting officer since September 2021 and previously served as controller since joining our company in 2017. Ms. Alexander previously served as controller of Johnson Specialty Tools, LLC and in a variety of finance and accounting management positions for Trican Well Services, L.P., Nabors Industries Ltd. and Ernst & Young, LLP. Ms. Alexander is a certified public accountant and received her B.B.A. from the University of Oklahoma.

## **Significant Shareholders**

We have valuable relationships with Invus, L.P. and its affiliates, which we collectively refer to as Invus. Invus currently owns approximately 50% of the outstanding shares of our common stock.

## **Human Capital Resources**

As of March 21, 2024, we employed 285 persons, of whom 22 hold M.D. or Ph.D. degrees and another 73 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.

Our company culture is supported by our five core values: innovation, transparency, ownership, respect and integrity. We value a diverse workforce and proudly reflect a company culture developed with a variety of ethnic backgrounds, nationalities, races, religions, military service, sexual preferences and abilities. We are committed to promoting and maintaining an inclusive, high-performing environment where all team members embrace and leverage each other's talents and backgrounds and nourish innovative thinking in order to achieve their full potential and contribute to our success.

Our most valued resource is the collective talent and time that our employees dedicate to support and advance our mission. Accordingly, we offer our employees a comprehensive compensation and benefits package that is competitive within the industry and make investing in the growth and development of our employees an important priority. Employee development is advanced through talent management, promotions, mentoring, stretch assignments, internships, formal training, speaker series, conferences, continuing education and educational reimbursement.

## **Research and Development Expenses**

In 2023, 2022 and 2021, respectively, we incurred expenses of \$58.9 million, \$52.8 million and \$55.0 million in company-sponsored as well as collaborative research and development activities, including \$5.1 million, \$4.3 million and \$4.3 million of stock-based compensation expense in 2023, 2022 and 2021, 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.

### **Risk Factor Summary**

Below is a summary of the material risks to our business, operations and the investment in our common stock. This summary does not include all of the risks we face and you should carefully review and consider the full discussion of our risk factors below, together with the other information in this annual report on Form 10-K.

#### *Risks Related to Our Business and Industry*

- We depend heavily on the commercial success of INPEFA in heart failure. If we do not achieve commercial success with INPEFA, our business will suffer and our stock price will likely decline.
- We depend heavily on our ability to obtain regulatory approval in the United States for sotagliflozin in patients with type 1 diabetes and CKD. If we fail to obtain such regulatory approval, our business will suffer and our stock price will likely decline.
- We depend heavily on our ability to successfully complete and obtain positive results from our PROGRESS Phase 2b clinical trial of LX9211 in DPNP. If we fail to successfully complete and obtain positive results from the PROGRESS clinical trial on our expected timeline, our business will suffer and our stock price will likely decline.
- 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.
- 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.
- 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.
- Our competitors may develop products that impair the value of any products that we or our collaborators may develop.

#### *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 research and development programs.
- We may not have sufficient capital to support Phase 3 development of LX9211. If we are unable to establish a strategic collaboration or other arrangement for that purpose, our capital needs will be substantially higher and we may be unable to obtain financing sufficient to fund Phase 3 development of LX9211 on acceptable terms, or at all, and may be required to forego or reduce the scope of any such Phase 3 development program.
- We have a history of net losses, and we expect to continue to incur net losses and may not achieve or maintain profitability.

#### *Risks Related to Our Relationships with Third Parties*

- We depend on our ability to establish collaborations with pharmaceutical and biotechnology companies for the development and commercialization of our other drug candidates. If we are unable to establish such collaborations, or if pharmaceutical products are not successfully and timely developed and commercialized under such collaborations, our opportunities to generate revenues from our other drug candidates will be greatly reduced.

#### *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.

### *Risks Related to Our Employees and Facilities*

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

### *Risks Related to Environmental and Product Liability*

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

### *Risks Related to Our Common Stock*

- Invus, L.P. and its affiliates own a substantial interest in our outstanding common stock and may have interests which conflict with those of our other stockholders.
- Invus has additional rights under its stockholders' agreement relating to the membership of our board of directors and under our certificate of incorporation relating to preemptive and consent rights, which provide Invus with substantial influence over significant corporate matters.

### ***Risks Related to Our Business and Industry***

*We depend heavily on the commercial success of INPEFA in heart failure. If we do not achieve commercial success with INPEFA, 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 INPEFA for heart failure in the United States, but we cannot be certain that INPEFA will be commercially successful. Our future sales of INPEFA will depend on numerous factors, including:

- the number of patients suffering from heart failure;
- competition from dapagliflozin, empagliflozin and, to some extent, other classes of drugs used in the treatment of heart failure, such as the combination drug sacubitril/valsartan;
- the effectiveness of our commercial strategy for marketing INPEFA and our execution of that strategy, in particular the effectiveness of our efforts to obtain and maintain adequate third-party reimbursement;
- the safety profile of INPEFA, 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 commercial use of INPEFA;
- the acceptance of INPEFA by patients, the medical community and third-party payers; and
- our ability to meet the demand for commercial supplies of INPEFA and to maintain and successfully monitor commercial manufacturing arrangements for INPEFA 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 INPEFA has a competitive commercial profile, our current estimates of the revenues that INPEFA 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 INPEFA 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 INPEFA 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 ability to obtain regulatory approval in the United States for sotagliflozin in patients with type 1 diabetes and CKD. If we fail to obtain such regulatory approval, our business will suffer and our stock price will likely decline.*

We are currently preparing to resubmit our NDA for sotagliflozin as an adjunct to insulin therapy for patients with type 1 diabetes and CKD. We cannot offer any assurances that the FDA will grant marketing approval for sotagliflozin in that patient population, on acceptable timelines or at all. Furthermore, regulatory approval in the United States for sotagliflozin, even if obtained, may further limit the types of patients in which sotagliflozin may be used or otherwise require specific

warning or labeling language, such as with respect to the risk of diabetic ketoacidosis, any of which may reduce the commercial potential of sotagliflozin in type 1 diabetes. Should we fail to obtain regulatory approval in the United States or obtain regulatory approval with limits that disadvantage us as compared to competitive products, 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 ability to successfully complete and obtain positive results from our ongoing PROGRESS Phase 2b clinical trial of LX9211 in DPNP. If we fail to successfully complete and obtain positive results from such clinical trial, or if the progress of such clinical trial is delayed beyond our expected timelines, our business will suffer and our stock price will likely decline.*

We are conducting the PROGRESS Phase 2b clinical trial of LX9211 in DPNP. We cannot offer any assurances or predict with any certainty that the PROGRESS clinical trial will be successfully completed, generate positive clinical data or demonstrate a competitive commercial profile for LX9211, in any such case on our expected timeline. Should we fail to obtain positive results from the PROGRESS clinical trial, or if the PROGRESS clinical trial is not completed on our expected timeline due to delays in planned patient enrollment or otherwise, our opportunity to establish a strategic collaboration or other arrangement for the further development and commercialization of LX9211 would be negatively affected, 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, 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 preclinical 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. Negative or inconclusive results from a preclinical study or a clinical trial could cause us, our collaborators or the FDA or other equivalent foreign regulatory agencies to terminate a preclinical 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 preclinical or clinical test may fail to produce results satisfactory to the FDA or foreign regulatory authorities. Preclinical 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 cGCP requirements. 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 cGMP requirements.

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 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. 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 preclinical testing, and data obtained from preclinical 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 any 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 or our collaborators' ability to commercialize any products that we or they may develop will be highly dependent upon the extent to which such products gain market acceptance among physicians, patients, health care payers, such as commercial health insurers, Medicare and Medicaid, and the medical community. If such 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 such 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 any products that we or our collaborators may develop.*

In order to successfully commercialize any product that we or our collaborators may develop, we or they must establish or maintain an effective commercialization infrastructure supporting such product, including sales force, marketing organization and distribution capabilities. Factors that may hinder efforts to effectively establish, manage and maintain such infrastructure for 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, pharmacies, third-party manufacturers and other third parties instrumental in the commercial manufacture and distribution of such products;
- inability to establish or implement internal controls and procedures required in connection with sales of such products;
- inability of sales personnel to obtain access to or convince adequate numbers of physicians to prescribe such products; and
- potential lack of complementary products to be offered by sales personnel, which may put us or our collaborators at a competitive disadvantage relative to companies with more extensive product lines.

If we or our collaborators are unable to sustain our or their sales force, marketing infrastructure and distribution capability for such products, we may not be able to generate any product revenue, may generate increased expenses and may never become profitable.

We or our collaborators will need to expend significant time and resources to train our sales forces to be credible, persuasive and compliant in discussing such products with the physicians treating the patients indicated under the label. We or our collaborators will also need to continue to train our sales forces to ensure that a consistent and appropriate message about such products is being delivered to potential customers. If we or our collaborators are unable to effectively train our sales forces 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 such products and their proper administration, our and their ability to successfully commercialize such products could be diminished, which could have a material adverse effect on our financial condition, stock price and operations.

*If we are unable to establish adequate coverage and reimbursement from third-party payers for any products that we or our collaborators may develop, our revenues and prospects for profitability will suffer.*

Our ability to successfully commercialize any 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 the 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 such 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 products that we or our collaborators may develop in commercial quantities, which would impair our ability to commercialize such products.*

Our drug candidates other than INPEFA have been manufactured in relatively small quantities for preclinical 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 approved product 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 any such product, the regulatory approval or commercial launch of that product may be delayed or there may be a shortage in supply. Pharmaceutical products typically 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 any products that we or our collaborators may develop.*

We and our collaborators 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 any 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 Statute, which constrains our marketing practices, educational programs, pricing policies, relationships with healthcare providers or other entities, and other business activities, 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;
- 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 expenditure tracking and reporting laws, which generally require certain types of expenditures in the United States to be tracked and reported. For example, the Physician Payments Sunshine Act, among other things, imposes reporting requirements on certain manufacturers to annually report to CMS information related to payments and other transfers of value to physicians and certain advanced non-physician health care practitioners and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. 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.*

In the United States and some foreign countries, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of pharmaceutical products, restrict or regulate post-approval activities, and affect the ability to profitably sell pharmaceutical products that obtain marketing approval. The FDA’s and other regulatory authorities’ policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we otherwise may have obtained and we may not achieve or sustain profitability. Moreover, complying with any new legislation or regulatory changes could be time-intensive and expensive, resulting in a material adverse effect on our business.

For example, the Inflation Reduction Act imposed significant changes to how drugs are covered and paid for under the Medicare program, including the creation of financial penalties for drugs whose prices rise faster than the rate of inflation, redesign of the Medicare Part D program to require manufacturers to bear more of the liability for certain drug benefits, and government price-setting for certain Medicare Part D drugs, starting in 2026, and Medicare Part B drugs starting in 2028. The long-term implications of the Inflation Reduction Act remain uncertain and subject to various factors, including the manner in which the DHHS decides to implement the statute.

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, such as the Inflation Reduction Act, that may have the effect of reducing the prices that we are able to

charge for 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 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 products we or our collaborators may develop due to the increasing influence of health maintenance organizations and additional legislative proposals.

*Our competitors may develop products that impair the value of any 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. INPEFA competes and any additional 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 and commercialize products that would render INPEFA and any other products that we or our collaborators develop obsolete and noncompetitive.

For example, dapagliflozin and empagliflozin were being marketed by AstraZeneca and through an alliance between Boehringer Ingelheim and Eli Lilly, respectively, for the treatment of heart failure and certain other indications for a lengthy period in advance of INPEFA's approval. Each of those products act through SGLT2, one of the targets of INPEFA. Our principal competition for INPEFA for the treatment of heart failure includes such selective SGLT2 inhibitors which have already received or may gain regulatory approval for the treatment of heart failure, as well as other classes of drugs used in the treatment of heart failure, such as the combination drug sacubitril/valsartan, currently marketed for the treatment of heart failure by Novartis, and vericiguat, currently marketed for the treatment of heart failure by Merck. In addition, there may also be drug candidates of which we are not aware at an earlier stage of development that may compete with our drugs and drug candidates.

*The outbreak of the novel coronavirus, or COVID-19, had an adverse impact on our business operations and clinical trials and another novel coronavirus could adversely affect our business in the future.*

Our business was disrupted and adversely affected by the COVID-19 pandemic. The emergence of any new, more virulent SARS-CoV-2 variants could negatively affect the health and availability of our workforce and cause new disruptions to our business operations. Any such disruptions could negatively impact productivity and delay our ongoing commercialization of INPEFA and research and development efforts with respect to our drug candidates.

The emergence of new, more infectious and virulent variants may also negatively impact future clinical trials by impeding our ability to effectively recruit and retain patients, principal investigators and site staff due to concerns for patient safety and prioritization of healthcare resources. In addition, significant disruption in the operations of third party manufacturers and research and development organizations upon whom we rely may occur and, as a result, our business operations could be severely impacted. These and similar, and perhaps more severe, disruptions in our operations due to the emergence of a novel coronavirus could negatively impact our business, operating results and financial condition.

The pandemic also resulted in the disruption of global financial markets and supply chains. Any disruption could make it more difficult for us to access capital, which could in the future negatively affect our liquidity, and effectively manage the clinical and commercial supply of our products. In addition, a recession or market correction resulting from the spread of a novel coronavirus could materially affect our business and the value of our common stock. The ultimate impact of a health pandemic or epidemic is highly uncertain and subject to change. These effects could have a material impact on our operations.

## ***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 research and 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, 2023, we had \$170.0 million in cash, cash equivalents and investments. In March 2024, we entered into an agreement with certain accredited investors in a private placement of convertible preferred stock in which we received net proceeds of approximately \$242 million (please refer to Note 13 of the Notes to Consolidated Financial Statements for further details). We anticipate that our existing capital resources and revenues will enable us to fund our currently planned operations for at least the next 12 months from the date of this report. 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 INPEFA for the treatment of heart failure, preparations for the potential commercial launch of sotagliflozin for patients with type 1 diabetes and CKD and the continued research and development of sotagliflozin, LX9211, LX9851 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 commercialization of INPEFA for the treatment of heart failure;
- the success of our commercial launch of sotagliflozin for patients with type 1 diabetes and CKD, if approved;
- the timing, progress and results of our research and development efforts for sotagliflozin, LX9211, LX9851 and our other drug candidates and our ability to obtain necessary regulatory approvals based on clinical trials of those drug candidates;
- our success in establishing new collaborations and licenses;
- the amount and timing of our research, development and commercialization expenditures;
- the effect of competing programs and products, and of technological and market developments; and
- the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights.

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 all of our assets as collateral under our existing term loans with Oxford Finance LLC, or the Oxford Term Loans, 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.

*We may not have sufficient capital to support Phase 3 development of LX9211 in DPNP and do not have sufficient capital to support Phase 3 development of LX9211 in neuropathic pain broadly. If we are unable to establish a strategic collaboration or other arrangement for that purpose, our capital needs will be substantially higher and we may be unable to obtain financing sufficient to fund Phase 3 development of LX9211 on acceptable terms, or at all, and may be required to forego or reduce the scope of any such Phase 3 development program.*

Our existing resources may be insufficient to support Phase 3 development of LX9211 in DPNP and will be insufficient to support Phase 3 development of LX9211 in neuropathic pain broadly. Although we seek to collaborate with another pharmaceutical or biotechnology company or strategic partner under terms which would enable reliance on their resources, in whole or in part, and provide additional funding for such Phase 3 development program, we may be unable to successfully enter into any such collaboration or other arrangement on reasonable terms, or at all. In such event, our capital needs will be substantially higher and we will be reliant on obtaining financing in support of any such Phase 3 development program from alternative sources. We cannot be certain that such financing will be available in amounts or on terms acceptable

to us, if at all. If we are unable to secure such financing, we may be required to forego or reduce the scope of any such Phase 3 development program.

*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 aggregate net losses since our inception, including an aggregate net loss of \$366.8 million for the three years ended December 31, 2023. As of December 31, 2023, we had an accumulated deficit of \$1.8 billion. Because of the numerous risks and uncertainties associated with successfully developing and commercializing drug products, 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 continue making significant investments in the commercialization of INPEFA for the treatment of heart failure, preparations for the potential commercial launch of sotagliflozin for patients with type 1 diabetes and CKD and the continued research and development of sotagliflozin, LX9211, LX9851 and our other drug candidates.

We have derived a substantial portion of our revenues from strategic collaborations and other research and development collaborations and technology licenses. 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 products developed or commercialized 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 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 have spent and expect to continue spending significant amounts to fund our commercialization of INPEFA for the treatment of heart failure, preparations for our potential commercial launch of sotagliflozin for patients with type 1 diabetes and CKD and our continued research and development of sotagliflozin, LX9211, LX9851 and our other drug candidates. As a result, we will need to generate substantial additional revenues to achieve profitability in future periods. Even if we do achieve profitability in future periods, we may not be able to sustain or increase such profitability on a quarterly or annual basis.

*Our operating results have fluctuated 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:

- the success of our commercialization of INPEFA for the treatment of heart failure;
- the success of our ongoing research and development efforts and our ability to obtain regulatory approval of our drug candidates as a result of such efforts;
- the timing and amount of expenses incurred with respect to our research, development and commercialization efforts;
- our success in establishing new collaborations and technology licenses and the timing and financial terms of such arrangements;
- 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; and
- 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 \$99.5 million of indebtedness. Although the affirmative and restrictive covenants and the pledge of substantially all of our assets as collateral under the Oxford Term Loans 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 Oxford Term Loans, our financial condition and results of operations could be adversely affected.*

Our obligations under the Oxford Term Loans are secured by a first lien security interest in substantially all of our assets. In addition, the Oxford Term Loans require that we comply with certain affirmative and restrictive covenants, including financial covenants relating to net sales of INPEFA and minimum cash balance requirements and additional 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 Oxford Term Loans, 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 depend on our ability to establish collaborations with pharmaceutical and biotechnology companies for the development and commercialization of our other drug candidates. If we are unable to establish such collaborations, or if pharmaceutical products are not successfully and timely developed and commercialized under such collaborations, our opportunities to generate revenues from our other drug candidates will be greatly reduced.*

We have derived a substantial majority of our revenues to date from collaborative arrangements with other pharmaceutical and biotechnology companies for the research, development and commercialization of our drug candidates and other research and development collaborations and technology licenses. Future revenues from our existing and future collaborations depend upon the achievement of milestones and payment of royalties we earn from any future products developed under those arrangements. If our relationship terminates with any collaborator, 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 collaborations or strategic alliances. If milestones are not achieved 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 arrangements.

We have limited or no control over the resources that any third party may devote to the development and commercialization of products under our collaborations. Any of our present or future collaborators may not perform their obligations as expected. Our 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 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 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 rely on third parties to carry out our preclinical studies and clinical trials, which may harm or delay our research and development efforts.*

We rely on clinical research organizations and other third-party contractors to carry out many of our drug development activities, including the performance of preclinical 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 commercial supplies of INPEFA and any other products which gain regulatory approval and other materials for our research and development activities relating to our drug candidates. Our reliance on third parties to manufacture our drugs and drug candidates may harm or delay our research, development and commercialization efforts.*

We currently do not have the manufacturing capabilities or experience necessary to produce commercial supplies of INPEFA and any other products which gain regulatory approval and other materials for our research and development activities relating to our drug candidates 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 cGMP regulations 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 and commercialization timelines and applicable regulatory requirements. In addition, there are a limited number of manufacturers that operate under the FDA's cGMP regulations 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 or commercialization efforts may be delayed. Moreover, noncompliance with the FDA's cGMP regulations 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 commercial 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 other intellectual property rights, or are effectively maintained as trade secrets or otherwise protected from disclosure by non-disclosure agreements. 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. Further, as we customarily assess whether to apply for new patents based on our ongoing research and development activities, this assessment and the filing for additional patent protection may require significant expenditures and therefore may not be commercially practicable.

Our patents and other intellectual property rights may be challenged by third parties and may be invalidated, cancelled or held unenforceable under U.S. or foreign laws, or they may be infringed or misappropriated 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 other intellectual property rights, such as trademarks and trade secrets, 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 may 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 from a third party that may not be available on reasonable terms, if at all. Further, others may discover uses for our products and technology other than those covered in or claimed by our issued or pending patents, such as other uses for our drug targets and drug candidates, 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 a similar 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 and misappropriation.

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 or duplicate substantially equivalent proprietary information or may otherwise gain access to or misappropriate our trade secrets. For example, publicly available information, such as information in issued patents, published patent applications and scientific literature, can be used by third parties to independently develop technology and we cannot provide assurance that any such independently developed technology will not be equivalent or superior to our proprietary technology.

We rely on registered trademarks to protect our investment in our brand and goodwill. However, competitors may challenge the validity of those trademarks and other brand names in which we have invested or may invest. Such challenges can be expensive and may adversely affect our ability to maintain the goodwill gained in connection with a particular trademark.

*We may be involved in patent litigation and other disputes regarding intellectual property rights and may require licenses from third parties for our planned research, 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 research and development efforts, may give rise to claims that they infringe or misappropriate the patents or other intellectual property rights 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, and may issue in the future, 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 research and 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 may 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 or other dispute resolution proceedings 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 or other dispute resolution proceedings based on intellectual property indemnification undertakings that we have given to certain of our collaborators. Patent and other intellectual property litigation is expensive and requires substantial amounts of management attention. The eventual outcome of any such litigation or dispute resolution proceedings is uncertain and involves substantial risks. If we are sued for infringement or misappropriation and lose, we could be required to pay substantial damages and/or be enjoined from using or selling the allegedly infringing or misappropriation products or technology. The results or costs of any such litigation or dispute resolution proceedings may have an adverse effect on our business, operating results and financial condition.

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, reputational harm and financial loss.*

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 and personal data. The secure maintenance of this information is critical to our business and reputation. Companies have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access and unintentional breaches. 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 information security breaches 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, particularly for cyber incidents such as advanced persistent threats. 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 and information security breaches 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 able to detect or prevent every attempted breach and may not permit us to respond effectively to every breach. These incidents could also subject us to liability, expose us to significant expense and cause significant harm to our reputation and business. Reputational harm resulting from a significant cyber incident may cause unquantifiable damage to our established goodwill. Moreover, as cyber incidents continue to evolve, we will likely be required to expend additional resources to enhance our security posture and cybersecurity defenses or to investigate and remediate any vulnerability to or consequences of cyber incidents. Our insurance coverage may not be sufficient to prevent or recover from cyberattacks, including coverage of applicable resulting losses arising from the incident.

Further, each foreign jurisdiction and U.S. state in which we operate may have laws governing how we must respond to a cyber incident that results in the unauthorized access, disclosure, or loss of personal information. Additionally, new laws and regulations governing data privacy and unauthorized disclosure of confidential information, including recent California legislation providing for a private right of action, pose increasingly complex compliance challenges and could potentially elevate our costs over time. As legislation continues to develop and cyber incidents continue to evolve, we will likely be required to expend significant resources to continue to modify or enhance our protective measures to comply with such legislation and to detect, investigate and remediate vulnerabilities to cyber incidents. Any failure by us to comply with such laws and regulations could result in reputational harm, loss of goodwill, penalties, liabilities and/or mandated changes in our business practices.

*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 or other dispute resolution proceedings may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation or other dispute resolution proceedings 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 Our Employees and Facilities***

*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 may continue to experience substantial growth in the number of our employees and in the scope of our operations. This growth will likely place 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 have increased our commercial, medical, clinical, 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 or retaining 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 and clinical staff, the loss of whose services might adversely impact the achievement of our objectives. Retaining and, where advisable, recruiting qualified commercial, medical and clinical personnel will be critical to the commercialization of INPEFA for heart failure, the potential commercial launch of sotagliflozin for patients with type 1 diabetes and CKD and the advancement of our research and development efforts for sotagliflozin, LX9211, LX9851 and our other drug candidates. Competition is intense for experienced commercial, medical and clinical 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.

*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 Bridgewater, 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 substances in our business. Any claims relating to improper handling, storage or disposal of these substances could be time consuming and costly.*

Our research and development processes have historically involved the controlled use of hazardous substances, including chemicals and radioactive and biological materials, and our operations have produced hazardous waste products. See “Part I, Item 1. Business – Government Regulation – Environmental and Worker Safety Matters” for more discussion on these and other environmental matters. 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 INPEFA or any other product that we or our collaborators develop or commercialize, or any other 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 INPEFA or our other 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 commercialization of INPEFA and clinical trials of our drug candidates. 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. and its affiliates own a substantial interest in our outstanding common stock and may have interests which conflict with those of our other stockholders.*

Invus, L.P. and its affiliates, which we collectively refer to as Invus, currently own approximately 50% of the outstanding shares of our common stock and are thereby able to exert substantial control over the election and removal of our directors and determination of 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 its stockholders' agreement relating to the membership of our board of directors and under our certificate of incorporation relating to preemptive and consent rights, which provide Invus with substantial influence over significant corporate matters.*

Under its stockholders' agreement, 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 eight 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 (a) 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 (b) 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, and no Invus-designated directors currently serve on the audit committee of our board of directors.

Our certificate of incorporation also grants holders of 20% or more of our issued and outstanding common stock customary preemptive rights and consent rights prior to us taking any of the following actions: (a) creating or issuing any new class or series of shares of capital stock (or securities convertible into or exercisable for shares of capital stock) having rights, preferences or privileges senior to or on parity with the common stock, (b) subject to certain exceptions, repurchasing, retiring, redeeming or otherwise acquiring any equity securities (or securities convertible into or exchangeable for equity securities) or any subsidiary and (c) adopting, or proposing to adopt, or maintaining any shareholders' rights plan, "poison pill" or other similar plan or agreement, unless such stockholder is exempt from such plan or agreement. Invus currently has such preemptive and consent rights as a result of its ownership position in our issued and outstanding common stock.

Each of these rights provide Invus with substantial influence over significant corporate matters and Invus' interest in those matters may not be aligned with the interests of other holders of our common stock.

*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 INPEFA and the revenues we generate from sales of INPEFA;
- results or delays in our or our collaborators' clinical trials;
- 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 sotagliflozin, LX9211, LX9851 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 misappropriation, 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.

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

A substantial number of shares of our common stock is reserved for issuance upon the exercise of stock options and vesting of restricted stock units. If we or our stockholders issue or sell substantial amounts of our common stock (including shares issued upon the 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. In addition, any such issuance or sale of our common stock will dilute the ownership interests of existing stockholders and may cause the market price of our common stock to decline.

*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 unfavorable research about our business, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause our stock price and trading volume to decline.

#### **Item 1B. Unresolved Staff Comments**

None.

## Item 1C. Cybersecurity

Cybersecurity represents an important component of our overall approach to enterprise risk management. Our cybersecurity policies, standards, processes and practices are fully integrated into our enterprise risk management program and are based on recognized frameworks established by the National Institute of Standards and Technology, the International Organization for Standardization and other applicable industry standards. In general, we seek to address cybersecurity risks through a comprehensive, cross-functional approach that is focused on preserving confidentiality, security and availability of the information that we collect and store by identifying, preventing and mitigating cybersecurity threats and effectively responding to cybersecurity threats when they occur.

Our cybersecurity program is focused on the following key areas:

- *Technical Safeguards.* We deploy technical safeguards that are designed to protect our information systems from cybersecurity threats, including firewalls, intrusion prevention and detection systems, an endpoint protection platform system, anti-malware functionality, email filtering, url filtering and access controls, which are evaluated and improved through vulnerability assessments and cybersecurity threat intelligence.
- *Education and Awareness.* We provide regular, mandatory training for personnel regarding cybersecurity threats, as well as periodic decoy and honeypot testing, as a means to equip our personnel with effective tools to address cybersecurity threats, and to communicate our evolving information security policies, standards, processes and practices.
- *Assessments of Third Party Service Providers.* We regularly evaluate the cybersecurity policies, standards, processes and practices of our key third party service providers in order to effectively identify and address any vulnerabilities or other risks.
- *Incident Response and Recovery Planning.* We have established and maintain comprehensive incident response and recovery plans that fully address our response to a cybersecurity incident, and such plans are tested and evaluated on a regular basis.
- *Collaborative Approach.* We have implemented a comprehensive, cross-functional approach to identifying, preventing and mitigating cybersecurity threats and incidents, while also implementing controls and procedures that provide for the prompt escalation of certain cybersecurity incidents so that decisions regarding the public disclosure and reporting of such incidents can be made by management in a timely manner.

We engage in the periodic assessment and testing of our policies, standards, processes and practices that are designed to address cybersecurity threats and incidents. These efforts include a wide range of activities, including audits, assessments, tabletop exercises, threat modeling, vulnerability testing and other exercises focused on evaluating the effectiveness of our cybersecurity measures and planning. We regularly engage third parties to perform assessments on our cybersecurity measures, including information security maturity assessments, audits and independent reviews of our information security control environment and operating effectiveness. The results of such assessments, audits and reviews are reported to our executive management and board of directors, and we adjust our cybersecurity policies, standards, processes and practices as necessary based on the information provided by these assessments, audits and reviews.

Our executive management and board of directors oversee our enterprise risk management process, including the management of risks arising from cybersecurity threats. Our executive management and board of directors each receive regular presentations and reports on cybersecurity risks, which address a wide range of topics including recent developments, evolving standards, vulnerability assessments, third party and independent reviews, the threat environment, technological trends and information security considerations arising with respect to our peers and third parties. Our executive management and board of directors also receive prompt and timely information regarding any cybersecurity incident that meets established reporting thresholds, as well as ongoing updates regarding any such incident until it has been addressed.

Our vice president, information operations works collaboratively across our company to implement a program designed to protect our information systems from cybersecurity threats and to promptly respond to any cybersecurity threats in accordance with our incident response and recovery plans. To facilitate the success of our cybersecurity risk management program, multidisciplinary teams are deployed to address cybersecurity threats and respond to cybersecurity incidents. Through ongoing communications with these teams, our vice president, information operations monitors the prevention, detection, mitigation and remediation of cybersecurity threats and incidents in real time, and report such threats and incidents to executive management when appropriate. Our vice president, information systems has served in such role since October 2021 and in various roles in information security and information technology for over 25 years.

Cybersecurity threats, including as a result of any previous cybersecurity incidents, have not materially affected our company to date, including our business strategy, results of operation or financial condition. For a description of the risks from cybersecurity threats that may materially affect us and how they may do so, see our risk factors under Part 1. Item 1A. Risk Factors in this Annual Report on Form 10-K, including “Data breaches and cyber-attacks could compromise our intellectual property or other sensitive information and cause significant damage to our business, reputational harm and financial loss.”

## **Item 2. *Properties***

In February 2021, we leased a 25,000 square-foot office space in The Woodlands, Texas. The term of the sublease extends from March 2021 through August 2025, and provides for escalating yearly base rent payments starting at \$506,000 and increasing to \$557,000 in the final year of the lease.

In July 2022, our subsidiary, Lexicon Pharmaceuticals (New Jersey), Inc. leased a 22,000 square-foot office space in Bridgewater, New Jersey. The term of the lease extends through January 2034 and provides for escalating yearly base rent payments starting at \$820,000 and increasing to \$986,000 in the final year of the lease.

We believe that our facilities are well-maintained, in good operating condition and acceptable for our current operations.

## **Item 3. *Legal Proceedings***

We are from time to time party to claims and legal proceedings that arise in the normal course of our business and that we believe will not have, individually or in the aggregate, a material adverse effect on our results of operations, financial condition or liquidity. We are currently not aware of any material legal proceedings affecting our company.

## **Item 4. *Mine Safety Disclosures***

Not applicable.

## PART II

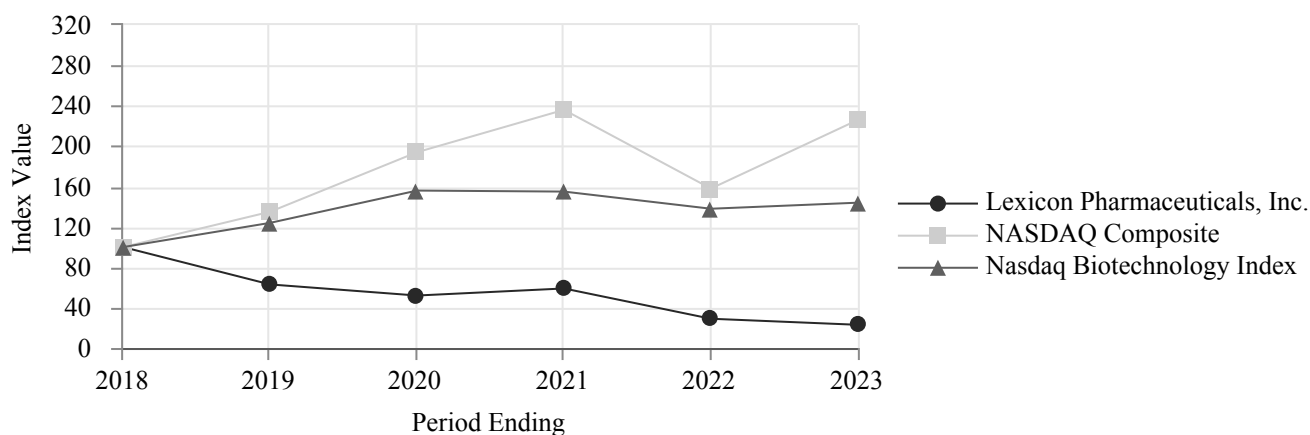
### Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is quoted on The Nasdaq Global Select Market under the symbol “LXRX.” As of March 21, 2024, there were approximately 313 holders of record of our common stock.

We have never paid cash dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the expansion and operation of our business and do not anticipate paying cash dividends in the foreseeable future.

#### Performance Graph

The following performance graph compares the performance of our common stock to the Nasdaq Composite Index and the Nasdaq Biotechnology Index for the period beginning December 31, 2018 and ending December 31, 2023. The graph assumes that the value of the investment in our common stock and each index was \$100 at December 31, 2018, and that all dividends were reinvested. The stock performance shown on the graph below represents historical performance and is not necessarily indicative of future stock price performance.



	December 31,					
	2018	2019	2020	2021	2022	2023
Lexicon Pharmaceuticals, Inc.	100	63	52	59	29	23
Nasdaq Composite Index	100	135	194	236	158	226
Nasdaq Biotechnology Index	100	124	156	155	138	144

The foregoing stock price performance comparisons shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference by any general statement incorporating by reference this annual report on Form 10-K into any filing under the Securities Act of 1933 or under the Securities Exchange Act of 1934, except to the extent that we specifically incorporate such comparisons by reference.

#### Item 6. [Reserved]

Not applicable.

## Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

*The following discussion and analysis should be read with our financial statements and notes included elsewhere in this annual report on Form 10-K.*

### Overview

We are a biopharmaceutical company with a mission of pioneering medicines that transform patients' lives. We are devoting most of our resources to the commercialization of our approved drug, INPEFA, for heart failure and the research and development of our most advanced drug candidates:

- We are commercializing INPEFA, an orally-delivered small molecule drug, in the United States to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visits in adults with heart failure or type 2 diabetes mellitus, chronic kidney disease, or CKD, and other cardiovascular risk factors.

We are separately pursuing regulatory approval of sotagliflozin as a treatment for type 1 diabetes. The U.S. Food and Drug Administration, or FDA, issued a complete response letter regarding our New Drug Application, or NDA, for sotagliflozin in type 1 diabetes in March 2019, which we appealed. Following FDA feedback from recent discussions, we are now preparing to resubmit our NDA for patients with type 1 diabetes and CKD. We have reported positive results from three Phase 3 clinical trials of sotagliflozin in type 1 diabetes.

We are also developing sotagliflozin as a treatment for hypertrophic cardiomyopathy, or HCM, and are preparing to initiate a Phase 3 clinical trial of sotagliflozin in HCM.

- We are developing LX9211, an orally-delivered small molecule drug candidate, as a treatment for neuropathic pain. We are conducting a Phase 2b clinical trial of LX9211 in diabetic peripheral neuropathic pain, or DPNP, and have received Fast Track designation from the FDA for development of LX9211 in that indication. We have reported positive results from a Phase 2 clinical trial of LX9211 in DPNP and top-line results from a separate Phase 2 clinical trial of LX9211 in post-herpetic neuralgia which also demonstrated evidence of effect.
- We are conducting preclinical development of LX9851, an orally-delivered small molecule drug candidate, as a treatment for obesity and tool for weight management.
- We are conducting preclinical research and development and preparing to conduct clinical development of compounds from a number of additional drug programs originating from our internal drug discovery efforts.

INPEFA, LX9851 and compounds from a number of additional drug programs originated from our own internal drug discovery efforts, and LX9211 originated from our collaborative neuroscience drug discovery efforts with Bristol-Myers Squibb. Our 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 have worked both independently and through collaborations and strategic alliances with third parties to capitalize on our drug target discoveries and research and development programs. We seek to retain exclusive or co-exclusive rights to the benefits of certain research 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 with respect to the research, development and commercialization of certain of our drug candidates, particularly with respect to commercialization in territories outside the United States or 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.

We have derived substantially all of our revenues from strategic collaborations and other research and development collaborations and technology licenses, as well as from commercial sales of our approved drug products. To date, we have generated a substantial portion of our revenues from a limited number of sources.

Our operating results and, in particular, our ability to generate additional revenues are dependent on many factors, including the success of our commercialization of INPEFA in the United States and the amount of revenues generated from



sales of INPEFA; the success of our ongoing research and development efforts and the ability to obtain necessary regulatory approvals of the drug candidates which are the subject of such efforts; our success in establishing new collaborations and licenses and our receipt of milestones, royalties and other payments under such arrangements; and general and industry-specific economic conditions which may affect research, development and commercialization expenditures.

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 INPEFA in heart failure, 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.

Since our inception, we have incurred significant losses and, as of December 31, 2023, we had an accumulated deficit of \$1.8 billion. Our losses have resulted principally from costs incurred in research and development, selling, general and administrative costs associated with our operations, and non-cash stock-based compensation expenses associated with stock options and restricted stock units granted to employees and consultants. Research and development expenses consist primarily of salaries and related personnel costs, external research costs related to our preclinical and clinical efforts, material costs, facility costs, depreciation on property and equipment, and other expenses related to our drug discovery and development programs. Selling, general and administrative expenses consist primarily of salaries and related expenses for executive, sales and marketing, and administrative personnel, professional fees and other corporate expenses, including information technology, facilities costs and general legal activities. We expect to continue to incur significant research and development costs in connection with the continuing research and development of our drug candidates and significant selling, general and administrative expenses in connection with our commercialization of INPEFA. As a result, we will need to generate significantly higher revenues to achieve profitability.

### **Critical Accounting Policies**

Our Consolidated Financial Statements included in this Annual Report on Form 10-K have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP, which require that we make numerous estimates and assumptions. Actual results could differ from those estimates and assumptions, thus impacting our reported results of operations and financial position. The critical accounting policies and estimates described in this section are those that are most important to the depiction of our financial condition and results of operations and the application of which requires our most subjective judgments in making estimates about the effect of matters that are inherently uncertain. We describe our significant accounting policies more fully in Note 2, “Summary of Significant Accounting Policies,” to the Consolidated Financial Statements included in this Annual Report on Form 10-K.

#### ***Research and Development Expenses***

Research and development expenses consist of costs incurred for research and development activities solely sponsored by us as well as collaborative research and development activities. These costs include direct and research-related overhead expenses and are expensed as incurred. Technology license fees for technologies that are utilized in research and development and have no alternative future use are expensed when incurred.

We are presently devoting most of our resources to the commercialization of INPEFA for heart failure, preparations for the potential commercial launch of sotagliflozin for patients with type 1 diabetes and CKD and the continued research and development of sotagliflozin, LX9211, LX9851 and our other drug candidates.

INPEFA, LX9851 and compounds from a number of additional drug programs originated from our own internal drug discovery efforts, and LX9211 originated from our collaborative neuroscience drug discovery efforts with Bristol-Myers Squibb. Those 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.

The drug development process takes many years to complete. The cost and length of time varies due to many factors including the type, complexity and intended use of the drug candidate. We estimate that drug development activities are typically completed over the following periods:

Phase	Estimated Completion Period
Preclinical development	1-2 years
Phase 1 clinical trials	1-2 years
Phase 2 clinical trials	1-2 years
Phase 3 clinical trials	2-4 years

We expect research and development costs to remain substantial in the future as we continue to fund our research and development efforts and advance new drug candidates into clinical development. Due to the variability in the length of time necessary for drug development, the uncertainties related to the cost of these activities and ultimate ability to obtain regulatory approval for commercialization, accurate and meaningful estimates of the ultimate costs to bring our drug candidates to market are not available.

We record significant accrued liabilities related to unbilled expenses for products or services that we have received from service providers, specifically related to ongoing preclinical studies and clinical trials. These costs primarily relate to clinical study management, monitoring, laboratory and analysis costs, drug supplies, toxicology studies and investigator grants. We may have multiple drug candidates in concurrent preclinical studies and clinical trials at clinical sites throughout the world. In order to ensure that we have adequately provided for ongoing preclinical and clinical development costs during the period in which we incur such costs, we maintain accruals to cover these expenses. Substantial portions of our preclinical studies and clinical trials are performed by third party laboratories, medical centers, contract research organizations and other vendors. For preclinical studies, we accrue expenses based upon estimated percentage of work completed and the contract milestones remaining. For clinical studies, expenses are accrued based upon milestones and the number of patients enrolled over the duration of the study. We monitor patient enrollment, the progress of clinical studies and related activities to the extent possible through internal reviews of data reported to us by the vendors and clinical site visits. Our estimates depend on the timeliness and accuracy of the data provided by our vendors regarding the status of each program and total program spending. We periodically evaluate the estimates to determine if adjustments are necessary or appropriate based on information we receive. Although we use consistent milestones or subject or patient enrollment to drive expense recognition, the assessment of these costs is a subjective process that requires judgment. Upon settlement, these costs may differ materially from the amounts accrued in our consolidated financial statements.

The financial terms of these agreements are subject to negotiation and vary from contract to contract. In accruing the relevant costs, we estimated the time period over which services were to be performed and the level of effort required to complete or wind down each study. Upon completion and settlement, these costs may differ materially from the amounts accrued in our consolidated financial statements.

We record our research and development costs by type or category, rather than by project. Significant categories of costs include personnel, facilities and equipment costs and third-party and other services. In addition, a significant portion of our research and development expenses is not tracked by project as it benefits multiple projects. Consequently, fully-loaded research and development cost summaries by project are not available.

#### **Recent Accounting Pronouncements Issued But Not Yet Adopted**

See Note 2, Summary of Significant Accounting Policies, of the Notes to Consolidated Financial Statements, for a discussion of the impact of new accounting standards issued but not yet adopted on our consolidated financial statements.

## Results of Operations

The following discussion and analysis should be read with “Results of Operations” and our financial statements and notes included in our annual report on Form 10-K for the year ended December 31, 2022.

### Revenues

Revenues for the year ended December 31, 2023 were approximately \$1.2 million, primarily from product revenues recognized from sales of INPEFA following its regulatory approval in May 2023.

### Cost of Sales

Cost of sales during the year ended December 31, 2023 consist of third-party manufacturing costs and freight associated with sales of INPEFA. Prior to receiving regulatory approval on May 26, 2023, we had completed or begun the manufacturing of certain INPEFA raw materials. These raw materials were either received at “zero-cost” to us in conjunction with a terminated agreement in 2019 or recorded as research and development expense. Based on our expectations for future manufacturing costs, we estimate these amounts totaled approximately \$39.0 million. We began capitalizing inventory manufactured subsequent to regulatory approval of INPEFA as the related costs were expected to be recoverable through the commercialization of the product. At December 31, 2023, substantially all of the “zero-cost” INPEFA raw materials remains available to us. The “zero-cost” inventory is expected to be consumed over approximately the next three years, which will result in a lower average per unit cost of materials during that period; however, the time period over which this inventory is consumed will depend on a number of factors, including the amount of future INPEFA sales, use of this inventory in clinical development or other research activities, production lead times, and/or the ability to utilize inventory prior to its expiration date. We estimate our cost of goods sold as a percentage of net product revenue will be less than 10% subsequent to the utilization of all of the remaining “zero-cost” inventory.

### Research and Development Expenses

Research and development expenses and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

	Year Ended December 31,		
	2023	2022	2021
Total research and development expense	\$ 58.9	\$ 52.8	\$ 55.0
Dollar increase (decrease)	\$ 6.1	\$ (2.2)	
Percentage increase (decrease)	12 %	(4)%	

Research and development expenses consist primarily of third-party services principally related to preclinical and clinical development activities, salaries and other personnel-related expenses, facility and equipment costs, stock-based compensation, and other costs each of which are described below.

#### Years Ended December 31, 2023 and 2022

- *Third-party services* – Third-party services relate principally to our clinical trial and related development activities, such as preclinical and clinical studies and contract manufacturing. Overall, third-party services increased 16% in 2023 to \$34.6 million, primarily related to increased manufacturing and external research and development costs. These costs were partially offset by lower professional and consulting fees in 2023 when compared to costs incurred in 2022 related to preparations for the submission of our application for regulatory approval to market INPEFA for heart failure in the United States.
- *Personnel* – Personnel costs increased 6% in 2023 to \$14.3 million from \$13.5 million in 2022, due to increased headcount in 2023. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.
- *Stock-based compensation* – Stock-based compensation expense increased 21% in 2023 to \$5.1 million as compared to 2022, partially due to increased headcount.

- *Facilities, equipment, and other* – Facilities, equipment, and other costs relate primarily to rent, insurance, travel and training, and software licensing costs. Facilities, equipment, and other costs were \$4.9 million and \$5.2 million in 2023 and 2022, respectively.

### ***Selling, General and Administrative Expenses***

Selling, general and administrative expenses and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

	Year Ended December 31,		
	2023	2022	2021
Total selling, general and administrative expense	\$ 114.0	\$ 48.1	\$ 32.3
Dollar increase	\$ 65.9	\$ 15.8	
Percentage increase	137 %	49 %	

Selling, general and administrative expenses consist primarily of personnel costs to support the commercialization of INPEFA and support of our research and development activities, professional and consulting fees, stock-based compensation expense, and facilities, equipment, and other costs each of which are described further below.

#### *Years Ended December 31, 2023 and 2022*

- *Personnel* – Personnel costs increased 181% in 2023 to \$53.0 million, primarily due to higher employee salaries and benefit costs as a result of increased headcount during 2023 in conjunction with the June 2023 commercial launch of INPEFA. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.
- *Professional and consulting fees* – Professional and consulting fees increased 137% in 2023 to \$38.7 million, primarily due to higher marketing and professional fees in conjunction with the commercial launch of INPEFA.
- *Stock-based compensation* – Stock-based compensation expense increased 27% in 2023 to \$9.2 million as compared to 2022, due to increasing headcount in the current year.
- *Facilities, equipment, and other* – Facilities, equipment, and other costs were \$13.1 million and \$5.6 million in 2023 and 2022, respectively. The increase in these costs in 2023 was primarily due to travel, training, and software licensing in conjunction with the commercial launch of INPEFA.

### ***Interest and Other Expense***

*Interest and Other Expense.* Interest and other expense increased to \$13.1 million in 2023 from \$2.8 million in 2022, primarily due to the Oxford debt financings of \$25 million in December 2022 and \$50 million in June 2023.

### ***Interest Income and Other, Net***

*Interest Income and Other, Net.* Interest income and other, net was \$7.7 million and \$1.6 million in the years ended December 31, 2023 and 2022, respectively.

### ***Net Loss and Net Loss per Common Share***

Net loss was \$177.1 million, or a loss of \$0.80 per share, in 2023, as compared to a net loss of \$101.9 million, or \$0.62 per share in 2022.

### **Liquidity and Capital Resources**

We have financed our operations from inception primarily through sales of common and preferred stock, contract and milestone payments we received under our collaborations and strategic licenses, target validation, database subscription and technology license agreements, government grants and contracts, and financing under debt, lease and other project financing arrangements, as well as from commercial sales of our approved drug products.

In March 2022, we entered into a loan and security agreement with Oxford Finance LLC that provides up to \$150 million in borrowing capacity, available in five tranches, under which \$100 million has been funded under the first three tranches. The loan and security agreement was subsequently amended in August 2022, May 2023, June 2023, December 2023 and March 2024. The fourth \$25 million tranche is available for draw at our option upon the achievement of specified INPEFA net sales and until April 25, 2025. The fifth \$25 million tranche is available for draw at our option, subject to Oxford's consent, at any time prior to the expiration of the 36-month interest-only payment period. The loan and security agreement includes a financial covenant relating to INPEFA net sales and a separate financial covenant which requires us to maintain a minimum cash and investments balance of \$10 million until the achievement of specified INPEFA net sales. Upon funding of the fourth tranche, the minimum cash and investments balance will increase to \$25 million.

In December 2023, we entered into an Open Market Sale Agreement<sup>SM</sup> with Jefferies LLC pursuant to which we may offer and sell shares of our common stock having an aggregate sales price of up to \$75 million from time to time through Jefferies as sales agent.

On March 11, 2024, we entered into an agreement with certain accredited investors in a private placement in which we agreed to sell 2,304,147 shares of Series A Convertible Preferred Stock of the Company, par value \$0.01 per share, at a price of \$108.50 per share. We received net proceeds of approximately \$242 million, after deducting placement agent fees and offering expenses from the private placement offering. Each share of preferred stock will automatically convert into 50 shares of our common stock upon the filing and acceptance of an amendment to our certificate of incorporation by the Secretary of State of Delaware increasing the number of authorized shares of our common stock to 450,000,000 shares. For additional information on the private placement offering, please refer to Note 13 of the Notes to Consolidated Financial Statements.

As of December 31, 2023, we had \$170.0 million in cash, cash equivalents and short-term investments. As of December 31, 2022, we had \$138.4 million in cash, cash equivalents and short-term investments. We used cash of \$161.9 million in our operations in 2023 largely reflective of the net loss for the year of \$177.1 million which included non-cash charges of \$12.6 million primarily related to stock-based compensation expense. Investing activities used cash of \$49.9 million in 2023, primarily due to net purchases of investments. Financing activities provided cash of \$188.0 million, primarily from approximately \$139.0 million in net proceeds from the sale of an aggregate of 55,288,460 shares of common stock at a price of \$2.60 per share in a public offering and concurrent private placement to an affiliate of Invus, L.P. and \$50.0 million in net proceeds from the funding of the third tranche under the Oxford Term Loans.

*Other commitments.* Upon the regulatory approval of sotagliflozin for the treatment of type 1 diabetes in a major market, we will be required to make certain royalty payments, totaling \$4.5 million, in three equal annual installments of \$1.5 million.

Under our drug discovery alliance with Bristol-Myers Squibb, we will be required to make a royalty payment of \$5 million upon dosing of the first patient in a Phase 3 clinical trial of LX9211.

For a further discussion of our commitments and contingencies see Note 10 of the Notes to Consolidated Financial Statements.

Our future capital requirements will be substantial and will depend on many factors, including the success of our commercialization of INPEFA in the United States; the success of our commercial launch of sotagliflozin for patients with type 1 diabetes and CKD, if approved; the success of our ongoing research and development efforts and the ability to obtain necessary regulatory approvals of the drug candidates which are the subject of such efforts; our success in establishing new collaborations and licenses and our receipt of milestones, royalties and other payments under such arrangements; the amount and timing of our research, development and commercialization expenditures; the resources we devote to commercializing, developing and supporting our products and other factors. Our capital requirements will also be affected by any expenditures we make in connection with license agreements and acquisitions of and investments in complementary technologies and businesses.

We expect to continue to devote substantial capital resources to the commercialization of INPEFA for heart failure, the commercial launch of sotagliflozin for patients with type 1 diabetes and CKD, if approved, the research and development of our drug candidates and for other general corporate activities. We believe that our current unrestricted cash and investment balances and cash and revenues we expect to derive from strategic and other collaborations and other sources will be sufficient to fund our currently planned operations for at least the next 12 months from the date of this report. During or after this period, if cash generated by operations is insufficient to satisfy our liquidity requirements, we will need to sell additional equity or debt securities or obtain additional credit arrangements. If we are unable to obtain adequate financing when needed, we may have to delay or reduce the scope of our commercialization efforts or one or more of our clinical trials and other research and development programs. Additional financing may not be available on terms acceptable to us or at all. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders.

From time to time, our board of directors may authorize us to repurchase shares of our common stock. If and when our board of directors should determine to authorize any such action, it would be on terms and under market conditions that our board of directors determines are in the best interest of us and our stockholders. Any such actions could deplete significant amounts of our cash resources and/or result in additional dilution to our stockholders.

### **Disclosure about Market Risk**

We are exposed to limited market and credit risk on our cash equivalents which have maturities of three months or less at the time of purchase. We had approximately \$170.0 million in cash and cash equivalents and short-term investments as of December 31, 2023. We maintain a short-term investment portfolio which consists of U.S. Treasury bills and corporate debt securities that mature three to 12 months from the time of purchase, which we believe are subject to limited market and credit risk. We currently do not hedge interest rate exposure or hold any derivative financial instruments in our investment portfolio.

We are subject to interest rate sensitivity on our outstanding Oxford Term Loans which bear interest at a floating rate equal to the 1-month CME Term SOFR rate. Interest on the Oxford Term Loans is payable in cash monthly and the term loans are fully matured by March 2027, unless earlier repaid in accordance with their terms.

We have operated primarily in the United States and substantially all sales to date have been made in U.S. dollars. Accordingly, we have not had any material exposure to foreign currency rate fluctuations.

### **Item 7A. *Quantitative and Qualitative Disclosures About Market Risk***

See “Disclosure about Market Risk” under “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations” for quantitative and qualitative disclosures about market risk.

### **Item 8. *Financial Statements and Supplementary Data***

The financial statements required by this Item are incorporated under Item 15 in Part IV of this report.

### **Item 9. *Changes in and Disagreements with Accountants on Accounting and Financial Disclosure***

None.

### **Item 9A. *Controls and Procedures***

#### **Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) as of the end of the period covered by this report. Based on that evaluation, our principal executive officer and principal financial officer have concluded that our disclosure controls and procedures were effective as of December 31, 2023 to ensure that the information required to be disclosed by us in the reports we file under the Securities Exchange Act is gathered, analyzed and disclosed with adequate timeliness, accuracy and completeness.

#### **Management’s Report on Internal Control over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act).

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2023. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control-Integrated Framework* (2013 Framework).

Based on such assessment using those criteria, management concluded that, as of December 31, 2023, our internal control over financial reporting was effective.

### **Changes in Internal Control Over Financial Reporting**

Subsequent to our evaluation described above, there were no significant changes in internal controls or other factors during the fiscal quarter ended December 31, 2023 that could significantly affect internal controls, including any corrective actions with regard to significant deficiencies and material weaknesses.

### **Item 9B. *Other Information***

#### **Insider Trading Arrangements**

During the three months ended December 31, 2023, none of our directors or executive officers adopted or terminated a “Rule 10b5-1 trading arrangement” or “non-Rule 10b5-1 trading arrangement,” as each term is defined in Item 408(a) of Regulation S-K.

### **Item 9C. *Disclosure Regarding Foreign Jurisdictions that Prevent Inspections***

None.

## PART III

### **Item 10. *Directors, Executive Officers and Corporate Governance***

The information required by this Item is hereby incorporated by reference from (a) the information appearing under the captions “Election of Directors,” “Stock Ownership of Certain Beneficial Owners and Management,” “Corporate Governance” and “Executive and Director Compensation” in our definitive proxy statement which involves the election of directors and is to be filed with the SEC pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2023 and (b) the information appearing under Item 1 in Part I of this report.

### **Item 11. *Executive Compensation***

The information required by this Item is hereby incorporated by reference from the information appearing under the captions “Corporate Governance” and “Executive and Director Compensation” in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2023. Notwithstanding the foregoing, in accordance with the instructions to Item 407(e)(5) of Regulation S-K, the information contained in our proxy statement under the sub-heading “Compensation Committee Report” shall not be deemed to be filed as part of or incorporated by reference into this annual report on Form 10-K.

### **Item 12. *Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required by this Item is hereby incorporated by reference from the information appearing under the captions “Stock Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2023.

### **Item 13. *Certain Relationships and Related Transactions, and Director Independence***

The information required by this Item is hereby incorporated by reference from the information appearing under the captions “Corporate Governance” and “Transactions with Related Persons” in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2023.

### **Item 14. *Principal Accountant Fees and Services***

The information required by this Item as to the fees we pay our principal accountant is hereby incorporated by reference from the information appearing under the caption “Ratification and Approval of Independent Auditors” in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2023.



## PART IV

### Item 15. *Exhibit and Financial Statement Schedules*

(a) Documents filed as a part of this report:

1. Consolidated Financial Statements

	<u>Page</u>
Report of Independent Registered Public Accounting Firm (PCAOB ID: 42)	F-1
Consolidated Balance Sheets	F-3
Consolidated Statements of Comprehensive Loss	F-4
Consolidated Statements of Stockholders' Equity	F-5
Consolidated Statements of Cash Flows	F-6
Notes to Consolidated Financial Statements	F-7

2. Financial Statement Schedules

All other financial statement schedules are omitted because they are not applicable or not required, or because the required information is included in the financial statements or notes thereto.

3. Exhibits

#### Exhibit No.

#### Description

- 1.1 — Open Market Sale Agreement<sup>SM</sup>, dated December 29, 2023, with Jefferies LLC (filed as Exhibit 1.1 to the Company's Current Report on Form 8-K dated December 29, 2023 and incorporated by reference herein).
- 3.1 — Fifth Amended and Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K dated May 20, 2022 and incorporated by reference herein).
- 3.2 — Certificate of Designations, dated March 12, 2024 (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K dated March 12, 2024 and incorporated by reference herein).
- 3.3 — Second Amended and Restated Bylaws (filed as Exhibit 3.2 to the Company's Current Report on Form 8-K dated April 26, 2012 and incorporated by reference herein).
- 4.1 — Securities Purchase Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein).
- 4.2 — Amendment, dated October 7, 2009, to Securities Purchase Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated October 7, 2009 and incorporated by reference herein).
- 4.3 — Registration Rights Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein).
- 4.4 — Stockholders' Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.4 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein).
- 4.5 — Supplement to Transaction Agreements, dated March 15, 2010, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated March 15, 2010 and incorporated by reference herein).
- 4.6 — Supplement No. 2 to Transaction Agreements, dated February 23, 2012, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated February 23, 2012 and incorporated by reference herein).
- 4.7 — Supplement No. 3 to the Transaction Agreements, dated December 16, 2020, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated December 16, 2020 and incorporated by reference herein).
- 4.8 — Description of Common Stock (filed as Exhibit 4.8 to the Company's Annual Report on Form 10-K for the period ended December 31, 2021 and incorporated by reference herein).
- 10.1 — Offer Letter, dated July 1, 2014, with Lonnel Coats, as amended (filed as Exhibit 10.1 to the Company's Annual Report on Form 10-K for the period ended December 31, 2018 and incorporated by reference herein).
- 10.2 — Employment Agreement, dated January 1, 1999, with Jeffrey L. Wade (filed as Exhibit 10.3 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).

- 10.3 — Offer Letter, dated July 27, 2021, with Craig B. Granowitz, M.D., Ph.D. (filed as Exhibit 10.3 to the Company's Annual Report on Form 10-K for the period ended December 31, 2021 and incorporated by reference herein).
- 10.4 — Employment Agreement, dated July 12, 2001, with Alan J. Main, Ph.D. (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2001 and incorporated by reference herein).
- 10.5 — Form of Indemnification Agreement with Officers and Directors (filed as Exhibit 10.6 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
- \*10.6 — Summary of Non-Employee Director Compensation
- 10.7 — 2017 Equity Incentive Plan, as amended (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated April 27, 2023 and incorporated by reference herein).
- 10.8 — 2017 Non-Employee Directors' Equity Incentive Plan, as amended (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated April 27, 2023 and incorporated by reference herein).
- 10.9 — Form of Stock Option Agreement with Officers under the 2017 Equity Incentive Plan (filed as Exhibit 10.11 to the Company's Annual Report on Form 10-K for the period ended December 31, 2017 and incorporated by reference herein).
- \*10.10 — Form of Restricted Stock Unit Agreement with Officers under the 2017 Equity Incentive Plan
- 10.11 — Form of Notice of Stock Option Grant to Directors under the 2017 Non-Employee Directors' Equity Incentive Plan (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2019 and incorporated by reference herein).
- 10.12 — Form of Notice of Restricted Stock Unit Grant to Directors under the 2017 Non-Employee Directors' Equity Incentive Plan (filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2019 and incorporated by reference herein).
- 10.13 — Collaboration and License Agreement, dated December 17, 2003, with Bristol-Myers Squibb Company (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2015 and incorporated by reference herein).
- 10.14 — First Amendment, dated May 30, 2006, to Collaboration and License Agreement, dated December 17, 2003, with Bristol-Myers Squibb Company (filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2015 and incorporated by reference herein).
- †10.15 — Second Amendment, dated November 2, 2016, to Collaboration and License Agreement, dated December 17, 2003, with Bristol-Myers Squibb Company (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated November 2, 2016 and incorporated by reference herein).
- 10.16 — Sublease Agreement, dated February 8, 2021, with Repsol Oil & Gas USA, LLC (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated February 8, 2021 and incorporated by reference herein).
- †10.17 — Loan and Security Agreement, dated March 17, 2022, with Oxford Finance, LLC and the lenders listed therein (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2022 and incorporated by reference herein).
- †10.18 — First Amendment to Loan and Security Agreement, dated August 29, 2022, with Oxford Finance, LLC and the lenders listed therein (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated August 29, 2022 and incorporated by reference herein).
- †10.19 — Second Amendment to Loan and Security Agreement, dated May 1, 2023, with Oxford Finance, LLC and the lenders listed therein (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated May 1, 2023 and incorporated by reference herein).
- †10.20 — Third Amendment to Loan and Security Agreement, dated June 23, 2023, with Oxford Finance, LLC and the lenders listed therein (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated June 23, 2023 and incorporated by reference herein).
- †10.21 — Fourth Amendment to Loan and Security Agreement, dated December 29, 2023, with Oxford Finance, LLC and the lenders listed therein (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated December 29, 2023 and incorporated by reference herein).
- †10.22 — Fifth Amendment to Loan and Security Agreement, dated March 6, 2024, with Oxford Finance, LLC and the lenders listed therein (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated March 6, 2024 and incorporated by reference herein).
- 10.23 — Purchase Agreement, dated May 31, 2023, with Artal International S.C.A., Artal Group S.A., Artal International Management S.A., Invus Advisors, L.L.C., Invus Public Equities, L.P., Invus, L.P., Mr. Amaury Wittouck, Stichting Administratiekantoor Westend and Westend S.A. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated May 31, 2023 and incorporated by reference herein).

- 10.24 — Preferred Stock Purchase Agreement, dated March 11, 2024, with the purchasers party thereto (filed as Exhibit 10.1 to the Company’s Current Report on Form 8-K dated March 6, 2024 and incorporated by reference herein).
- 21.1 — Subsidiaries (filed as Exhibit 21.1 to the Company’s Annual Report on Form 10-K for the period ended December 31, 2021 and incorporated by reference herein).
- \*23.1 — Consent of Independent Registered Public Accounting Firm.
- \*24.1 — Power of Attorney (contained in signature page).
- \*31.1 — Certification of Principal Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
- \*31.2 — Certification of Principal Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
- \*32.1 — Certification of Principal Executive and Principal Financial Officers Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
- \*97.1 — Incentive-Based Compensation Clawback Policy
- \*101.INS — XBRL Instance Document.
- \*101.SCH — XBRL Taxonomy Extension Schema Document.
- \*101.CAL — XBRL Taxonomy Extension Calculation Linkbase Document.
- \*101.DEF — XBRL Taxonomy Extension Definition Linkbase Document.
- \*101.LAB — XBRL Taxonomy Extension Label Linkbase Document.
- \*101.PRE — XBRL Taxonomy Extension Presentation Linkbase Document.

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\* Filed herewith.

† Confidential treatment has been requested for portions of this exhibit (indicated by “[\*\*]”). The confidential portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission.

**Item 16. *Form 10-K Summary***

Not applicable.

### Signatures

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: March 25, 2024	Lexicon Pharmaceuticals, Inc. By: <u>/s/ LONNEL COATS</u> Lonnel Coats <i>Chief Executive Officer</i>
Date: March 25, 2024	By: <u>/s/ JEFFREY L. WADE</u> Jeffrey L. Wade <i>President and Chief Financial Officer</i>

### Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Lonnel Coats and Jeffrey L. Wade, or either of them, each with the power of substitution, his or her attorney-in-fact, to sign any amendments to this Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, here ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ LONNEL COATS Lonnel Coats	Chief Executive Officer and Director (Principal Executive Officer)	March 25, 2024
/s/ JEFFREY L. WADE Jeffrey L. Wade	President and Chief Financial Officer (Principal Financial Officer)	March 25, 2024
/s/ KRISTEN L. ALEXANDER Kristen L. Alexander	Vice President, Finance and Accounting (Principal Accounting Officer)	March 25, 2024
/s/ RAYMOND DEBBANE Raymond Debbane	Chairman of the Board of Directors	March 25, 2024
/s/ PHILIPPE J. AMOUYAL Philippe J. Amouyal	Director	March 25, 2024
/s/ SAMUEL L. BARKER Samuel L. Barker, Ph.D.	Director	March 25, 2024
/s/ ROBERT J. LEFKOWITZ Robert J. Lefkowitz, M.D.	Director	March 25, 2024
/s/ CHRISTOPHER J. SOBECKI Christopher J. Sobecki	Director	March 25, 2024
/s/ DIANE E. SULLIVAN Diane E. Sullivan	Director	March 25, 2024
/s/ JUDITH L. SWAIN Judith L. Swain, M.D.	Director	March 25, 2024

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Lexicon Pharmaceuticals, Inc.

### **Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of Lexicon Pharmaceuticals, Inc. (the Company) as of December 31, 2023 and 2022, the related consolidated statements of comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2023, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

### **Basis for Opinion**

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

### **Critical Audit Matter**

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

***Accrued research and development expenses***

*Description of the Matter* As described in Note 2 and Note 5 to the consolidated financial statements, the Company records accruals for estimated costs of research and development activities that include contract services for clinical trials. Clinical trial expenses are accrued based upon milestones and the number of patients enrolled over the duration of the study. The accrual for these third-party clinical trial research and development expenses includes estimates of services completed.

Auditing management’s accounting for accrued third-party clinical trial research and development expenses is especially challenging because of the judgment applied by management to determine the estimate of services completed related to the activities under the Company’s research and development agreements.

*How We Addressed the Matter in Our Audit* Our audit procedures included, among others, testing the accuracy and completeness of the underlying inputs used in management’s analysis to determine costs incurred. We compared expenses incurred to budgeted amounts per executed vendor contracts and to expenses incurred in prior periods and obtained an understanding of the reasons for changes. We inspected the terms and conditions of vendor contracts, change orders and trial budgets, and clerically tested the cost models to track progress against trial budgets. We evaluated estimated services incurred by third parties by understanding the terms and timeline of significant projects, evaluating management’s estimate of work performed and costs incurred by meeting with members of the Company’s clinical operations team, and obtaining external confirmation of key inputs to the clinical trial expense calculation, such as total approved trial budgets and amounts invoiced, and number and timing of patients enrolled in clinical studies. Further, we inspected invoices received from third parties during the year as well as after the balance sheet date and performed a lookback analysis to evaluate the completeness of accrued research and development expenses.

/s/ Ernst & Young LLP

We have served as the Company’s auditor since 2002.

Houston, Texas

March 25, 2024

**Lexicon Pharmaceuticals, Inc.**  
**Consolidated Balance Sheets**  
(In thousands, except par value and share amounts)

	As of December 31,	
	2023	2022
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 22,465	\$ 46,345
Short-term investments	147,561	92,012
Accounts receivable, net	1,010	28
Inventory	381	—
Prepaid expenses and other current assets	5,130	2,481
Total current assets	176,547	140,866
Property and equipment, net of accumulated depreciation and amortization of \$4,538 and \$3,984, respectively	1,987	2,071
Goodwill	44,543	44,543
Operating lease right-of-use-assets	5,524	6,407
Other assets	828	412
Total assets	\$ 229,429	\$ 194,299
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 14,389	\$ 10,395
Accrued liabilities	17,157	12,777
Total current liabilities	31,546	23,172
Long-term debt, net	99,508	48,579
Long-term operating lease liabilities	5,265	5,424
Total liabilities	136,319	77,175
Commitments and contingencies (Note 10)		
Stockholders' Equity:		
Preferred stock, \$0.01 par value; 5,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, \$0.001 par value; 300,000,000 shares authorized; 245,792,668 and 189,213,948 shares issued, respectively	245	189
Additional paid-in capital	1,862,558	1,709,144
Accumulated deficit	(1,766,839)	(1,589,720)
Accumulated other comprehensive income (loss)	31	(428)
Treasury stock, at cost, 867,973 and 488,205 shares, respectively	(2,885)	(2,061)
Total stockholders' equity	93,110	117,124
Total liabilities and stockholders' equity	\$ 229,429	\$ 194,299

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

**Lexicon Pharmaceuticals, Inc.**

**Consolidated Statements of Comprehensive Loss**  
(In thousands, except per share amounts)

	Year Ended December 31,		
	2023	2022	2021
<b>Revenues:</b>			
Net product revenue	\$ 1,110	\$ —	\$ —
Royalties and other revenue	94	139	298
Total revenues	1,204	139	298
<b>Operating expenses:</b>			
Cost of sales	85	—	—
Research and development, including stock-based compensation of \$5,139, \$4,253 and \$4,284 respectively	58,887	52,816	55,046
Selling, general and administrative, including stock-based compensation of \$9,201, \$7,267 and \$6,293, respectively	113,982	48,083	32,342
Total operating expenses	172,954	100,899	87,388
Loss from operations	(171,750)	(100,760)	(87,090)
Interest and other expense	(13,101)	(2,780)	(802)
Interest income and other, net	7,732	1,596	134
Net loss	<u>\$ (177,119)</u>	<u>\$ (101,944)</u>	<u>\$ (87,758)</u>
Net loss per common share, basic and diluted	<u>\$ (0.80)</u>	<u>\$ (0.62)</u>	<u>\$ (0.60)</u>
Shares used in computing net loss per common share, basic and diluted	221,130	165,733	145,652
<b>Other comprehensive loss:</b>			
Unrealized gain (loss) on investments	459	(418)	(4)
Comprehensive loss	<u>\$ (176,660)</u>	<u>\$ (102,362)</u>	<u>\$ (87,762)</u>

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



**Lexicon Pharmaceuticals, Inc.**

**Consolidated Statements of Stockholders' Equity  
(In thousands)**

	Common Stock		Additional	Accumulated	Accumulated	Treasury	Total
	Shares	Par Value	Paid-In Capital	Deficit	Other Comprehensive Gain (Loss)	Stock	
Balance at December 31, 2020	142,289	\$ 142	\$ 1,561,096	\$ (1,400,018)	\$ (6)	\$ (4,843)	\$ 156,371
Stock-based compensation	—	—	10,577	—	—	—	10,577
Issuance of common stock under an Open Market Sale Agreement, net of issuance fees	6,177	6	35,485	—	—	—	35,491
Issuance of common stock under Equity Incentive Plans	1,616	2	1,591	—	—	—	1,593
Repurchase of common stock	—	—	—	—	—	(2,675)	(2,675)
Net loss	—	—	—	(87,758)	—	—	(87,758)
Unrealized loss on investments	—	—	—	—	(4)	—	(4)
Balance at December 31, 2021	150,082	\$ 150	\$ 1,608,749	\$ (1,487,776)	\$ (10)	\$ (7,518)	\$ 113,595
Stock-based compensation	—	—	11,520	—	—	—	11,520
Issuance of common stock under Equity Incentive Plans	32	—	—	—	—	—	—
Issuance of common stock, net of issuance fees	39,100	39	94,166	—	—	—	94,205
Issuance of equity-classified warrants	—	—	1,030	—	—	—	1,030
Issuance of treasury stock	—	—	(6,321)	—	—	6,321	—
Repurchase of common stock	—	—	—	—	—	(864)	(864)
Net loss	—	—	—	(101,944)	—	—	(101,944)
Unrealized loss on investments	—	—	—	—	(418)	—	(418)
Balance at December 31, 2022	189,214	\$ 189	\$ 1,709,144	\$ (1,589,720)	\$ (428)	\$ (2,061)	\$ 117,124
Issuance of equity-classified warrants	—	—	307	—	—	—	307
Stock-based compensation	—	—	14,340	—	—	—	14,340
Issuance of common stock, net of fees	55,288	55	138,768	—	—	—	138,823
Issuance of common stock under Equity Incentive Plans	1,291	1	(1)	—	—	—	—
Repurchase of common stock	—	—	—	—	—	(824)	(824)
Net loss	—	—	—	(177,119)	—	—	(177,119)
Unrealized gain on investments	—	—	—	—	459	—	459
Balance at December 31, 2023	245,793	\$ 245	\$ 1,862,558	\$ (1,766,839)	\$ 31	\$ (2,885)	\$ 93,110

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

**Lexicon Pharmaceuticals, Inc.**  
**Consolidated Statements of Cash Flows**  
(In thousands)

	<b>Year Ended December 31,</b>		
	<b>2023</b>	<b>2022</b>	<b>2021</b>
<b>Cash flows from operating activities:</b>			
Net loss	\$ (177,119)	\$ (101,944)	\$ (87,758)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	554	427	292
Stock-based compensation	14,340	11,520	10,577
Amortization of debt-related costs	1,774	741	54
Loss on disposal of property and equipment	—	3	49
Other non-cash adjustments	(4,105)	—	—
Changes in operating assets and liabilities:			
(Increase) decrease in accounts receivable	(982)	(14)	381
Increase in inventories	(381)	—	—
(Increase) decrease in prepaid expenses and other current assets	(2,899)	(316)	2,885
Decrease in other long-term assets	467	656	661
Increase (decrease) in accounts payable and other liabilities	6,454	76	(14,158)
Net cash used in operating activities	(161,897)	(88,851)	(87,017)
<b>Cash flows from investing activities:</b>			
Purchases of property and equipment	(470)	(1,326)	(1,221)
Purchases of investments	(223,343)	(133,949)	(34,261)
Maturities of investments	173,870	64,197	37,592
Net cash (used in) provided by investing activities	(49,943)	(71,078)	2,110
<b>Cash flows from financing activities:</b>			
Proceeds from issuance of common stock, net of fees	138,823	94,205	37,084
Repurchase of common stock	(824)	(864)	(2,675)
Proceeds (repayment) of debt borrowings, net of fees	49,961	48,868	(11,700)
Net cash provided by financing activities	187,960	142,209	22,709
Net decrease in cash and cash equivalents	(23,880)	(17,720)	(62,198)
Cash and cash equivalents at beginning of year	46,345	64,065	126,263
Cash and cash equivalents at end of year	<u>\$ 22,465</u>	<u>\$ 46,345</u>	<u>\$ 64,065</u>
<b>Supplemental disclosure of cash flow information:</b>			
Cash paid for interest	\$ 10,057	\$ 2,289	\$ 799
<b>Supplemental disclosure of noncash investing and financing activities:</b>			
Right-of-use assets obtained in exchange for operating lease liability	\$ —	\$ 5,206	\$ 1,704
Issuance of equity-classified warrants	\$ 307	\$ 1,030	\$ —
Issuance of treasury stock	\$ —	\$ 6,321	\$ —
Accrual of deferred financing costs	\$ 250	\$ —	\$ —

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

## Lexicon Pharmaceuticals, Inc.

### Notes to Consolidated Financial Statements

#### 1. Organization and Operations

Lexicon Pharmaceuticals, Inc. (“Lexicon” or the “Company”) is a Delaware corporation incorporated on July 7, 1995. Lexicon was organized to discover the functions and pharmaceutical utility of genes and use those gene function discoveries in the discovery and development of pharmaceutical products for the treatment of human disease.

Lexicon has financed its operations from inception primarily through sales of common and preferred stock, contract and milestone payments to it under strategic collaborations and other research and development collaborations, target validation, database subscription and technology license agreements, product sales, government grants and contracts and financing under debt and lease arrangements. The Company’s future success is dependent upon many factors, including, but not limited to, the success of its commercialization efforts for INPEFA for heart failure; the success of its commercial launch of sotagliflozin for patients with type 1 diabetes and CKD, if approved; its ongoing research and development efforts and its ability to obtain necessary regulatory approvals of the drug candidates which are the subject of such efforts; its success in establishing new collaborations and licenses and its receipt of milestones, royalties and other payments under such arrangements; the amount and timing of research, development and commercialization expenditures; the resources devoted to developing and supporting its products; general and industry-specific economic conditions which may affect research, development and commercialization expenditures; and its ability to obtain and enforce patents and other proprietary rights in its discoveries, comply with federal and state regulations, and maintain sufficient capital to fund its activities. As a result of the aforementioned factors and the related uncertainties, there can be no assurance of the Company’s future success.

#### 2. Summary of Significant Accounting Policies

*Basis of Presentation.* The accompanying consolidated financial statements include the accounts of Lexicon and its wholly-owned subsidiaries. Intercompany transactions and balances are eliminated in consolidation. Lexicon has made certain reclassification adjustments to conform prior-period amounts to the current presentation. In the opinion of management, all adjustments (consisting of normal recurring adjustments) considered necessary for a fair presentation have been included.

*Use of Estimates.* The preparation of financial statements in conformity with U. S. generally accepted accounting principles (“GAAP”) requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the period. Actual results could differ from those estimates.

*Cash, Cash Equivalents and Short-Term Investments.* Lexicon considers all highly-liquid investments with original maturities of three months or less to be cash equivalents. As of December 31, 2023 and 2022, short-term investments consist primarily of U.S. treasury bills as well as certain corporate and other debt securities. The Company’s short-term investments are available for use in current operations regardless of the stated maturity date of the security. These short-term investments are classified as available-for-sale securities as the Company has not historically or does not intend to sell any of its available-for-sale securities prior to their maturity dates.

Short-term investments are carried at fair value, based on quoted market prices of the securities. The costs of securities sold is based on the specific identification method. Any net realized gains and losses, interest and dividends, and amortization of premium or accretion of discount are included in interest and other income. Unrealized gains and losses on such securities are reported as a separate component of stockholders’ equity. The Company reviews its portfolio of available-for-sale debt securities in an unrealized loss position. For those investments whose fair value is less than amortized cost, to the extent the Company decided to sell these investments prior to their maturity dates or was required to sell such investments, the Company would evaluate the expected cash flows to be received as compared to amortized cost and to determine if an expected credit loss has occurred.

*Accounts Receivable.* Lexicon records trade accounts receivable in the normal course of business related to the sale of products or services, net of an allowance for expected credit losses.

*Concentration of Credit Risk.* Lexicon’s cash equivalents, investments and accounts receivable represent potential concentrations of credit risk. The Company attempts to minimize potential concentrations of risk in cash equivalents and investments by placing investments in high-quality financial instruments. The Company has not experienced any realized losses on its cash equivalents or short-term investments. The Company’s accounts receivable are unsecured and are primarily

concentrated in large pharmaceutical and biotechnology companies located in the United States. The Company has not experienced any significant credit losses to date.

*Segment Information and Significant Customers.* Lexicon operates in one business segment, which primarily focuses on the discovery, development and commercialization of pharmaceutical products for the treatment of human disease. Substantially all of the Company's revenues have been derived from drug discovery alliances, target validation collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses, subscriptions to its databases, product sales, government grants and contracts and compound library sales, as well as from commercial sales of its approved drug products. In support of the commercial launch of INPEFA in 2023, the Company entered into distribution agreements with wholesalers and limited retail pharmacies. The Company's net product sales are generated from sales to these customers. In 2023, 11 United States-based customers accounted for all of the Company's net product revenue. Three large wholesalers, each of which account for greater than 10% of total revenues and in the aggregate account for greater than 85% of total revenues. In 2022 and 2021, the Company's revenues were solely derived from royalties and other revenues from one and two customers, respectively.

*Property and Equipment.* Property and equipment that is held and used is carried at cost and depreciated using the straight-line method over the estimated useful life of the assets, which ranges from three to 40 years. Maintenance, repairs and minor replacements are charged to expense as incurred. Leasehold improvements are amortized over the shorter of the estimated useful life or the remaining lease term. Significant renewals and betterments are capitalized.

*Impairment of Long-Lived Assets.* Long-lived assets and right-of-use assets for leases are reviewed for impairment when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Recoverability of assets to be held and used is measured by comparison of the carrying amount of an asset to future net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount that the carrying amount of the assets exceeds the fair value of the assets. Assets to be disposed of are reported at the lower of the carrying amount or fair value less costs to sell. There were no impairments of long-lived assets, in 2023, 2022, or 2021.

*Goodwill.* Goodwill is not amortized, but is tested at least annually for impairment at the reporting unit level which the Company has determined is the single operating segment disclosed in its current financial statements. An impairment exists when the carrying amount of goodwill exceeds its implied fair value. Additional impairment assessments may be performed on an interim basis if the Company encounters events or changes in circumstances that would indicate that, more likely than not, the carrying value of goodwill has been impaired.

*Leases.* Lexicon determines if a contract is or contains a lease at inception or upon modification of the contract. A contract is or contains a lease if it conveys the right to control the use of an identified asset for a period in exchange for consideration. Control over the use of the identified asset means the lessee has both (a) the right to obtain substantially all of the economic benefits from the use of the asset and (b) the right to direct the use of the asset. Lexicon does not apply this accounting to those leases with terms of twelve (12) months or less. Operating lease right-of-use assets and associated lease liabilities are recorded in the balance sheet at the lease commencement date based on the present value of future lease payments to be made over the expected lease term. As the implicit rate is not determinable in its leases, Lexicon uses its incremental borrowing rate based on the information available at the commencement date to determine the present value of lease payments.

*Inventory:* Inventory is comprised of INPEFA, the Company's approved product that it is commercializing in the United States. Inventories are determined at the lower of cost or market value, with cost determined under the specific identification method.

*Revenue Recognition.* The Company performs the following five steps in determining the amount of revenue to recognize as it fulfills its performance obligations under each of its collaborative agreements: (a) identify the contract(s) with a customer; (b) identify the performance obligation in the contract; (c) determine the transaction price; (d) allocate the transaction price to the performance obligation in the contract, and (e) recognize revenue when (or as) the Company satisfies the performance obligation. The Company applies this five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. The Company develops assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract.

### Product Revenues

Product revenues consist of U.S. sales of INPEFA, which Lexicon began shipping to its customers in the U.S. in June 2023. These customers primarily include wholesalers and limited retail pharmacies. The Company is continuing to contract with certain managed care programs or pharmacy benefit managers (“PBMs”) and has legislatively mandated contracts with the federal and state governments under which rebates are provided based on product utilization. Product revenues are recognized when control is transferred to the customer upon delivery.

The Company recognizes product revenue net of applicable estimates of reserves for variable consideration using the expected value method. These estimates consider relevant factors such as current contractual and statutory requirements, industry data and forecasted customer buying and payment patterns. Net product revenue includes variable consideration only to the extent that it is probable that a significant reversal in revenue recognized will not occur in a future period. As necessary, these estimates will be adjusted in the period that such variances to actuals become known. Listed below is a further discussion of these reserves and sales return allowances:

*Customer Credits.* The Company’s customers were offered various forms of consideration, including allowances, service fees and prompt payment discounts. The Company records allowances, deducts the full amount of prompt payment discounts, and deducts service fees from total product sales when revenues are earned and recognized.

*Rebates.* Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program reflecting amounts owed after final dispensing of the product to participants. The Company’s estimates for rebates is based on statutory discount rates, third party market research data and data from sales to its customers. As rebates are generally invoiced and paid in arrears, the Company accrues an estimate of rebates based on the current quarter’s activity, plus any known unpaid prior quarter rebates.

*Chargebacks.* Chargebacks are discounts that occur when contracted healthcare providers purchase directly from a wholesaler. Generally, the contracted healthcare providers purchase INPEFA at a discounted price. The wholesaler, in turn, charges back to Lexicon the difference between the price paid by the wholesaler and the discounted price that the wholesaler’s customer pays for that product.

*Medicare Part D Coverage Gap.* The Medicare Part D prescription drug benefit mandates manufacturers to fund a portion of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients. The Company’s estimates for the expected Medicare Part D coverage gap are based on sales data received from a third party and projections based on historical data. As funding of the coverage gap is generally invoiced and paid in arrears, the Company accrues an estimate based on the current quarter’s activity, plus any known unpaid prior quarter estimates.

*Co-payment assistance.* Patients with commercial insurance who meet certain eligibility requirements are eligible to receive co-payment assistance. The Company accrues a liability for co-payment assistance based on actual program participation and estimates of program redemption using data provided by third-party administrators.

*Sales returns.* The Company records allowances for product returns, if appropriate, as a reduction of revenue at the time product sales are recorded based on an assessment of market exclusivity of the product, the patient population, the customers’ return rights and the Company’s historical experience with returns. Because approval is recent and there is a limited number of patients, most customers and retailers carry a limited inventory.

### Collaborative Agreements

Revenues under collaborative agreements include both license revenue and contract research revenue. At contract inception, the Company evaluates whether development milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal will not occur, the associated development milestone value is included in the transaction price. Development milestones that are not within the control of the Company or the licensee, including those requiring regulatory approval, are not considered probable of being achieved until those approvals are received. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue when (or as) the performance obligation is satisfied. At the end of each reporting period, the Company re-evaluates the probability of achievement of the development milestones and any related constraint, and if necessary, adjusts its estimates of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues in the period of adjustment.

For agreements in which a license to the Company's intellectual property is determined distinct from other performance obligations identified in the agreement, the Company recognizes revenue when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For agreements that include sales-based royalties, including milestones based on a level of sales, the license is deemed to be the predominant item to which the royalties relate and the Company recognizes revenue at the later of (a) when the related sales occur, or (b) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). The Company may receive payments from its licensees based on billing schedules established in each contract. Upfront payments and fees are recorded as deferred revenue upon receipt or when due, and may require deferral of revenue recognition to a future period until the Company performs its obligations under these agreements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional.

*Cost of Sales.* Cost of sales consists of third-party manufacturing costs, product shipping and handling costs and freight associated with sales of INPEFA. The Company began capitalizing inventory manufactured subsequent to regulatory approval of INPEFA in June 2023, as the related costs were expected to be recovered through the commercialization of the product. Costs related to manufacturing inventory prior to the approval of INPEFA have been recorded as research and development expense in the consolidated statements of comprehensive loss.

*Research and Development Expenses.* Research and development expenses consist of costs incurred for company-sponsored as well as collaborative research and development activities. These costs include direct and research-related overhead expenses and are expensed as incurred. Technology license fees for technologies that are utilized in research and development and have no alternative future use are expensed when incurred. Substantial portions of the Company's preclinical and clinical trials are performed by third-party laboratories, medical centers, contract research organizations and other vendors. For preclinical studies, the Company accrues expenses based upon estimated percentage of work completed and the contract milestones remaining. For clinical studies, expenses are accrued based upon the number of patients enrolled and the completion of milestones. The Company monitors patient enrollment, the progress of clinical studies and related activities to the extent possible through internal reviews of data reported to the Company by the vendors and clinical site visits. The Company's estimates depend on the timeliness and accuracy of the data provided by the vendors regarding the status of each program and total program spending. The Company periodically evaluates the estimates to determine if adjustments are necessary or appropriate based on information it receives.

*Stock-Based Compensation.* Compensation expense related to stock options and restricted stock units ("RSUs") is determined based on the fair value of the award on the date of the grant and is recognized on a straight-line basis over the vesting period in which an employee is required to provide service. Forfeitures of share-based payment awards are recognized in the period in which they occur. Compensation expense is recorded in research and development expense and selling, general, and administrative expense as noted on the Company's consolidated statements of comprehensive loss.

*Income Taxes.* The Company recognizes deferred tax liabilities and assets for the expected future tax consequences of events that have been recognized differently in the financial statements and tax returns. The Company uses the liability method in accounting for income taxes. Under this method, deferred tax liabilities and assets are determined based on the difference between the financial statement carrying amounts and tax bases of liabilities and assets using enacted tax rates and laws in effect in the years in which the differences are expected to reverse. Deferred tax assets are evaluated for realization based on a more-likely-than-not criteria in determining if a valuation allowance should be provided. In evaluating our valuation allowances, we consider cumulative book losses, the reversal of existing temporary differences, tax planning strategies and estimates of future taxable income, the latter two of which involve the exercise of significant judgment.

*Net Loss per Common Share.* Net loss per common share is computed using the weighted average number of shares of common stock outstanding. Shares associated with warrants, stock options and restricted stock units that could potentially dilute earnings per share in the future are not included in the computation of diluted earnings per share because they are antidilutive.

*Recent Accounting Pronouncements Issued But Not Yet Adopted.* In November 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280) – Improvements to Reportable Segment Disclosures*, which is effective retrospectively for fiscal years beginning after December 15, 2023 and interim periods within fiscal years beginning after December 15, 2024. In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740) – Improvements to Income Tax Disclosures*, which is effective prospectively for annual periods beginning after December 15, 2024. Early adoption is permitted for both standards. We do not expect these accounting pronouncements to have a material impact on our financial statements.

### 3. Cash, Cash Equivalents and Investments

The fair value of cash and cash equivalents and investments held at December 31, 2023 and 2022 are as follows:

	As of December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(in thousands)			
Cash and cash equivalents	\$ 22,465	\$ —	\$ —	\$ 22,465
Securities maturing within one year:				
U.S. treasury securities	141,577	31	(12)	141,596
Corporate debt securities	5,954	11	—	5,965
Total short-term investments	\$ 147,531	\$ 42	\$ (12)	\$ 147,561
Total cash and cash equivalents and investments	\$ 169,996	\$ 42	\$ (12)	\$ 170,026
	As of December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(in thousands)			
Cash and cash equivalents	\$ 46,345	\$ —	\$ —	\$ 46,345
Securities maturing within one year:				
U.S. treasury securities	74,022	—	(342)	73,680
Corporate debt securities	18,418	—	(86)	18,332
Total short-term investments	\$ 92,440	\$ —	\$ (428)	\$ 92,012
Total cash and cash equivalents and investments	\$ 138,785	\$ —	\$ (428)	\$ 138,357

For the years ended December 31, 2023 and 2022, our investments in an unrealized loss position had an estimated fair value of \$58.5 million and \$89.0 million, respectively. There were no realized gains or losses for the years ended December 31, 2023, 2022, and 2021.

### 4. Fair Value Measurements

The Company uses various inputs in determining the fair value of its investments and measures these assets on a recurring basis. Assets and liabilities recorded at fair value in the consolidated balance sheets are categorized by the level of objectivity associated with the inputs used to measure their fair value. The following levels are directly related to the amount of subjectivity associated with the inputs to fair valuation of these assets and liabilities:

- Level 1 – quoted prices in active markets for identical assets, which include U.S. treasury securities
- Level 2 – other significant observable inputs (including quoted prices for similar investments, market corroborated inputs, etc.), which include corporate debt securities
- Level 3 – significant unobservable inputs

The inputs or methodology used for valuing securities are not necessarily an indication of the credit risk associated with investing in those securities. The following tables provide the fair value measurements of applicable Company assets that are measured at fair value on a recurring basis according to the fair value levels defined above as of December 31, 2023 and 2022. There were no transfers between Level 1 and Level 2 during the periods presented.

Assets at Fair Value				
As of December 31, 2023				
	Level 1	Level 2	Level 3	Total
(in thousands)				
Cash and cash equivalents	\$ 22,465	\$ —	\$ —	\$ 22,465
Short-term investments	141,596	5,965	—	147,561
Total cash and cash equivalents and investments	<u>\$ 164,061</u>	<u>\$ 5,965</u>	<u>\$ —</u>	<u>\$ 170,026</u>

Assets at Fair Value				
As of December 31, 2022				
	Level 1	Level 2	Level 3	Total
(in thousands)				
Cash and cash equivalents	\$ 46,345	\$ —	\$ —	\$ 46,345
Short-term investments	73,680	18,332	—	92,012
Total cash and cash equivalents and investments	<u>\$ 120,025</u>	<u>\$ 18,332</u>	<u>\$ —</u>	<u>\$ 138,357</u>

The carrying amount of cash and cash equivalents, prepaid expenses and other assets, accounts payable and accrued expenses are generally considered to be representative of their respective fair values because of the short-term nature of those instruments. The fair value of the Oxford Term Loans (see Note 9) is determined under Level 2 in the fair value hierarchy and approximates carrying value as the loans bear interest at a rate that approximates prevailing market rates for instruments with similar characteristics.

## 5. Supplemental Financial Information

The following tables show the Company's additional balance sheet information as of December 31, 2023 and 2022:

	As of December 31,	
	2023	2022
(in thousands)		
<i>Inventories:</i>		
Raw materials	\$ —	\$ —
Work-in-progress	100	—
Finished goods	281	—
Inventory	<u>\$ 381</u>	<u>\$ —</u>

	As of December 31,	
	2023	2022
(in thousands)		
<i>Accrued Liabilities:</i>		
Accrued research and development services	\$ 3,705	\$ 3,252
Accrued compensation and benefits	9,591	7,830
Short term lease liability	1,291	1,291
Other	2,570	404
Accrued liabilities	<u>\$ 17,157</u>	<u>\$ 12,777</u>



## 6. Property and Equipment

Property and equipment at December 31, 2023 and 2022 are as follows:

	Estimated Useful Lives In Years	As of December 31,	
		2023	2022
(in thousands)			
Computers and software	3-5	\$ 2,408	\$ 2,209
Furniture and fixtures	5-7	1,939	1,794
Leasehold improvements	3-7	2,178	2,052
Total property and equipment		6,525	6,055
Less: Accumulated depreciation and amortization		(4,538)	(3,984)
Net property and equipment		<u>\$ 1,987</u>	<u>\$ 2,071</u>

## 7. Income Taxes

*Effective Tax Rate Reconciliation.* A reconciliation of the statutory tax rate to the effective tax rate for the years ended December 31, 2023, 2022 and 2021 consists of the following:

	Year Ended December 31,		
	2023	2022	2021
(in thousands)			
Expected income tax expense (benefit) at 21%	\$ (37,196)	\$ (21,408)	\$ (18,429)
State income taxes, net of federal benefit	(3,895)	—	—
Equity compensation	1,530	1,627	851
Research and development credit	(712)	—	—
State income taxes, tax rate change	(4,723)	—	—
Change in valuation allowance	44,410	19,543	17,210
Other <sup>(1)</sup>	586	238	368
Income tax benefit	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>

(1) Other is primarily comprised of expiring NOLs and nondeductible expenses for the year ended December 31, 2023 and nondeductible expenses for the years ended December 31, 2022 and 2021.

*Deferred Tax Assets and Liabilities.* Lexicon recognizes deferred tax liabilities and assets for the expected future tax consequences of events that have been recognized differently in the financial statements and tax returns. The components of Lexicon's deferred tax assets (liabilities) at December 31, 2023 and 2022 are as follows:

	As of December 31,	
	2023	2022
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	\$ 288,264	\$ 251,331
Research and development tax credits	30,002	29,290
Orphan drug credits	24,524	24,524
Capitalized research and development	37,357	33,813
Stock-based compensation	6,965	5,445
Interest	1,359	398
Other	3,308	2,255
Total deferred tax assets	391,779	347,056
Deferred tax liabilities:		
Other	(1,608)	(1,295)
Total deferred tax liabilities	(1,608)	(1,295)
Less: valuation allowance	(390,171)	(345,761)
Net deferred tax liabilities	\$ —	\$ —

*Net Operating Losses/Valuation Allowance.* At December 31, 2023, Lexicon had both federal and state NOL carryforwards of approximately \$1.3 billion and \$169.6 million, respectively. The Company had \$606.5 million of U.S. federal NOL carryforwards as of December 31, 2023, which can be carried forward indefinitely. The remaining federal and state NOL carryforwards will begin to expire in 2024.

The Company maintains a valuation allowance on net operating losses and other deferred tax assets. Accordingly, the Company has not reported any tax benefit relating to the remaining net operating loss carryforwards and income tax credit carryforwards that are available for utilization in future periods. On a periodic basis, the valuation allowance is reassessed on deferred income tax assets, weighing positive and negative evidence to assess the recoverability of the deferred tax assets. In 2023, the Company reassessed the valuation allowance and considered negative evidence, including the cumulative losses over the three years ended December 31, 2023 and positive evidence including the projections of future income. After assessing both the negative and the positive evidence, the Company concluded that it should continue to maintain the valuation allowance on net operating losses and other deferred tax assets as of December 31, 2023 given the significance of the weight of the negative evidence. Based on recent financial performance and future projections, the Company could record a reversal of all, or a portion of the valuation allowance associated with U.S. deferred tax assets in future periods. However, any such change is subject to actual performance and other considerations that may present positive or negative evidence at the time of the assessment. Significant judgment is required in making these assessments to maintain or reverse valuation allowances and, to the extent future expectations change the Company would have to assess the recoverability of these deferred tax assets at that time.

Based on the federal tax law limits and the Company's cumulative loss position, the Company concluded it was appropriate to establish a full valuation allowance for its net deferred tax assets until an appropriate level of profitability is sustained. During the year ended December 31, 2023, the valuation allowance increased \$44.4 million, primarily due to NOLs generated, increases in deferred tax assets associated with capitalized research and development expense and deferred tax assets for state jurisdictions.

*Other.* As of December 31, 2023 and 2022, the Company did not have any unrecognized tax benefits and had no accruals for interest or penalties related to income tax matters. Any interest and penalties related to uncertain tax positions will be reflected as a component of income tax expense. The Company is subject to U.S. federal and state income taxes. The tax years 2020 through 2022 remain open to examination by the Internal Revenue Service of the United States and the tax years 2019 through 2022 remain open to examination by various state tax authorities.

## 8. Goodwill

Lexicon recorded goodwill from previous acquisitions prior to 2011 of \$44.5 million, representing the excess of purchase price over the fair value of the underlying net identifiable assets including the effects of deferred taxes. Goodwill is not subject to amortization, but is tested at least annually on its assessment date for impairment at the reporting unit level, which is the Company's single operating segment. There was no impairment of goodwill in 2023, 2022 or 2021.

## 9. Debt Obligations

*Oxford Term Loans.* In March 2022, Lexicon and one of its subsidiaries entered into a loan and security agreement with Oxford Finance LLC ("Oxford") that provides up to \$150 million in borrowing capacity (the "Oxford Term Loans"). The loan and security agreement was subsequently amended in August 2022, May 2023, June 2023 and December 2023. The Company incurred debt issuance costs of \$0.3 million in connection with the December 2023 amendment which extended the fourth tranche period and modified the existing financial covenant relating to net sales of INPEFA and the minimum cash and investments balance requirement. In March 2024, the Company entered into a fifth amendment further modifying the existing financial covenant relating to net sales of INPEFA.

The Oxford Term Loans are available in five tranches, each maturing in March 2027. The first \$25 million tranche was funded in March 2022, the second \$25 million tranche was funded in December 2022 and the third \$50 million tranche was funded in June 2023. The fourth \$25 million tranche will be available for draw at Lexicon's option upon the achievement of specified INPEFA net sales and until April 15, 2025. An unused fee will be due in the event Lexicon does not draw the full amount available under the fourth tranche. The fifth \$25 million tranche is available for draw at Lexicon's option, subject to Oxford's consent, at any time prior to the expiration of the interest-only payment period as described below. A final payment exit fee equal to 6% of the amount funded under the Oxford Term Loans is due upon prepayment or maturity. The final payment exit fee of \$6 million as of December 31, 2023, in the aggregate for the three borrowed tranches, is recorded as a debt discount on the consolidated balance sheet.

Concurrent with the funding of the first three tranches, Lexicon granted Oxford warrants to purchase 420,673 shares of Lexicon's common stock at an exercise price of \$2.08 per share, 224,128 shares of Lexicon's common stock at an exercise price of \$1.95 per share and 183,824 shares of Lexicon's common stock at an exercise price of \$2.38 per share, respectively. Subject to and upon funding of the fourth tranche, Lexicon will grant Oxford a warrant to purchase shares of its common stock having a value equal to 1.75% of such tranche, as determined by reference to a 10-day average closing price of the shares, and having an exercise price equal to such average closing price. All warrants are exercisable for five years from their respective grant dates and feature a net cashless exercise provision. The Company allocated the proceeds from each term loan tranche to the corresponding warrant using the relative fair value method and used the Black-Scholes model to calculate the fair value of the warrants.

As of December 31, 2023, the carrying value of the Oxford Term Loans on the consolidated balance sheet was \$99.5 million, reflecting an unamortized discount of \$6.5 million to the face value of long-term debt for the final payment exit fee, the warrant fair value, and debt issuance costs, which are being amortized into interest and other expense throughout the life of the term loan using the effective interest rate method.

Monthly interest-only payments are due during an initial 36-month period from the original March 2022 borrowing date. The interest-only period will be followed by an amortization period extending through the maturity date. Payments of \$34.8 million, \$52.2 million, and \$19.0 million, including debt principal and final exit fee payments, will be due during the fiscal years ended December 31, 2025, December 31, 2026 and December 31, 2027, respectively, with respect to all borrowed loan tranches as of December 31, 2023.

Prior to the June 2023 amendment to the loan and security agreement, the Oxford Term Loans bore interest at a floating rate equal to the 30-day U.S. Dollar LIBOR plus 7.90%, but not less than 8.01%, subject to additional interest if an event of default occurs and is continuing. Following such amendment, the floating interest rate is based on the sum of (a) the 1-month CME Term Secured Overnight Financing Rate (SOFR), (b) 0.10%, and (c) 7.90% for the first and second tranches and 7% for the third and fourth tranches. As of December 31, 2023, the weighted average interest rate of the Oxford Term Loans was 12.9%. During the year ended December 31, 2023, the Company recognized interest expense of \$11.6 million, including \$1.5 million in amortization of discount and related debt issuance costs.

If an event of default occurs and is continuing, Oxford may declare all amounts outstanding under the loan and security agreement to be immediately due and payable. Additionally, Lexicon may prepay the Oxford Term Loans in whole at its option at any time. Any prepayment of the Oxford Term Loans is subject to prepayment fees for up to three years after the funding of each tranche of the loans.

Lexicon's obligations under the Oxford Term Loans are secured by a first lien security interest in all of the assets of the Company and its subsidiaries. The loan and security agreement contains certain customary representations and warranties, affirmative and negative covenants and events of default applicable to Lexicon and its subsidiaries. In addition to the financial covenants, additional covenants include those restricting dispositions, fundamental changes to its business, mergers or acquisitions, indebtedness, encumbrances, distributions, investments, transactions with affiliates and subordinated debt. The loan and security agreement includes a financial covenant which requires Lexicon to maintain a minimum cash and investments balance of \$10 million until the achievement of specified INPEFA net sales. Upon funding of the fourth tranche, the minimum cash and investments balance will increase to \$25 million. The loan and security agreement includes a separate financial covenant relating to net sales of INPEFA as noted above. The Company was in compliance with its debt covenants as of December 31, 2023, and has classified its debt as long-term based on its intent and ability to refinance with completed equity financing (see Note 13) if the Company is unable to meet these financial covenants within one year.

## **10. Commitments and Contingencies**

*Operating Lease Obligations.* Lexicon's operating leases include leases of office space in The Woodlands, Texas and Bridgewater, New Jersey that will expire in August 2025 and January 2034, respectively. The Texas lease provides for escalating yearly base rent payments which started at \$506,000 and increase to \$557,000 in the final year of the lease. The New Jersey lease provides for escalating yearly base rent payments which started at \$820,000 and increase to \$986,000 in the final year of the lease. Under its lease agreements, Lexicon is obligated to pay property taxes, insurance, and maintenance costs.

As of December 31, 2023 and 2022, the right-of-use assets for the office space leases had a balance of \$5.5 million and \$6.4 million, respectively, which are included in operating lease right-of-use-assets in the consolidated balance sheet. Current and long-term liabilities as of December 31, 2023, relating to the leases were \$1.3 million and \$5.3 million, respectively, which are included in accrued liabilities and long-term operating lease liabilities in the consolidated balance sheet, respectively. Current and long-term liabilities as of December 31, 2022, relating to the leases were \$1.3 million and \$5.4 million, respectively, which are included in accrued liabilities and long-term operating lease liabilities in the consolidated balance sheet, respectively. During the years ended December 31, 2023 and 2022, the Company incurred lease expense of \$1.6 million and \$1.8 million, respectively.

During the years ended December 31, 2023 and 2022, the Company made cash payments for lease liabilities of \$0.8 million and \$1.1 million, respectively. As of December 31, 2023 and 2022, the weighted-average remaining lease terms were 9 years and 9.5 years, respectively, with weighted-average discount rates of 9.6% for each year.

The following table reconciles the undiscounted cash flows of the operating lease liability to the recorded lease liability at December 31, 2023:

	(in thousands)
2024	\$ 1,378
2025	1,220
2026	865
2027	881
2028	898
Thereafter	4,746
Total undiscounted operating lease liability	\$ 9,988
Less: amount of lease payments representing interest	(3,432)
Present value of future lease payments	6,556
Less: short-term operating lease liability	(1,291)
Long-term operating lease liability	\$ 5,265

*Employment Arrangements.* Lexicon has entered into employment arrangements with certain of its corporate officers. Under the arrangements, each officer receives a base salary, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The employment arrangements are at-will and some contain non-competition agreements. Some of the arrangements also provide for certain severance payments for either six or 12 months and, in some cases, payment of a specified portion of the officer's bonus target for such year, in the event of a specified termination of the officer's employment.

*Legal Proceedings.* Lexicon is from time to time party to claims and legal proceedings that arise in the normal course of its business and that it believes will not have, individually or in the aggregate, a material adverse effect on its results of operations, financial condition or liquidity.

## 11. Equity Incentive Awards

The Company has stockholder-approved equity incentive plans further described below that permit the grant of stock options, restricted stock unit awards, and other stock-based awards to employees, directors, and consultants of the Company.

*2017 Equity Incentive Plan.* The Company's 2017 Equity Incentive Plan permits the grant of incentive stock options to employees and nonstatutory stock options to employees, directors and consultants of the Company. The plan also permits the grant of stock bonus awards, restricted stock awards, restricted stock unit awards, stock appreciation rights and performance stock awards. Incentive and nonstatutory stock options have an exercise price of 100% or more of the fair market value of the Company's common stock on the date of grant. Most stock options granted under the 2017 Equity Incentive Plan become vested and exercisable over a period of four years. Stock options granted under the Equity Incentive Plan have a term of 10 years from the date of grant. Vesting of restricted stock units issued under this plan generally vest in three annual installments.

*2017 Non-Employee Directors' Equity Incentive Plan (the "Directors' Plan").* Under the Company's Directors' Plan, non-employee directors may be granted awards under the plan with an aggregate grant date fair value of no more than \$500,000 during any calendar year, taken together with any cash fees paid to such non-employee director in compensation for service on Lexicon's board of directors during such calendar year. Stock options granted under the Directors' Plan have an exercise price equal to the fair market value of the Company's common stock on the date of grant and a term of 10 years from the date of grant. Vesting of restricted stock units granted under this plan occurs on the first anniversary of the grant date.

The total number of shares of common stock that may be issued pursuant to stock awards under the Equity Incentive Plan and the Directors' Plan shall not exceed in the aggregate 55,000,000 and 2,000,000 shares at December 31, 2023, respectively. Under the combined plans, as of December 31, 2023, an aggregate of 23,719,712 shares of common stock were reserved for issuance upon exercise of outstanding stock options and vesting of outstanding restricted stock units and 24,047,212 additional shares were available for future grants. The Company has a policy of using either authorized and unissued shares or treasury shares, including shares acquired by purchase in the open market or in private transactions, to satisfy equity award exercises. As of December 31, 2023, options to purchase 18,705,022 shares and 5,014,690 restricted stock

units were outstanding, 2,285,702 shares had been issued upon the exercise of stock options, 6,730,226 shares had been issued pursuant to restricted stock units and 217,148 shares had been issued pursuant to stock bonus awards or restricted stock awards granted under the aggregate of both plans.

For the years ended December 2023, 2022, and 2021 stock-based compensation costs was \$14.3 million, \$11.5 million, and \$10.6 million, respectively. As of December 31, 2023, future stock-based compensation cost for all outstanding unvested stock options and restricted stock units was \$26.8 million, which is expected to be recognized over a weighted-average period of 1.2 years.

*Stock Options.* The following is a summary of stock option activity under Lexicon's equity incentive plans for the year ended December 31, 2023:

<b>As of December 31, 2023</b>		
<b>(in thousands, except exercise price data)</b>	<b>Options</b>	<b>Weighted Average Exercise Price</b>
Outstanding at beginning of year	12,349	\$ 5.10
Granted	8,091	2.29
Exercised	—	—
Expired	(152)	14.68
Forfeited	(1,583)	3.66
Outstanding at end of year	<u>18,705</u>	3.93
Exercisable at end of year	<u>8,280</u>	\$ 5.58

The weighted average estimated grant date fair value of stock options granted during the years ended December 31, 2023, 2022 and 2021 were \$1.78, \$2.30 and \$4.85, respectively. The weighted average remaining contractual term of stock options outstanding and exercisable was 7.5 and 5.6 years, respectively, as of December 31, 2023. At December 31, 2023, the aggregate intrinsic value of the outstanding stock options was \$0.4 million. At December 31, 2023, the intrinsic value of exercisable stock options was \$0.

The fair value of stock options is estimated at the date of grant using the Black-Scholes method requiring the input of subjective assumptions. For purposes of determining the fair value of stock options, the Company segregates its options into two homogeneous groups, based on exercise and post-vesting employment termination behaviors, resulting in different assumptions used for expected option lives. Historical data is used to estimate the expected option life for each group. Expected volatility is based on the historical volatility in the Company's stock price. The following weighted-average assumptions were used for stock options granted in the years ended December 31, 2023, 2022 and 2021, respectively:

	<b>Expected Volatility</b>	<b>Risk-free Interest Rate</b>	<b>Expected Term</b>	<b>Dividend Rate</b>
December 31, 2023:				
Employees	110%	3.9%	4	0 %
Officers and non-employee directors	98%	4.0%	6	0 %
December 31, 2022:				
Employees	109%	2.8%	4	0 %
Officers and non-employee directors	91%	1.9%	7	0 %
December 31, 2021:				
Employees	104%	0.7%	4	0 %
Officers and non-employee directors	90%	1%	6	0 %

*Restricted Stock Units.* During the years ended December 31, 2023, 2022 and 2021, Lexicon granted its employees restricted stock units in lieu of or in addition to annual stock option awards. The total fair value of shares vested in 2023, 2022 and 2021 was \$2.9 million, \$2.9 million and \$8.7 million, respectively.

During the years ended December 31, 2023, 2022 and 2021, Lexicon granted its non-employee directors 64,256, 74,416 and 32,192 restricted stock units, respectively. The restricted stock granted in 2023, 2022 and 2021 had weighted average grant date fair values of \$2.36, \$1.77 and \$5.04 per share, respectively.

The following is a summary of restricted stock units activity under Lexicon’s stock-based compensation plans for the year ended December 31, 2023:

	Shares	Weighted Average Grant Date Fair Value
	(in thousands)	
Outstanding at December 31, 2022	2,748	\$ 3.78
Granted	4,199	2.43
Vested	(1,291)	3.80
Forfeited	(641)	2.72
Outstanding at December 31, 2023	5,015	\$ 2.78

During the year ended December 31, 2022, the Company issued \$6.3 million of Treasury shares in lieu of issuing additional authorized common shares in order to satisfy the annual vesting of restricted stock units for its employees and officers.

## 12. Benefit Plan

Lexicon maintains a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code. The plan covers substantially all full-time employees. Participating employees may defer a portion of their pretax earnings, up to the Internal Revenue Service annual contribution limit. The Company matches employee contributions according to a specified formula. The matching contributions totaled \$1.2 million, \$0.7 million and \$0.4 million in the years ended December 31, 2023, 2022 and 2021, respectively. Company contributions are vested based on the employee’s years of service, with full vesting after four years of service.

## 13. Other Capital Agreements

*Common Stock.* In June 2023, Lexicon sold an aggregate of 55,288,460 shares of its common stock at a price of \$2.60 per share in a public offering and concurrent private placement to an affiliate of Invus, L.P., resulting in net proceeds of approximately \$139 million, after deducting underwriting discounts and commissions and offering expenses.

In August 2022, Lexicon sold an aggregate of 39,100,000 shares of its common stock at a price of \$2.50 per share in a public offering and concurrent private placement to two affiliates of Invus, L.P., resulting in net proceeds of \$94.2 million, after deducting underwriting discounts and commissions and offering expenses.

In January 2021, Lexicon sold 2,000,000 shares of its common stock at a price of \$8.463 per share under a previous Open Market Sale Agreement™ with Jefferies LLC, resulting in net proceeds of \$16.4 million. In August and September 2021, Lexicon sold an aggregate of 4,176,953 shares of its common stock at a price of \$4.732 per share under the sales agreement, resulting in net proceeds of \$19.1 million. The net proceeds from each of these sales are reflected as issuances of common stock in the accompanying financial statements.

*Convertible Preferred Stock.* On March 11, 2024, Lexicon entered into an agreement with certain accredited investors pursuant to which the Company agreed to sell 2,304,147 shares of its Series A Convertible Preferred Stock, par value \$0.01 per share, in a private placement at a price of \$108.50 per share. The Company received net proceeds of approximately \$242 million, after deducting placement agent fees and offering expenses from the private placement offering. Each share of preferred stock is convertible into 50 shares of common stock. An affiliate of Invus, L.P. elected to participate on the same terms as each other purchaser on a pro rata basis and also agreed to vote at the Company’s 2024 annual meeting of stockholders in favor of the approval of an amendment to the Company’s certificate of incorporation increasing the total authorized common shares thereunder from 300,000,000 to 450,000,000 shares (the “New Charter”).

Following the approval of the New Charter by the Company's shareholders, the adoption of the New Charter by the Company's board of directors, and the filing and acceptance of the New Charter by the Secretary of State of Delaware, each share of preferred stock will automatically convert into 50 shares (subject to adjustments) of common stock.





# CORPORATE SUMMARY

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## EXECUTIVE OFFICERS

**LONNEL COATS**  
Chief Executive Officer and Director

**JEFFREY L. WADE**  
President and Chief Financial Officer

**ALAN J. MAIN, PH.D.**  
Executive Vice President,  
Innovation and Chemical Sciences

**BRIAN T. CRUM**  
Senior Vice President and General Counsel

**THOMAS A. GARNER**  
Senior Vice President and Chief  
Commercial Officer

**CRAIG B. GRANOWITZ, M.D., PH.D.**  
Senior Vice President and Chief  
Medical Officer

**KENNETH B. KASSLER-TAUB, M.D.**  
Senior Vice President,  
Regulatory and Quality Assurance

**WENDY E. MCDERMOTT**  
Vice President, Human Resources

**KRISTEN L. ALEXANDER**  
Vice President, Finance and Accounting

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## BOARD OF DIRECTORS

**RAYMOND DEBBANE**  
Chairman  
President and Chief Executive Officer,  
The Invus Group, LLC

**PHILIPPE J. AMOUYAL**  
Managing Director,  
The Invus Group, LLC

**SAMUEL L. BARKER, PH.D.**  
Former President, U.S. Pharmaceutical  
Group, Bristol-Myers Squibb Company

**LONNEL COATS**  
Chief Executive Officer and Director,  
Lexicon Pharmaceuticals, Inc.

**ROBERT J. LEFKOWITZ, M.D.**  
Investigator, Howard Hughes Medical  
Institute and James B. Duke Professor  
of Medicine and Professor of Biochemistry  
Duke University Medical Center; Recipient  
of 2012 Nobel Prize in Chemistry

**CHRISTOPHER J. SOBECKI**  
Managing Director, The Invus Group, LLC

**DIANE E. SULLIVAN**  
Former Chief Commercial Officer,  
DalCor Pharmaceuticals  
Former Chief Commercial Officer,  
The Medicines Company

**JUDITH L. SWAIN, M.D.**  
Visiting Professor of Medicine,  
National University of Singapore and  
Chief Medical Officer, Physiowave, Inc.

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## CORPORATE HEADQUARTERS

2445 Technology Forest Blvd.  
11th Floor  
The Woodlands, TX 77381  
Tel: (281) 863-3000  
[www.lexpharma.com](http://www.lexpharma.com)

## TRANSFER AGENT

Computershare  
PO Box 505000  
Louisville, KY 40233-5000  
Tel: (877) 854-4583  
[www-us.computershare.com/investor](http://www-us.computershare.com/investor)

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## ANNUAL REPORT

Our 2023 annual report on Form 10-K is available, without charge, upon request by contacting our Investor Relations Department at (281) 863-3000.

## ANNUAL MEETING

Our annual meeting of shareholders will be held at 8:00 a.m. CDT on May 10, 2024. The annual meeting will be held entirely online at:  
[www.virtualshareholdermeeting.com/LXR2024](http://www.virtualshareholdermeeting.com/LXR2024)

This annual report to shareholders contains forward-looking statements relating to Lexicon's commercial products, clinical and preclinical development programs and the potential therapeutic and commercial potential of those programs. These statements involve risks, uncertainties and other important factors that may cause Lexicon's actual results to be materially different from any future results expressed or implied by such forward-looking statements. Information identifying such risks, uncertainties and other important factors is contained in the section entitled "Risk Factors" and elsewhere in our annual report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission and included as part of the annual report to shareholders.





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