Risk Factors Comparison 2025-03-07 to 2024-03-25 Form: 10-K

Legend: **New Text** ~~Removed Text~~ Unchanged Text Moved Text Section

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 **the ongoing research** and ~~obtain~~ **development of our drug programs. If we fail to successfully complete and gain** positive results from **such research** ~~our PROGRESS Phase 2b clinical trial of LX9211 in DPNP. If we fail to successfully complete~~ and **development efforts** ~~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~~ **pilavapadin in DPNP and do not have sufficient capital to support Phase 3 development of pilavapadin 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~~ **pilavapadin** 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 **or other arrangements** with pharmaceutical and biotechnology companies for the development and commercialization of our ~~other~~ drug candidates. If we are unable to establish such collaborations **or arrangements**, or if pharmaceutical products are not successfully and timely developed and commercialized under such collaborations **or arrangements**, our opportunities to generate revenues from **milestones and royalties or** 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. 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 **heavily** 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~~ **our ability** ~~increased incidence or severity of known side effects as compared~~ to **successfully complete** ~~those~~ -- **the** ~~seen during~~ **ongoing research and** 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~~ **our** ~~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. **If we fail to successfully complete and gain positive results from such research and development efforts, our business will suffer and our stock price will likely decline.** We are **developing pilavapadin** ~~currently preparing to resubmit our NDA~~ for **neuropathic pain, LX9851 for obesity and cardiometabolic disorders and** sotagliflozin ~~as an adjunct to insulin therapy~~ for **HCM** ~~patients with type 1 diabetes~~ and ~~CKD~~ **conducting research and development of compounds from a number of additional drug programs**. 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~~ **our ongoing research and development efforts, including our IND- enabling studies for LX9851 and SONATA- HCM Phase 3** clinical trial **of sotagliflozin in HCM,** will be successfully completed, generate positive **data or demonstrate competitive** clinical ~~data~~ or ~~demonstrate a competitive~~ commercial ~~profile~~ **profiles** ~~for LX9211~~, in any ~~such~~ case on our expected ~~timeline~~ **timelines**. Should we fail to obtain positive results from ~~the PROGRESS clinical trial~~ **any ongoing research and development efforts**, or if **any such efforts are** ~~the PROGRESS clinical trial is~~ not completed on our expected ~~timeline~~ **timelines** ~~due to delays in planned patient enrollment~~ **, the likelihood of gaining regulatory approval** ~~or~~ **for** ~~otherwise~~ **the impacted drug program would be reduced**, our opportunity to establish a strategic collaboration or other arrangement for the further **research,** development and commercialization of ~~LX9211~~ **the impacted drug program** 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. 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, 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~~ **establish** 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. **We no longer maintain a significant commercial infrastructure following our restructuring and reduction of commercial operations for INPEFA and would need to reestablish sales capabilities in order to effectively commercialize any future products.** Factors that may hinder efforts to effectively ~~establish~~ **reestablish** , 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 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. 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. **Any** ~~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. **Changes in government trade policies could disrupt our supply chain or increase the costs of our clinical and commercial supply, negatively impacting our ability to conduct our clinical and commercial operations, price our commercial product competitively and conduct clinical development in a cost effective manner. We rely on third party drug product contract manufacturers in Canada and China who then manufacture, package and label finished commercial supply of INPEFA and clinical supply of our drug candidates. Recent changes in U. S. foreign trade policies, including changes to trade regulations, proposed tariffs or other import or export restrictions with countries such as Canada, Mexico and China, could disrupt our supply chains and jeopardize the commercial availability of INPEFA and our conduct of planned clinical development activities for our drug candidates. Such trade dynamics could also increase our costs for raw materials or products that we source internationally, which would negatively impact our business margins and financial results. We cannot predict what other changes to trade policy, if any, will be made by the current or a future administration or Congress, including whether existing tariff policies will be maintained or modified.** 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~~ **2024** , we had $ ~~170~~ **238** . 0 million in cash, cash equivalents and **short- term** 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~~ **research and development** of **pilavapadin** ~~INPEFA for the treatment of heart failure~~ , **LX9851,** ~~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 **and the continued limited commercialization of INPEFA for the treatment of heart failure** . 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 **pilavapadin, LX9851,** 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~~ **Our existing resources** may **be** ~~not have sufficient~~ **insufficient** ~~capital~~ to support Phase 3 development of ~~LX9211~~ **pilavapadin** in DPNP and **will be** ~~do not have sufficient~~ **insufficient** ~~capital~~ to support Phase 3 development of **pilavapadin** ~~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 incurred aggregate net losses since our inception, including an aggregate net loss of **approximately** $ ~~366~~ **479** . ~~8~~ **5** million for the three ~~-~~ ~~years~~ **year period** ended December 31, ~~2023~~ **2024** . As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of **approximately** $ ~~1~~ **2** . ~~8~~ **0** 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 **including** ~~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 **pilavapadin, LX9851,** 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 **pilavapadin, LX9851,** 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 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~~ **As of December 31, 2024, we** have incurred **approximately** $ ~~99~~ **100** . ~~5~~ **3** 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. 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 **. For example, we have entered into an exclusive license agreement with Viatris for the development and commercialization of sotagliflozin in all markets outside of the United States and Europe** . 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. 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~~ **that act on** the same drug targets ~~through~~ **upon** 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~~ **drugs** ~~targets~~ that **act on those** ~~we have identified and certain therapeutic products addressing such~~ targets. In some cases, patents have issued, and may issue in the future, from ~~these~~ **those** applications. In addition, many companies and institutions have ~~well- established~~ patent portfolios directed to ~~common~~ **commonly used** 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~~ **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. If we are unable to manage our ~~growth, our~~ business, financial condition, results of operations and prospects may be adversely affected. ~~We~~ **In the past 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~~ **If we experience it again, it** 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. 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 **pilavapadin, LX9851,** 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. 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. 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. 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 **pilavapadin, LX9851, sotagliflozin and our other drug candidates; • results** ~~our~~ **or** ~~,~~ **delays in our or** our collaborators ~~' or our competitors~~ ' 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 ~~sotagliflozin~~ **our** , **our collaborators'** ~~LX9211, LX9851 and our~~ **or** ~~other drug candidates~~ **our competitors' clinical trials** ; • 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. **If we are unable to meet Nasdaq continued listing requirements, including minimum trading price, Nasdaq may take action to delist our common stock. Our common stock trades on The Nasdaq Global Select Market, which has qualitative and quantitative listing criteria, including a requirement to maintain a minimum bid price of $ 1 per share. On January 3, 2025, we received a letter from Nasdaq' s listing qualifications staff indicating that we no longer meet such minimum bid price requirement. In accordance with Nasdaq rules, we have been provided a period of 180 calendar days, or until July 2, 2025, in which to regain compliance by ensuring the closing bid price of our common stock is at least $ 1 per share for a minimum of ten consecutive business days during such 180- day period. In the event that we do not regain compliance within such 180- day period, we may be eligible to seek an additional compliance period of 180 calendar days if we meet the continued listing requirement for market value of publicly held shares and all other Nasdaq initial listing standards, with the exception of the bid price requirement, and provide written notice to Nasdaq of our intent to cure the deficiency during this second compliance period, by effecting a reverse stock split, if necessary. However, if it appears to the**

Nasdaq staff that we will not be able to cure the deficiency, or if we are otherwise not eligible, Nasdaq will provide us notice that our common stock will be subject to delisting. Although we are monitoring the closing bid price of our common stock and considering our available options in the event that the closing bid price of our common stock remains below $ 1 per share, there can be no assurance that we will be able to regain compliance with the minimum bid price requirement or otherwise maintain compliance with the other Nasdaq listing requirements. A delisting of our common stock would likely negatively impact us and our shareholders by reducing the liquidity and market price of our common stock and potentially reducing the number of investors willing to hold or acquire our common stock.